Nutritional physiology / by Percy Goldthwait Stiles.

Contributors

Stiles, Percy Goldthwait, 1875-1936.

Publication/Creation

Philadelphia ; London : W.B. Saunders company, 1931.

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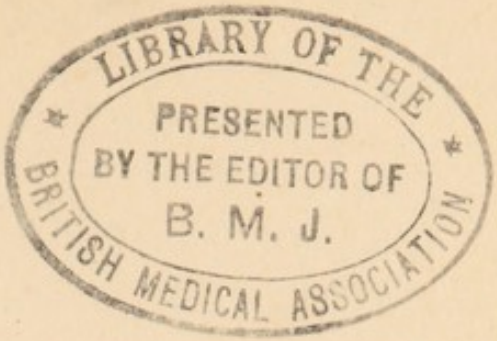
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NUTRITIONAL PHYSIOLOGY

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BY

PERCY GOLDTHWAIT STILES

ASSISTANT PROFESSOR OF PHYSIOLOGY IN HARVARD UNIVERSITY

SEVENTH EDITION

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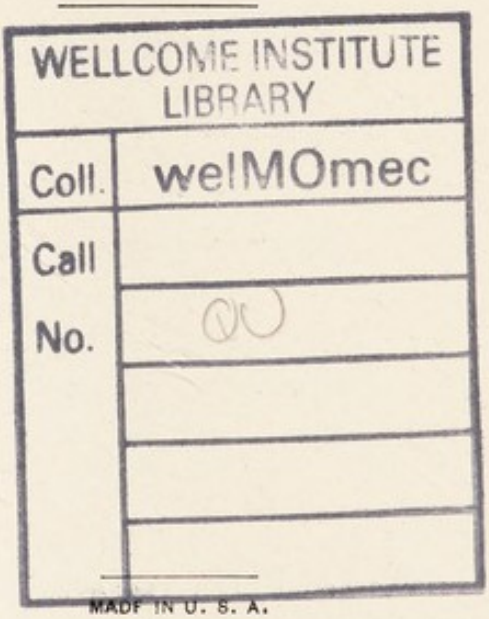
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TO

Graham Lusk

WHOSE DELICATE KINDNESS NO LESS THAN HIS SCHOLARLY POWER MADE MEMORABLE THE YEAR OF OUR ASSOCIATION

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PREFACE TO SEVENTH EDITION

It is still in order to emphasize the fact that this book should be liberally supplemented by other material. Since this was true eighteen years ago it must be clear that the development of the science has made it much more necessary today. The text has been but slightly increased though there is a wealth of new knowledge at hand. The references supplied are not numerous but always of first-class importance. As upon an earlier occasion (1918) the writer considers it both an obligation and a privilege to mention Lusk's "Elements of the Science of Nutrition" as an encyclopedic manual of information to which the student may always turn with advantage.

P. G. S.

Boston, Mass.,
June, 1931.

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PREFACE

THE making of this book has been a study in elimination. It is, therefore, necessary at the outset to indicate the limits of its scope. It is intended that it shall be used with other books. Supplementary reading upon general biology, human anatomy, food chemistry, and dietetics is greatly to be desired. In the field of physiology itself many fascinating topics are entirely ignored and others treated in bare outline, with the purpose of subordinating all else to the subject of nutrition. Chemical formulæ have been excluded from the text and used but sparingly in the notes.

A certain preliminary knowledge of elementary science is assumed. The key-word of the following discussion is "energy." The success of the reader in gaining clear conceptions of what is presented will depend upon his familiarity with the meaning of that term. It is essential that he shall understand that energy is latent or potential in those chemical compounds which are susceptible of oxidation. He must have learned to recognize the possibility of its unending transformation. The more readily he thinks in terms of molecules, the more profitably he can read these chapters.

Miss Ruth Bryant, Instructor in Biology in Simmons College, has borne a part in the work, which is to be described as collaboration rather than assistance.

P. G. S.

BOSTON, MASS.

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NUTRITIONAL PHYSIOLOGY

CHAPTER I

INTRODUCTION

The Modern Emphasis in Biology.—Living things are transformers of matter and energy. When we say *transformers* rather than *generators* we indicate the modern as contrasted with the old-time view. When we say that physiology is the physics and chemistry of living matter we suggest the same significant tendency to bring living and lifeless matter into direct comparison and to recognize the same laws as operating in both. The teaching that the same laws do hold sway in the living and the non-living is covered by the term "*mechanism*"; the earlier view that living things are not fairly to be compared with lifeless, and are to some extent exempt from physical principles and limitations, is expressed by the word "*vitalism.*" We have every reason to believe that the principle of the conservation of energy holds as rigidly for the plant or the animal as for the clock or the locomotive. This is perhaps the most important generalization of nineteenth century physiology.

But while scientific workers are now seeking to analyze the reactions of organisms in accordance with the data furnished by chemists and physicists whose work has been with materials not living, it is probable that the difficulties of their problems are better appreciated than was the case a few years ago. Living matter is found to be more complex in structure and more varied in response

than had been supposed. Physiologists are bound to be modest in their claims for progress. They are ignorant of many factors at work in even the simplest forms of plant and animal life. And the mystery of consciousness with its relation to nervous systems seems ever to defy approach.

Free-living Cells.—About the year 1840, at a time when investigators were profiting by important improvements in microscopes, it was found that the larger

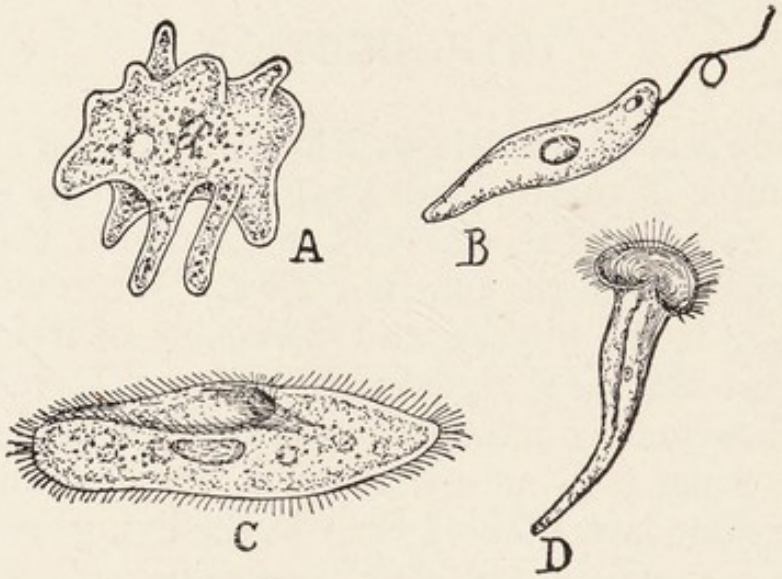


Fig. 1.—Four types of free-living animal cells: *A* is the ameba, distinguished for its changeable form; *B*, the euglena, shows the peculiar feature known as a flagellum, a writhing filament, which is its means of locomotion; *C* is the paramœcium, or "slipper animalcule," which has a ciliated surface; *D* is the interesting form known as the stentor.

plants and animals are made up of structural units assembled in vast numbers. These units are generally much too small to be seen without magnification. They are called *cells*, a term which is not especially appropriate, but not likely to be abandoned. Many microscopic forms, such as the swarming *Infusoria* of pools and ditches, are cells leading an independent existence. It will be helpful to consider what are the characteristic activities of such cells. They are for the most part equally characteristic of the higher forms.

The free-living animal cell takes something from its environment and returns something to it. It takes into itself a variety of organic substances together with small quantities of mineral salts. These constitute its *food.* It receives also a supply of *oxygen.* This is not ordinarily reckoned as a food and for a good reason. The term *food* is best restricted to material which can serve constructive purposes or at least be stored in the cell. The function of oxygen is not to promote constructive processes, but to release energy, a process of decomposition in which the stores of the cell are sacrificed. It is hard for the elementary student to realize that a destructive change can be other than disastrous. Yet he has only to reflect that money becomes useful in its expenditure. It is much the same with organic reserves. The process in which oxygen reacts with substances within the cell, giving rise to simple oxidized products in place of complex material rich in potential energy, is called *respiration.* (The word is, indeed, frequently used as a synonym for *breathing,* but we shall use it in its chemical sense.) Respiration is often compared with combustion, and while the two are not identical in all their stages, the fact remains that the initial and the final conditions are essentially the same for both. The release of energy is generally just as great in the physiologic change as in the actual burning of like quantities of the cell constituents.

The free-living animal cell is thus an accumulator of fuel and a furnace in which it is burnt. But this is a very imperfect comparison, for it has in addition the property of *self-repair,* and under favorable circumstances capacity for *growth* and *reproduction.* Cells multiply by cleaving into two similar parts, and the tendency to do this after a certain increase in size usually limits very definitely the dimensions to which a single cell may attain. When growth is taking place it is evident that not all the food is serving as fuel; a certain portion is becoming incorporated with the more permanent substance of the cell and is so changed as to become entirely typical *protoplasm.* The process through which food becomes an integral part

of the cell is called *assimilation*. The word emphasizes through its root-meaning the attainment of *likeness* to the material of the cell and indirectly implies that the food was originally foreign in its nature. We use the expression in much the same sense when we speak of the assimilation of immigrant peoples. The word *nutrition* is used in about the same way as assimilation, the only distinction being that we speak of the nutrition of *cells* (or cell-aggregates), while we speak of the assimilation of *food*, the former term referring to the structure nourished and the latter to the supplies worked over for the purpose. The word *digestion* is best restricted to the preliminary stages of the assimilation process; its application will be defined later.

Respiration has been said to be a process in course of which compounds are decomposed that their potential energy may be made available. The greater part of the released energy appears as heat. A smaller part manifests itself in movements through which resistances are overcome. The facts in regard to the production of energy are naturally better known for the larger animals than for the free-living cells, but "the whole is equal to the sum of its parts." The energy from respiration may in exceptional cases become kinetic, in the form of light or electric discharge (firefly, electric eel). The energy which shows itself in movement is of particular interest to us. Motion, when exhibited by animal cells, is almost always the expression of *contraction*, the word being used in a physiologic sense. So used, *contraction* does not mean diminution of volume, but does mean diminution of surface and active shortening in one or more dimensions. Although an increase in other dimensions attends such changes of form, we do not talk of the "expansion" of cells. It is the contraction which is the positive and forcible element in the movement. When this is said we intentionally leave out of account some types of movement occurring commonly in the plant world, in course of which the cells actually change their volume through gain or loss of water. Among free-living cells the type of move-

ment may be "ameboid," that is, a flowing of the cell contents to conform to an ever-changing outline. Contractile power may be limited in other cases to parts of cells, as in those forms which swim by the lashing of slender projections known as *flagella,* or by the waving of an animated nap or pile upon their surfaces, the *cilia,* of which more will be said. In all cases of energetic movement we feel justified in assuming that the source of the power is in destructive chemical reactions, and that a draft is being made upon the fuel stores of the cells.

The Association of Cells.—When many cells are massed, as in the body of a worm, the situation of the single unit differs significantly from that of the cell leading an independent existence. First of all, its environment is made for it to a great extent by other cells. A very small minority are in direct contact with the outside world; the great majority are submerged among their fellows. The typical cell is, therefore, shut in from food supplies of the casual sort on which the free-living cell depends. It is remote from the oxygen of the surrounding air or water. A cell so situated would perish were it not for one of the most striking features of the larger organisms, a *moving liquid medium,* which bathes the cells and acts as a common carrier. This fluid supplies food and oxygen and removes wastes.

The cells composing the body of any animal are of a common descent, but they have taken on widely different characters and have become adapted to particular functions. The cell which is in itself a complete living thing must perform all the essential activities for itself—the preparation of crude food, locomotion, etc. In the multicellular animal the individual cells have come to be far more restricted in their powers. Many have become passive structures serving only for mechanical support or surface protection. Such cells may or may not be living. Others, while clearly alive, have ceased to perform certain functions. With limited exceptions movement is exhibited only by those systematically arranged cells

which form the contractile tissues. Almost all the cells require their food to be in solution and of a few standard forms. In other words, the primitive capacity to digest and assimilate every kind of nutriment has been lost, but by a wonderful co-operative activity the internal medium has been made a depot of those particular foods which can still be utilized.

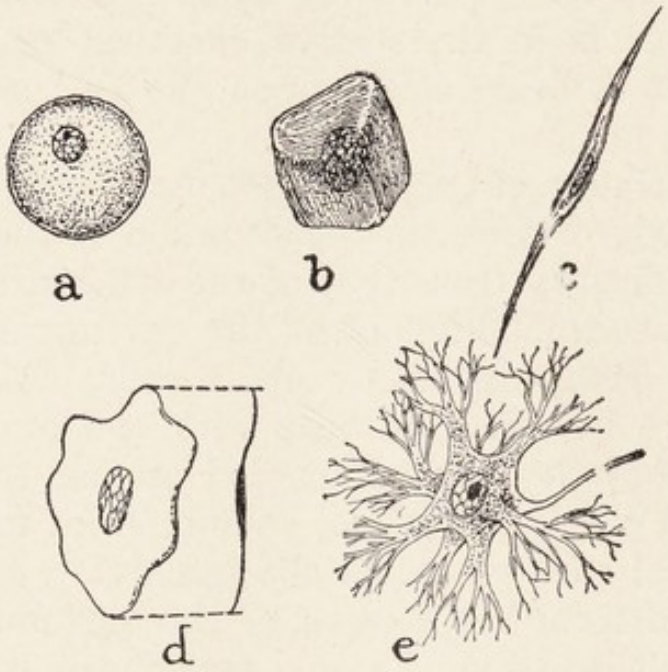


Fig. 2.—Drawings like the above are almost always made from tissues which have been prepared and colored by special means to make clear minute features: *a* Represents an ovum or egg-cell, the typical cell may be assumed to tend toward this spheric form; *b* is a cell from a compact tissue, to show how mutual pressure produces a faceted or polyhedral form; *c* is a contractile element such as occurs in the walls of the alimentary canal, it illustrates an elongated cell; *d* is an epithelial or lining cell of the order found on the inner surface of blood-vessels; this is an example of extreme flattening; *e*, from the nervous system, exhibits the possibility of a branching development.

As an animal grows larger its directly exposed surface becomes smaller in proportion to its weight. The transfers which must take place between the organism and the external world require ample surfaces, and they are secured by infoldings of the body wall at different places. The lining of the alimentary tract is an example of such an infolding and provides a large area for absorption. Among the higher forms the lining of the lungs constitutes a vastly

extended surface for gaseous exchange. The glands are organs in which are concealed great surfaces through which products of cell activity find an outlet.

The specialization which groups the cells of the animal body in a number of classes each with its definite work to do also entails the dependence of each class upon the others. If we compare the life of a savage with that of a civilized man we shall find an analogy not too far fetched to be helpful. We have seen that the free-living cell is self-sufficient, and, indeed, its chances of survival are better when there are but few of its own kind in the neighborhood. Such organisms are competitive rather than co-operative. Somewhat in the same way the solitary savage may be capable of self-maintenance, having the skill to find and prepare his food and after a fashion to shelter and clothe himself. The civilized man is accustomed to look to many other men—and women—to supply his needs. Yet if the man, like the cell, loses something of ruggedness and resourcefulness through becoming a member of a complex society, he evidently gains time and opportunity to concentrate his efforts upon a special pursuit. It is very much the same with the cell. Our analogy fails, as such devices are prone to do, when we consider how the civilized man may become a hermit or a Robinson Crusoe, whereas no single cell detached from one of the higher forms can exist by itself for any length of time.

Co-ordination.—We have emphasized above the services rendered to the organism by its internal medium. The composition of the circulating fluid is influenced by the ever-varying activities of all the organs and tissues. Accordingly, a contribution made to this medium by any group of cells may conceivably modify the conduct of any other group. We shall meet with numerous instances of such influence exerted through the chemical products of one organ upon another or upon the system as a whole. When we speak of an animal as an individual we imply that the parts of the body constantly interact. It is this interaction which makes it appropriate to regard

the body with all its complexity as still forming a *unity* rather than a *colony*. The term co-ordination is employed to express this purposeful working together of all parts for the advantage of the whole. The means of co-ordination may be chemical as just now suggested, but a more conspicuous agency in the highly developed types is that of the *nervous system*. While we must postpone until a later time any detailed description, we ought to indicate at this point the essential contrast between the two modes of co-ordination. One part of the body may affect another through the actual despatch of material to it. When the influence is through the nervous system instead of through the circulation there is no transfer of material. The nerves were once supposed to convey a fluid of strange properties, but the fact is established that they transmit a form of *energy* and not of matter. (The temptation to think of the nerves as conductors of electric currents and to compare the nervous mechanism with a telephone system is strong. Guardedly used, the comparison is valuable, but it is a symbolic rather than a literal representation of the facts. "Nerve impulses," so called, are not electric currents in the ordinary sense.)

In a great nation the prosperity of any section must depend to a large degree upon the commercial exchanges taking place between that section and others. Its factories may depend upon the mines of another province for coal and upon still another for raw material. Much in the same way a single organ of the human body is dependent upon others. A muscle, for instance, profits by the prepared foods or fuels forwarded to it from the digestive tract and by the oxygen borne to it from the lungs. The blood in this case is serving the purpose which is effected by trains and steamers in the case of the nation. Nor do we find lacking in our illustration an analogy for the nervous communication between parts of the living body. The type of such intercourse is furnished by the telegraphic messages which pass incessantly from place to place. *News*, in itself immaterial, may affect the course

of local events just as surely and much more quickly than can the material exports of another region. Reactions produced through the nervous system are correspondingly sharp and prompt in developing.

Blood and Lymph.—In the bodies of the higher animals the internal medium may be described as existing in two forms. In direct contact with the majority of the cells there is in scanty amount a fluid, the lymph.[1] From this they draw their needful supplies of oxygen and food; into it they discharge their waste. The limited resources

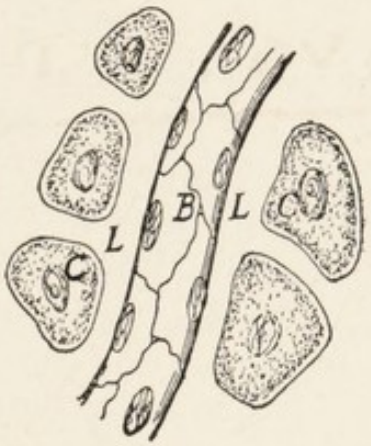


Fig. 3.—*B* is a blood-vessel of the smallest size—a capillary—with walls of flattened cells like that in Fig. 2, *d*. The blood flowing within is removed from direct contact with the cells (*C*, *C*), but dissolved substances may pass from one to the other through the capillary wall and the medium of the lymph (*L*).

of the lymph at a given point would be quickly exhausted were it not that the blood is passing close by in vessels whose delicate walls permit the passage of material in both directions. The blood is in rapid movement and it is constantly renewing the oxygen of the lymph with fresh supplies just brought from the lungs. It is at the same time receiving from the lymph the accumulated waste. The lymph itself is not absolutely stagnant; at a given place there is a certain formation of fresh portions, while that which was previously present is displaced along channels known as lymphatics.

[1] Or tissue-fluid. See p. 119.

CHAPTER II

THE ENERGY RELATIONS OF PLANTS AND ANIMALS

A CHEMICAL reaction can usually be assigned to one of two classes. Either it is exothermic, that is, attended by the evolution of heat, or it is endothermic, in which case heat must be supplied to cause its occurrence. When heat is evolved the products of the reaction are generally simpler and more stable than the original material. The most important reactions of this class are the oxidations. Heat, or other forms of energy applied from without, may effect the synthesis of complex substances rich in fuel value from initial material comparatively destitute of potential energy.

Broadly speaking, the constructive chemical processes in nature are the work of the higher plants. Animals, as well as those forms of plant life which lack pigment, carry on for the most part reactions of a destructive character. This makes evident the dependence of all other forms of living matter upon the pigmented plants. It is through the agency of light-waves, a form of kinetic energy, that the synthetic reactions resulting in the formation of starch and other energetic compounds are made possible. When light is excluded from the green plant it has no advantage over the animal, but pursues a similar course of decomposition. In fact, there is always going on in the plant, even when its constructive activity is most marked, an undercurrent of an opposite trend. Early writers commonly exaggerated the supposed contrast between the chemical conduct of plants and that of animals. They were disposed to deny that an animal could execute any synthesis whatever. It is true that animal cells make few

useful applications[1] of the energy showered upon them by the sun's rays. Nevertheless they do carry on synthetic reactions, although to a limited extent. Since much energy is released within such cells by the prevailing oxidative changes it is not difficult to see that some portion of it may be applied to promote endothermic reactions. When a hydraulic ram supplies with water a house considerably above the level of the stream which operates the device, we understand that the result is made possible because a great deal of water falls that a little may rise. The principle of the conservation of energy is not violated here, nor is it when animal cells erect from a portion of their food molecular structures more complex and energetic than anything in their current supply. The formation of fat from sugar is a case in point. Weight for weight, the fat is more highly endowed with potential energy than is the sugar, but we must take into account the fact that the quantity of sugar entering into this common transformation is much greater than the quantity of fat which can be produced. The energy in the product is more concentrated, but not absolutely larger in amount than it was in the sugar.

There are many species of green plants which are unicellular, just as there are many single-celled animal forms. It is suggestive to consider the reciprocal relations of one such plant and a solitary animal cell living beside it. A constant and pressing need of the animal is oxygen. Now oxygen is freely produced by plants when they avail themselves of the energy of light to carry on constructive processes. To this extent, then, the proximity of the plant to the animal is advantageous to the latter. This ceases to be true when light is succeeded by darkness. The animal meanwhile is giving off oxidized products, of which carbon dioxid is the most abundant. This, together with water, is the very material out of which the plant can build its stores of starch and sugar. The out-

[1] One such may be the development of a substance capable of preventing or correcting rickets, vitamin D. See p. 172.

put of the animal includes also various compounds of nitrogen. These, as well as the carbon dioxid, may be of service to the plant, although to be strictly accurate it must be added that they require some modification, usually effected in nature through the action of bacteria. In view of these exchanges one is tempted to the hasty conclusion that a single-celled green plant and a single-celled animal form a balanced system capable of continued maintenance—in short, a *microcosm*. There is, however, a fatal obstacle to the continuance of the partnership—the animal's need of organic food can only be satisfied by the sacrifice of the plant. To have a truly balanced system of an enduring character we must assume a multiplication of cells descended from the original unicellular plant, providing a surplus of vegetable tissue for the animal's consumption. This situation is sometimes realized in an aquarium.

The give and take which has been illustrated for single cells is proceeding on a vast scale everywhere.[1] It is hard to realize that the great harvests which support the races of mankind were formed for the most part from a gas present only very sparingly in the atmosphere, from water, and from the mineral salts of the soil. "The oak is but a foliated atmospheric crystal deposited from the aërial ocean that holds the future vegetable world in solution" (Holmes). While we rely partly upon animal food (meat, milk, and eggs), this does not alter the fact of our absolute dependence upon the green plants, which in turn owe their growth to the translated energy of the sun. It is amusing to note the apparent travesty upon our human life which can be read into the contrasted conduct of green plants and of animals. The plants are conserving, while the animals are spendthrift. Plants create and distribute wealth. They seem like the thrifty and industrious members of society upon whose charity others less competent depend. One is reminded irresistibly of the parent at

[1] For a most interesting discussion of this matter see Arrhenius, "Worlds in the Making," Harpers, New York, 1908.

home and the son at college. If the father does not literally subsist upon a diet of carbon dioxid and water that the son may have protein and alcohol, the approach to a parallel is too close for complacent attention.

The Body and the Diet.—Turning now to the definite problems of human nutrition, let us consider the respective make-up of the body and the diet. There must evidently be a degree of similarity between them, inasmuch as the one has been built from the other. Similar compounds are met with in both, but, as we shall find, in quite unlike proportions. The body is mainly water. Water makes up about two-thirds of the total weight and forms even a larger percentage of the most active tissues. No material reduction of its quantity can be tolerated. Even after death from thirst the amount is surprisingly little diminished. In the diet also water occupies the first place. It is likely to constitute fully five-sixths of the daily income. Its most obvious services are in connection with the absorption of food in solution and the removal of dissolved wastes. By its evaporation from the skin and the breathing passages it helps to keep the body temperature from rising above its normal level.

Second to water among the substances which compose the body we find the group of bewilderingly complex compounds known as the *proteins*. A protein always yields the five elements—carbon, oxygen, nitrogen, hydrogen, and sulphur[1]—when subjected to analysis. Some members of the group contain phosphorus also.

[1] The elements occur in proteins in about the following percentages: C 53, O 22, N 16, H 7, S 1 per cent. Phosphorus when present amounts to 1 per cent. more or less. It is quite impossible to convey an adequate impression of the complex fashion in which the five or six elements are combined. Many years ago the following formula was suggested for hemoglobin, the red protein of the blood, which is exceptional in containing iron:

$$C_{758}H_{1203}O_{228}N_{195}FeS_3.$$

It is not seriously maintained that these large numbers are precisely correct, but the order of their magnitude is probably typical. The scale cannot be less; it is now held that the hemoglobin molecule is more correctly represented by a multiple of such figures, perhaps four times the old estimate.

Merely to mention these constituent elements is to give no proper conception of the intricate manner in which they must evidently be combined. To appreciate this we need to consider the very long list of cleavage products, in themselves rather complex, which can be obtained by the decomposition of protein from a single source. The physiologic chemist is somewhat in the position of a person who sees the various parts of a watch—the wheels, springs, jewels, etc.—lying loose upon the table of the watchmaker. He may gain a fair notion of the intricacy of the watch, though he may be very far from knowing how the parts were related in the time-piece. We do well to use the plural number in speaking of the proteins, for all recent work tends to emphasize the distinctive molecular pattern which characterizes each form and makes it differ definitely from every other. "There is one flesh of men, another flesh of beasts, another of fishes, and another of birds." This is excellent and altogether modern chemical biology. The presence of the element nitrogen in the proteins distinguishes them sharply from the other prominent compounds in both the body and its daily income. Nitrogen makes up about 16 per cent. of protein, and the value of this figure in calculations will be apparent later. It has been said that the proteins are second only to water in their abundance in the body. This is not true of the diet unless we have to do with a carnivorous animal. Among the herbivora, and almost always among men, the second place in the list of supplies is occupied by the *carbohydrates*.

Third in quantity among the constituents of the body we find in most individuals the *mineral compounds*. These would not make so large a proportion if it were not for the skeleton. Bone is a tissue in which salts of lime are abundantly present. But in all the other tissues and in the fluids too we find a variety of salts, and it is well established that their presence is not accidental, but a matter of moment. Sodium, potassium, calcium, and magnesium at least, perhaps other bases also, must be

kept in certain balanced relations if the life processes are to go on. The acids represented are chiefly hydrochloric, phosphoric, and carbonic. Sodium chlorid, the one salt which we take pains to add to our food, is the one most abundant in blood and lymph. Potassium rather than sodium compounds predominate in the cells.

Next in amount to the salts in the body of average build, and not uncommonly exceeding them, are the *fats*.[1] The word " fat " is used sometimes in a chemical and sometimes in an anatomic sense. In the first case it denotes a compound of carbon, hydrogen, and oxygen, having a formula of a certain type. In the other usage the meaning is " adipose tissue," a form of connective tissue rich in such compounds. Fats have familiar physical characters. They are not soluble in water or to any great extent in the fluids of the body. They pass from solid to liquid form at moderate temperatures; the fats of the human body are regarded as in a fluid state when under the influence of its warmth. Fats which are familiarly observed as liquids we commonly speak of as *oils*.[2] No other common physiologic compounds have so much latent energy awaiting release by oxidation. Fats are more plentiful in apparently lean individuals than might be judged. A considerable store of adipose tissue is to be found in any condition short of imminent starvation.

It has been said above that *carbohydrates* usually have the leading place among the solid matters of the diet. This is owing to the large proportion of vegetable foods generally consumed. In the animal body the occurrence

[1] Fats are compounds which can be resolved into glycerin and organic acids. Those of chief interest in nutrition are the glycerids of palmitic, stearic, and oleic acids. The first mentioned has a composition indicated by the formula $C_3H_5(OOCH_{31}C_{15})_3$. The others are nearly related. The three common fats differ in their melting-points and in other respects. They are mingled in definite proportions to form the body fat of each animal species.

[2] Some oils are not fats nor subject to digestion. This is the case with the paraffins, which are not at all available as foods though valued as laxatives.

of carbohydrate is rather scant, and it is one of the chief problems of the physiologist to account for the daily disappearance of a great quantity of these compounds in the economy of the organism. The reader may already foresee what we shall later explain in detail, that this disappearance of carbohydrate is due in part to the fact that it is the fuel most constantly called upon to evolve energy, and in part to the ease with which the tissues transform to fat a surplus of these substances. Under the head of carbohydrates we distinguish the starches and the sugars. Starches[1] are of high molecular complexity, imperfectly soluble, and tasteless. Sugars are cleavage products of starches or, if they occur apart from previously existing starches, closely resemble such cleavage products. They are of definite and moderate molecular weight, they are soluble, crystallizable, and sweet. They contain the same elements which are found in fats—carbon, hydrogen, and oxygen—but the percentage composition is wholly different and the structure of the molecule also. While the carbohydrates are energetic, their fuel value is less than half that of fats.

We have now named this list of substances as uniting to form the body—water, proteins, mineral matter, fats, and carbohydrates—the order suggesting their relative abundance. We have said that in the diet water also takes the first place, but that carbohydrates ordinarily take the second. Either proteins or fats may stand third among the constituents of the diet. Often the amounts of the two are found to be about equal. A possible diet comprises 100 grams of protein, 100 grams of fat, and 250

[1] The three elements in starch are present in proportions represented by the formula $C_6H_{10}O_5$. But the number of atoms in the molecule is not correctly indicated by this formula; it requires to be multiplied throughout by an unknown, but considerable number. Sugars are of two common classes: the disaccharids, with the formula $C_{12}H_{22}O_{11}$, and the monosaccharids or hexoses, with the formula $C_6H_{12}O_6$. Cane-sugar, malt-sugar, and milk-sugar are disaccharids. The hexoses of direct interest in nutrition are glucose (also called dextrose), fructose (or levulose), and galactose (a derivative of milk-sugar).

grams of carbohydrate, illustrating this equality. The mineral matter in the ration is not likely to exceed 20 grams a day. Both the body and its income, of course, contain in small amounts substances which do not fall into any of the classes named. Such miscellaneous organic compounds are conveniently grouped as *extractives*. Many of them are nitrogenous and represent disintegration products of proteins. Reference to their significance will be made from time to time.

At the very outset the double service of food to the organism was indicated. It represents both building material and fuel. If we liken the living body to a power-house, we see clearly how both kinds of supplies are required. Coal is the most bulky supply of the power-plant and the one on which its operation immediately depends. But there must also be new parts to replace those which wear out. The up-keep of the building calls for new wood-work, for paint, etc. A certain difficulty is encountered in the attempt to show parallel conditions in the case of the body because the separation of the two functions is here much less sharp. Protein food, on the whole, has a peculiar title to be regarded as building material, but it is also an entirely available fuel. It is as if planks and beams designed primarily to repair the structure of the power-house were fed into its furnaces. The suggested comparison must not be pressed too far, for it conveys an impression of wanton destructiveness which we cannot assume to be just in the case of the organism. There are some minor supplies brought into the power-house which are not fuels nor precisely materials for repair. The oil is an example. Some of the extractives of the diet occupy an analogous position, being neither sources of energy nor of construction, but nevertheless favorably affecting the course of events. This comes near to our conception of a *drug* in relation to the processes of life.

CHAPTER III

THE NATURE AND THE MEANS OF DIGESTION

It has been said that one of the results of the specialization of cells is the loss of the primitive power to receive and utilize all kinds of food. The blood brings to the tissues of the body food of certain standard forms, and it is only these which can be used. The attempt to add various soluble foods to the blood by direct injection into the circulation has shown that in most cases such foods are offered in vain to the living cells. Milk introduced in this way is not a practical means of nutrition. Cane-sugar added in measured amounts to the blood is excreted promptly and in almost undiminished quantity by the kidneys. Thus it becomes clear that foods introduced directly into the blood are frequently treated like waste products, while the same foods after transformation in the alimentary canal are entirely acceptable to the body cells. The function of the alimentary canal is to work over the many foreign forms of nutriment into a few forms of the native type. From day to day the diet may be of quite variable character, but its variations hardly show themselves in the composition of the blood.

The term *digestion* is usually applied to those changes in the food-stuffs which precede absorption. To cover subsequent changes we use the word *metabolism*.

One of the more evident characteristics of digestion is that it is a refining process. It effects a separation of the useful and the useless portions of the ration. This is a very conspicuous fact with the herbivora, whose food contains much woody material from which the available nutriment must be laboriously extracted. With mankind, especially under modern conditions, a great part of

this work of separation is accomplished in the preparation of food, both industrial and domestic. In this way the task of the digestive organs is lightened, and, as we are often told, overeating is made easy. Some foods are quite devoid of residues when successfully digested and absorbed.

The early writers, having little knowledge of chemistry, were naturally led to make much of the mechanical reduction of food in the alimentary tract. Mastication subdivides the food, and it was held that the later operations, especially those of the stomach, were essentially further grindings of a similar sort. Such mechanical processes as do occur continue to be of interest, but they are now seen to be preliminary to actual digestion. Moreover, we shall see that it is easy to assume that they are of a more positive nature than is really the case. The human stomach is not a mill, though the gizzard of a bird may be fairly described by that word.

In the eighteenth century the emphasis passed from mechanical factors to the process of dissolving the food. Solution is plainly one of the features of digestion, but it is a somewhat superficial one. Of course, it is natural to believe that solid food must become liquid before it can penetrate the intestinal wall, but mere solubility, as we have already seen, is not a guarantee of fitness for the use of the cells. Freely soluble foods like cane-sugar and milk-sugar require to undergo digestive changes just as definite as those carried out in the case of fats or coagulated proteins. It is often stated that the object of digestion is to produce diffusible substances. This statement is inadequate, for diffusibility like solubility does not in itself determine the utility of a food. The sugars mentioned above are sufficiently diffusible, and the changes which they undergo before absorption serve a more fundamental purpose than the mere hastening of their passage through the lining of the intestine.

In the light of modern chemical knowledge we can be somewhat specific in regard to the molecular aspects of the

digestive processes. They are probably always *cleavages*, large molecules giving rise to smaller. When the original molecule is of extraordinary size, as with proteins and starches, these cleavages have a serial character and a number of intermediate products must accordingly be formed. That is to say, the earlier products are in turn subjected to digestion. Such cleavages are generally, if not always, *hydrolytic*, that is, water enters into the reaction and its elements are found combined in the products. For the simpler instances of digestion, as in the case of fats and of the disaccharids,[1] we can write precise chemical equations. We cannot do this with the same accuracy for the starches, and we are still farther from being able to express the exact manner in which the protein molecule undergoes hydrolysis. Yet we have sufficient evidence that the digestion is generally of a uniform type.

Some constituents of the diet need no digestion. This is the case with the mineral salts, so far as they are absorbed, with the simple sugars (monosaccharids), and with alcohol. It is hardly necessary to say that water is also ready for reception into the body fluids. The numerous extractives are for the most part absorbed in the form in which they are eaten. A diet entirely predigested seems not to be practicable. If one were prepared it would have to contain advanced decomposition products of the proteins, which are bitter to the taste, and an amount of sugar which would be cloying and subject to fermentation.

Digestion is anticipated to some extent by changes in our food which precede its actual arrival in the canal. The ripening of fruits and vegetables, as well as the corresponding processes in meat, illustrate this point. The influence of cooking is not so constantly of a sort to initiate digestion, yet in many instances it is so. For

[1] The following equation illustrates the hydrolysis of a disaccharid:

$$C_{12}H_{22}O_{11} + H_2O = 2C_6H_{12}O_6.$$

This means that one molecule of malt-sugar, reacting with one molecule of water, gives rise to two molecules of glucose.

example, when meat is boiled the common variety of connective tissue in it is converted to gelatin. This change is a typical hydrolysis, and if it were not executed in advance it would be an early task of the gastric juice. When cooking is attended by considerable drying of the food it is less likely to count definitely toward digestion. Most proteins are coagulated by heat, and this change to solid form seems opposed to the general course of events in the alimentary system. The action of microscopic organisms upon food substances is in line more or less with normal digestion; the maturing of cheese is an example. But bacterial action may depart so far from the normal decomposition as to generate products of strongly poisonous properties, the so-called *ptomains* being among them.

The Means of Digestion.—Hydrolytic cleavages closely resembling those of animal digestion may be caused to occur in various ways. Boiling food-stuffs with acids accomplishes this. So does treatment with alkalis. Similar results follow the application of superheated steam. But the striking fact is that such changes as are brought about in the laboratory by violent reagents, high temperatures, or both in conjunction, are caused to take place in the stomach and the intestine by bland juices acting at the mild temperature of the body. The changes effected by these juices are often modified by the simultaneous activity of bacteria, but the presence of the latter, at least in man, is to be regarded as accidental and non-essential.

The power to digest foods has been known for a long time to reside in the secretions which enter the alimentary tract. It was at first necessarily estimated simply by observing the progressive solution of solid food. The intimate nature of the process has become appreciated more recently. Comparison of the juices from different sources shows that they are individual and specific to the extent that each one, as a rule, acts upon certain classes of food and not on all. There is sufficient evidence for the belief that when a juice digests two or more classes

of food-stuffs it contains separate and distinct reagents for the performance of each line of work. We do not know the precise chemical nature of the active bodies, "digestive principles" as they were formerly called, but we know a great deal about the conditions of their working.

When a digestive secretion has a single well-marked effect upon one sort of food material we say that it contains an *enzyme*. We are thus naming a body which we know chiefly by its power to promote a certain chemical reaction. It is not many years since an able writer protested against this confident reference to a *substance* where it is a *property* rather than a compound which we are observing. It will be admitted that it is doubtful whether anyone has ever seen that which is an enzyme and nothing else. What we see and handle are solutions possessing characteristic powers or dry preparations capable of furnishing such solutions. But it has seemed altogether reasonable to connect the property with a substance and we shall continue to do so. Acting on this basis, we say of a juice which hydrolyzes starch that it contains a *diastatic enzyme*, and of one that acts in a parallel fashion on proteins that it contains a *proteolytic enzyme*. When the action is upon fats we call the enzyme *lipolytic*, or, using the substantive, we call it a *lipase*. It is unfortunate that there is much confusion at present in the use of such terms; there are a great many more in use than there need be. The simplest plan is, perhaps, to fall back upon our Saxon and speak of enzymes as starch-splitting, protein-splitting, sugar-splitting, and fat-splitting. We shall take pains, however, in our detailed discussion to introduce various equivalent terms. We shall find especially that enzymes are often named with reference to their sources as well as to their powers.

Enzymes are similar in many respects to the catalyzers of inorganic chemistry. Their presence accelerates reactions which in their absence might not be appreciable. We do not think of them as contributing either material

or energy to the process. They suggest the oil in a machine which lessens the resistance of its parts to the driving force. The enzyme in a digesting mixture is not forcibly compelling the molecules to disintegrate, but it is removing some hindrance to their spontaneous rearrangement. It is not definitely used up in this service. Accordingly, it follows that a limited quantity of a digestive juice, of course containing a still more limited quantity of enzyme, may be responsible for an amount of digestion practically unlimited. Unlimited time would be demanded for such a demonstration. (This form of statement should be qualified. Enzymes are somewhat unstable and liable to deteriorate.)

When a process of hydrolysis takes place under the influence of an enzyme and in a glass vessel, there must be a rising percentage of the products and a declining percentage of the initial substance as the reaction goes on. The velocity of the transformation is found to diminish and at last it seems entirely arrested. A mixture now exists which contains the first and the last members of the chemical system in proportions which have become constant. It is an instance of chemical equilibrium. The halting of the reaction does not mean that the enzyme is exhausted. If any means can be devised by which the accumulated end-products can be removed the hydrolysis will be continued. It was specified above that the trial should be made in a glass vessel. The reader will quickly recognize the important difference between such a container, from which nothing can escape, and the alimentary canal, from which active absorption processes withdraw the products of digestion. A clear field is thus provided for the continuance to substantial completion of the reactions which the enzymes are promoting. The contrast between laboratory conditions and those which prevail in the body did not escape the acute mind of Spallanzani, who was a pioneer among students of these matters. As early as 1777 he recorded that the solution of meat by gastric juice could be greatly facilitated by letting the

digestive fluid fall drop by drop upon the food and to trickle away, bearing the dissolved products.[1]

Enzymes are exceedingly sensitive to varying degrees of acidity and alkalinity in the medium. Most of them do not keep their efficacy if the solution is far from the neutral point. But they are somewhat individual in this as in other properties, the acid which is highly favorable for gastric digestion, for example, being quite prohibitive of salivary action. They are all destroyed when in solution by temperatures somewhat short of boiling. Cold suspends their activity, but does not prevent its return upon warming. They are most effective at a temperature not far from that of the blood, though in general a few degrees higher. These relations between the enzymes and temperature are much like those established in the case of the simpler living forms. Having this in mind, one easily adopts the common practice of speaking of the *killing* of enzymes by heat. It must not be forgotten that this is a figurative expression. We are not justified in thinking of enzymes as living. Living organisms when they grow and multiply in a nutrient medium may decompose it much as suitably assorted enzymes would do, and, in fact, the organisms in question are probably producing their own enzymes for the purpose. Formerly such living things as the yeasts and the bacteria were described as "organized ferments," and the detached enzymes, incapable of self-multiplication, were called "unorganized ferments." These terms are not much used at the present time. Enzymes are assumed to be products of living cells and may be very characteristic fragments of the cell's fabric, but they are not independently living.

The digestive changes to which we pay most attention are those which occur in the cavity of the alimentary canal, and which can be observed to take place also when the same mixtures are placed in the flasks and test-tubes of the laboratory. But we must not overlook the prob-

[1] Foster, "Lectures on the History of Physiology," University Press, Cambridge (England), 1901, p. 215.

able fact that similar changes are constantly occurring within the boundaries of every active cell. *Intracellular digestion*, presumably made possible by intracellular enzymes, obviously takes place when a protozoan cell engulfs a solid food particle, and has been thought to be as definite a process when a muscle-fiber of the human body nourishes itself at the expense of the surrounding lymph.

While the great majority of enzymes are hydrolytic and favor reactions of the class which we have been discussing, it must be added that there are other enzymes associated with other orders of chemical change. Enzymes which promote oxidations are believed to play a most important part in the activities of the tissues. When reactions are hydrolytic they proceed with but little evolution or absorption of heat. When they are oxidative the release of energy is a most characteristic attendant condition.

CHAPTER IV

THE WORK OF MUSCLES AND GLANDS

We cannot enter upon a description of the alimentary canal and its activities until we have devoted some space to the physiology of *contraction* and *secretion*. Movement is the most familiar manifestation of animal life. When visible to the naked eye it is the expression of the shortening of elongated units—cells or fibers—associated to form contractile tissues. In the human body there are three principal kinds of these tissues. The obvious external movements of the limbs and the features, the act of breathing, etc., are produced by what we call the skeletal muscles. Contractile tissue of another order forms the walls of the heart and furnishes the power for its beating. A third kind occurs in the walls of the alimentary tract, in the blood-vessels, and elsewhere.

The term *skeletal* applied to a type of contractile tissue implies relationship to the bones. It is easy to see that external movements are made effective through the connection of the muscles which produce them with bones acting as levers. In some instances the term is a misnomer, for there are some small muscles histologically like the rest which do not act upon bones. The large and conspicuous muscles are attached, usually at both ends, to the bones. We can generally observe that one end is more freely movable than the other. The comparatively fixed end is called the *origin* of the muscle, the end more subject to movement is its *insertion*.

What is called a skeletal muscle is a bundle in which we can distinguish an active and a passive part. There are the true contractile elements and there is the *connective tissue*. The inactive substance forms a sheath enclosing the rest and also partitions which subdivide the interior.

The arrangement is familiar in the cross-section of a piece of meat. The subdivision which is apparent to the unaided eye is repeated on a microscopic scale until the finest meshes of the connective tissue enclose the hair-like individual fibers of the muscle. Each of these slender fibers is a miniature muscle in principle. The function of the connective tissue is often overlooked. While this part of the muscle is entirely passive in character, and scarcely to be considered alive excepting for a certain power of renewal after injury, it is quite necessary to the act of contraction. It may fairly be said to constitute a harness through which all the numberless, minute contractile elements are enabled to unite their efforts. As the end of a muscle is approached the connective tissue increases in quantity at the expense of the typical contractile material. In most cases there is an extension of the muscle consisting of connective tissue only, and in a dense form, which attaches the whole to the bone. This is the *tendon*. It may be a long tough cord or it may form a wide thin sheet. A muscle deprived of its connective tissue would be simply a mass of unattached living fibers which might slip about among themselves, but which could not apply their combined tension to accomplish any external effect.

The fiber of skeletal muscle is a modified cell. It is exceptionally elongated; its length may be a thousand times its width. When it shortens it conforms to the general principle laid down in Chapter I, that is, it does not diminish in volume, but only in surface and, therefore, in length. How the chemical process which underlies the forcible shortening is made to contribute energy to carry it out has proved one of the most difficult problems of physiology. It cannot be dealt with here. But the fact is to be emphasized that we are in the presence of a mechanism somewhat like the steam-engine, inasmuch as it produces motion and does physical work at the cost of fuel destroyed. The resemblance goes farther than this, for both with the engine and with the muscle the ac-

complishment of a measured amount of work is attended by seemingly wasteful evolution of heat. An engine is considered economical if it turns 15 per cent. of the energy resident in its fuel into horsepower. Muscles sometimes do better than this, but much of the time they are even less efficient. It is fair to point out that the heat set free as an accompaniment of muscle contraction is often of value to the animal. In our own case the temperature of the body must be kept above that of its usual surroundings. By far the largest part of the heat devoted to this maintenance of a relatively high body temperature is produced in connection with muscular activity. Muscles are thus seen to be organs of heat production as well as organs to carry out movements. When the external temperature is high or the degree of muscular contraction is greatly above the average, the heat evolved does become distinctly an embarrassment to the organism.

The source of the energy displayed in muscular activity is chiefly the disruption of carbohydrate molecules. Sugar appears to be the preferred fuel of the muscular machine. While other foods are also available it may turn out that they have to be transformed to sugar before their energy can be utilized. Whether this is necessarily the case is now (1931) a matter of lively debate. When sugar is completely oxidized the only end-products are carbon dioxid and water, the same substances which would be formed by the literal burning of the sugar with an adequate supply of oxygen. These waste-products are very readily removed from the muscle, when its situation is normal, by the circulating blood. The carbon dioxid will almost immediately escape from the blood when it passes through the lungs. The water becomes part of the large total volume which is always passing into and out of the body, and may leave by all the main channels of excretion—the respiratory passages, the kidneys, and the skin. It will be noted that the quantity of water leaving the body is constantly in excess of the income. Ordinar-

ily the body excretes all the water which it receives plus the water which arises within it by oxidation.

A distinction must be borne in mind between the compounds which for the most part make up the muscle and those substances which it is generally found to use as sources of energy. The solid part of the muscle is mainly composed of proteins. But, as just stated, it is most apt to destroy carbohydrates when at work. One is reminded of the fact that a steam-engine is composed chiefly of steel, but burns coal as its fuel. The comparison is somewhat faulty, however, for it suggests a more radical difference between structure and fuel than we can safely infer for the muscle. Under some conditions muscular work may involve some destruction of protein material.

All that has been said of contraction up to this time applies equally to all three classes of muscle. Nevertheless each type is adapted to its particular work by peculiar properties. Skeletal muscle is capable of quick shortening and prompt relaxation. A contraction may occur and the return to an extended condition be accomplished in one-tenth of a second. The trained finger of a pianist may strike a key ten times in a second. Such movements are in strong contrast with those executed by the form of muscle found in the viscera. The contractions of the stomach develop very slowly, are maintained for some time, and are correspondingly slow in fading out. Of course, it is true that skeletal muscles may also make prolonged contractions, as in keeping the body erect, carrying a suit-case, and in countless other instances. Experimental study has shown that such contractions as these are really compounded of successive brief twitches occurring too rapidly to permit relaxation. In view of this the possibility of having prolonged contractions in skeletal muscle does not invalidate the statement that it is essentially a quick-acting tissue.

Muscle and Nerve.—The conception that muscular activity is due to the nervous system is probably sufficiently familiar. Every skeletal muscle has its own strand of nerve-fibers placing it in connection with the brain or

the spinal cord and under their control. If its connection is severed it becomes paralyzed and remains inactive, unless special local means, like electricity, are employed to excite it. Ordinarily we are justified in saying that skeletal muscle is *not automatic*, meaning that every movement which it makes is an indication of a previous act, or, as we say, a *discharge* on the part of the nervous system.

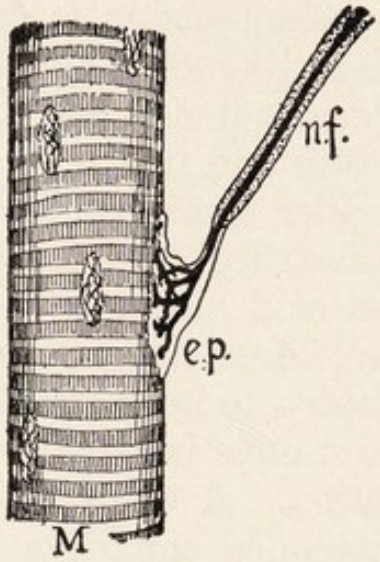


Fig. 4.—The above represents somewhat diagrammatically a very small fraction of the length of a fiber of skeletal muscle. To include the entire element with the length proportional to the width we should have to extend this drawing to a length of several yards. The fiber is cylindric and enclosed by a more definite membrane than is usual with animal cells. The cross-marking is not a feature of this membrane, but stands for a peculiar organization of the protoplasm inside. Nuclei are seen here and there near the surface. The segment shown is supposed to be the particular one about in the middle of the fiber within which falls the connection with the nervous system. A nerve-fiber (*n.f.*) is seen making a junction with the muscle-fiber (*M*) through the so-called end-plate (*e.p.*).

In somewhat sharp contrast is the behavior of the muscle composing the heart and of the form which is found in the viscera.[1] These two kinds of contractile tissue are described as *automatic*, in the sense that they show a tendency to rhythmic contraction and relaxation even when deprived of their nervous connections. The automatic property of the heart is the cause of its beating.

[1] Commonly called *smooth* muscle to emphasize the microscopic appearance of its cells: they lack the cross-markings featured above.

In varying degrees the different portions of the alimentary canal exhibit the same power, not ceasing to shorten and to extend when observed entirely outside the body of the animal. While we emphasize this remarkable tendency to rhythmic activity, we must hasten to add that tissues showing such capacities are nevertheless subject to some nervous control. Thus the heart beats primarily because of the peculiar nature of its own substance, but variations of rate and strength are constantly occurring as a result of the influence of the nervous system. In this connection it must be pointed out that such influence is not necessarily so applied as to excite increased activity, but may be *inhibitory*, that is, reducing the rate and force of the spontaneous contractions. A large place is now given to the inhibitory functions of the nervous system, and we shall meet with other examples of the restraint which it imposes upon various organs. A little reflection makes us realize that much of the highest work of the brain must be in the line of inhibition. A man is distinguished by the acts from which he refrains quite as much as by those which he performs.

Muscular Tone.—It will be well before we go farther to make clear what is meant by tone (tonus, tonicity) in connection with the behavior of contractile tissues. Muscle is said to exhibit tone when it is not completely relaxed. Tone is thus a mild, sustained contraction. It seems rarely to be absent altogether, but may vary much in degree. Tone in the skeletal muscles gives them a certain firmness and maintains a slight, steady pull upon their tendons. This is not likely to result in actual movement, because these muscles usually fall into antagonized groups, one of which opposes another. A heightened tone in the muscles of the arm may not change its position, since the force tending to bend it may be offset by an equal tension adapted to straighten it. Changes of tone in the walls of the hollow viscera, as the stomach, have a much more evident effect, since they alter the size of the cavity. One must discriminate carefully between stretch-

ing and tone change in such a case. A non-living, elastic sac may be distended by increasing its contents, but will react with a pressure proportional to the distention. A living organ which adapts itself to increased contents by a diminution of tone may exert no more pressure when full than when nearly empty. This principle is well illustrated by the urinary bladder. At one time this organ may have a capacity of a pint, and again its cavity may be nearly obliterated, but there is no strict correspondence between its size and the internal pressure. Indeed, a strong degree of tone and a high pressure may exist when the bladder is quite small.

Glands and Secretion.—We have taken time and space to deal with the elements of muscular activity, and we must also give a place to another type of tissue and to its work. Some appreciation of the physiology of glands is as much a prerequisite of the study of the alimentary process as is a knowledge of the mechanism of contraction. Everyone understands that the nervous system throws the skeletal muscles into their orderly activity, but the fact that the secretions of the body are often produced under nervous influences is not so familiar. Yet we do not have to look far for suggestive examples. The flow of tears as an accompaniment of an emotional experience is clear evidence that the small organs above the eyeballs which elaborate the tears are in connection with the brain and responsive to its changing conditions. A like relationship can be demonstrated for the glands that produce saliva and for those which secrete sweat. Secretion and contraction are two manifestations of metabolism which are alike regulated by the nervous system. In fact, if we set aside for the present the phenomena of consciousness, it is doubtful whether we have any expression of the working of the nerve-centers beside these two.

What, then, is a gland? The word is used sometimes to designate a large organ like the liver, the pancreas, or a kidney. Sometimes it is used with reference to a microscopic affair like an individual sweat-gland or one of the

minute pits in the inner surface of the stomach or the intestine. The fundamental structure is the same in both classes. The microscopic gland is a depression of a cellular surface—a pocket, one might say—out of which when it is active the secretion wells. The cells which

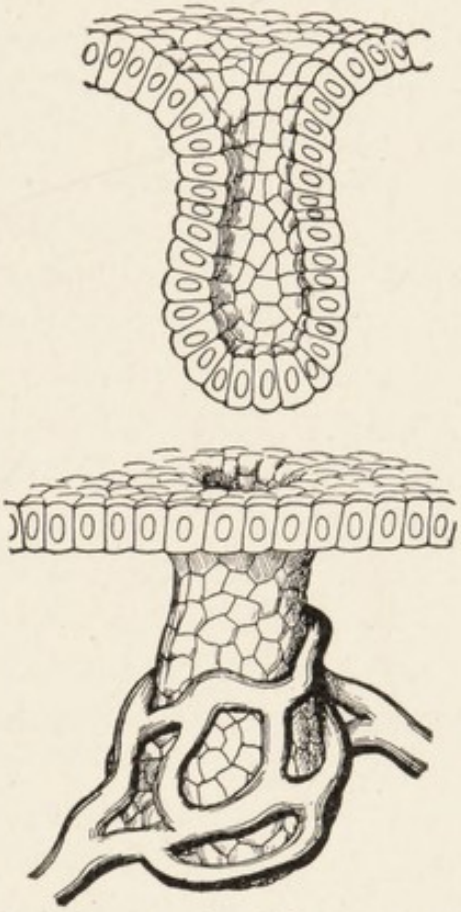


Fig. 5.—The principle of glandular structure. In the upper figure a simple microscopic gland is supposed to be laid open by a section along its vertical axis. The cells are seen to surround a recess into which they discharge their secretion. Below, the same structure is shown in its entirety, and in addition the encircling blood-vessels which contribute to make good the losses suffered by the secreting cells.

bound its cavity are the producers of the secretion, and are in turn dependent for renewal upon the lymph which underlies them and the blood which is flowing close by. A superficial view would suggest that such a gland is a filtering device adapted for straining off certain portions of the blood. This is, however, an entirely inadequate con-

ception. Most secretions contain substances which were not present in the blood at all, and which must, therefore, have been elaborated by the cells of the gland. When we remember that the same blood flows through all the glands we cannot fail to be impressed by the variety of the products which are made from the same raw material—products as unlike as milk and bile, urine and saliva.

A compound gland, like the pancreas, is an aggregate of numberless units, which are individually like the simple microscopic glands. Within the meshes of an abundant supporting tissue which is shot through with blood-vessels are these small pockets walled around with the characteristic cells of the gland. These ultimate recesses are called *alveoli* or *acini*. Each has a way open through which its liquid product may move toward an outlet. Usually there is a single main *duct* formed by the union of all the fine passages from the alveoli and bearing their combined contributions. A compound gland may have more than one duct. Glandular secretions may be discharged directly upon the surface of the skin, as in the case of the sweat, or they may enter cavities, as happens with the gastric juice, the pancreatic juice, and the secretion of the intestinal lining. The bile and the urine are two secretions which accumulate temporarily in special containers, the gall-bladder and the urinary bladder respectively, before they reach their final destination.

Internal Secretions.—It may not be premature to add at this point that any organ may yield some peculiar product of its own life process to the lymph or to the blood as well as to the cavities of the hollow viscera and to the exterior of the body. A product of this kind which merges with the circulating medium instead of appearing distinct and separate from it is called an *internal secretion*. One may maintain that every organ has such a secretion, for inasmuch as each has its unique chemical composition and its distinctive metabolism, it must give to the blood compounds which no other organ duplicates. As stated before, the actual make-up of the blood is the resultant

of the action of all the tissues upon it. But we shall find that internal secretion is a function much more clearly attributable to certain organs than to others and most evident in connection with a few small structures like the thyroid and the adrenal, to which later reference must be made. To have an internal secretion an organ need not be a typical gland. No duct will be required to carry such materials as its cells turn over to the blood-stream. In some cases organs believed to work along these lines are spoken of as *ductless glands*. A word recently introduced as an equivalent of the term "internal secretion" should be given. It is the word "hormone," meaning a chemical messenger, a very convenient and suggestive expression.

Absorption and Secretion.—Gland-cells have been said to draw upon the blood or the lymph for their raw material and to manufacture their secretions therefrom. In this process something enters the deeper boundary of the cell layer and in a more or less transformed state it is later discharged from the exposed surface. It is helpful to compare this operation with what takes place in the intestine when the products of the digestive cleavage are being removed to the circulation. When absorption is going on it is the exposed ends of the cells which receive dissolved substances and their deeper borders which are discharging to the fluids that underlie them. Such a process has been well called "reversed secretion," and there is the same possibility of an extensive making over of the transferred material in this case as in the other. In other words, the digestive products which are last detected in the intestine are not necessarily those which will be dealt out to the blood by the cells of the absorbing membrane. Both secretion and absorption are phenomena which can be completely carried out only by *living* cells. Each is probably promoted by a definite application of energy on the part of the cells concerned. In either case it is possible that there may be some transfer of material through the clefts *between* the cells as well as through the cell bodies.

CHAPTER V

REFLEX ACTION

In the previous chapter it was pointed out that all the work done by the skeletal muscles is in response to the discharges of the central nervous system. For the other types of muscle—the cardiac and the visceral—it was shown that there is an inherent tendency to rhythmic activity, but that over these tissues also the nervous system exercises a regulation. Finally, it was stated that the glands likewise are subject to central government, although not to the same degree in all cases. We must now proceed to consider how the nerve-centers are themselves prompted to throw muscles and glands into action.

As we observe the body at work we cannot fail to be impressed with the timeliness of its adjustments. It is constantly meeting with emergencies and adapting itself to new conditions. If we are inclined to attribute all these quick adaptations to intelligent choice of courses to be pursued we shall find that we cannot long defend such an explanation of the facts as they occur. We cannot pretend that we think of each inequality of the pavement as we cross the street, or of each individual in the crowd through which we make our way. The balancing of our bodies, standing or walking, is not a matter about which we are given to deliberating. These things seem to take care of themselves. It is such adjustments which " seem to take care of themselves " that are called *reflex actions*. A reflex is an adaptive change, brought about through the agency of the central nervous system, to meet some new external condition. We may or may not notice the occurrence of a reflex. If consciousness is at all involved, it is incidental and not causal. Often

the conscious effort is rather to prevent the reflex from taking place, as is apt to be true when we sneeze. Of some reflexes we are quite unlikely to be aware; this is the case with the narrowing of the pupil in response to increase of light.

Let us now go into some detail and analyze carefully the reflex process. We have seen that the primary cause is an external change of some sort, the word " external " meaning outside the central nervous system and not necessarily outside the body. The change which is at the root of the reflex is usually referred to as an external stimulus. It would be easy to give a long list of examples. A foreign particle comes in contact with the larynx; its contact is the stimulus which develops the coughing reflex. Slight drying of the exposed surface of the eyeball is a common cause of the winking reflex. Irritation of the lining of the stomach is the most frequent of the many possible stimuli through which vomiting can be excited.

External stimuli would fail of any extended effect if it were not for the nervous connections of the parts affected. In the last chapter the nervous system was spoken of as sending its impulses out to muscles and glands. But its work is twofold. It not only acts, but it is acted upon. Its fibers fall into two classes, those which are concerned with transmission of effects *outward* from the brain and the spinal cord, and those having the opposite function, the carrying *inward* of impulses started by external causes. The first class of conductors are usually called *motor;* the second, *sensory*. Both terms are open to objection, as a little consideration will show. The effects which the nervous system produces in the tissues of the body are not solely movements. The word " motor," then, is not inclusive enough. It is better to substitute the word *efferent*,[1] which means simply centrifugal, and which implies nothing whatever about the nature of the responses evoked. Efferent fibers may be motor, that is, exciting contraction, but they may also inhibit contraction, and

[1] *Efferre,* to bear away.

when they end in connection with the cells of glands they may be *secretory*. Probably also they may inhibit secretion.

Just as we have found the word "motor" inadequate and have agreed to replace it by "efferent," so the word "sensory" does not properly indicate the whole service of the fibers which bear impulses toward the brain and cord. *Sensory* implies "productive of sensation," and we cannot assign such a property to all the millions of fibers which assail the centers with their communications. In the great majority of cases we do not feel any consequences of their activity. The term *afferent* is free from this objection and is the logical complement of *efferent*. If one hastens to ask what is the significance of afferent fibers which do not arouse sensation, the answer is simple and definite: They produce reflexes.

If the first element in the reflex process is the application of an external stimulus, it is now clear that the next element is the *afferent transmission* of the impulses. What these impulses are cannot be discussed. It should be recalled that they are not fluid pulses nor electric currents in the usual sense of the expression. They represent energy of some kind in rapid, but not immeasurably rapid, motion. They pass along the nerves at rates in excess of 300 feet in a second, so that the longest paths in the human body are traversed almost instantaneously.

When the afferent impulses reach the central nervous system the third event in the development of the reflex act occurs. This is localized in the brain or the spinal cord, and we may speak of it as "a central process" without committing ourselves as to its exact character. What we actually observe is that the arrival of the afferent impulses is followed by the appearance of efferent ones. It is not necessary to decide whether these efferent impulses are the same currents which just entered the intricate fabric of the central organ and which have found a path open through its mazes which has led them out again. That is one way of picturing the phenomenon

and it appears to be gaining in favor. According to the older and more familiar view the impulses which come out are not those which went in, but a new set generated by an energetic metabolic process, a *discharge* on the part of cells in the brain or the cord. If this is the true conception the afferent impulses serve to "touch off" irritable nervous elements, much as these elements in their turn may touch off muscle-fibers or gland-cells.

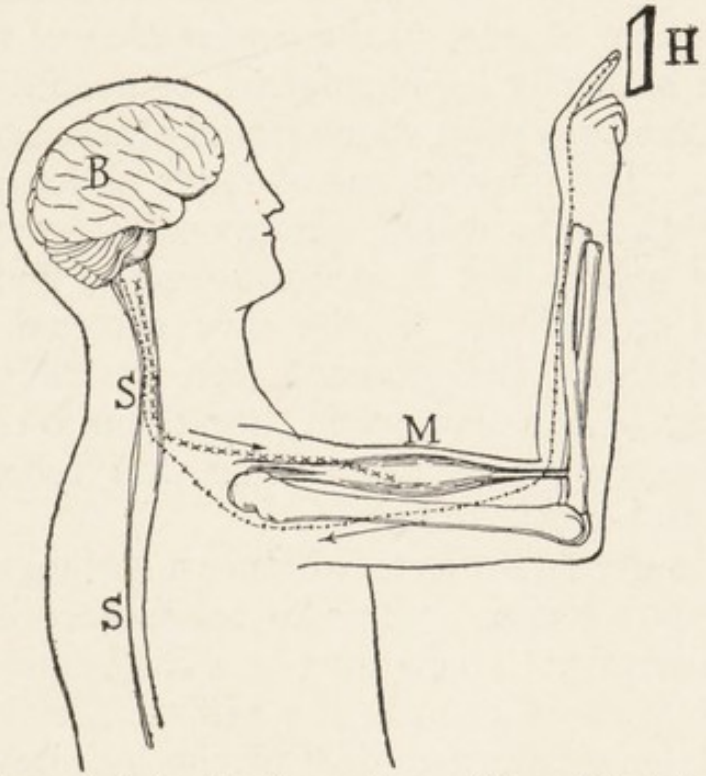


Fig. 6.—The principle of reflex action. The subject touches a hot object (*H*). Afferent nerve-impulses traverse the route marked by dots and dashes to the spinal cord (*S*). Efferent impulses return promptly along the route marked by little crosses to the muscle (*M*), which co-operates with others not shown to withdraw the finger from the stimulating surface. The situation of the co-ordinating center is left undetermined, whether in the brain or the cord.

The fourth step in the evolution of the reflex is the *efferent transmission.* This may be said always to be more voluminous than the afferent flow which went before. Impulses go out by many channels, where but few were engaged in bringing them in. A great characteristic of the "central process" is the spreading of the initial stimulation, so that there seems to be no proportion between the

cause and the response. The number of nerve-fibers which can be excited by the slender proboscis of a mosquito as it pierces the skin of a sleeper must be very small. The reflex movement which results may involve a very large share of his skeletal muscles.

The fifth and final occurrence completing the reflex is the reaction on the part of the muscles or the gland-tissue in which the efferent fibers end. As already indicated, this may be a movement, an outpouring of secretion, or it may have a negative character, the suppression of movements that would naturally have occurred, or possibly the withholding of some secretion which would otherwise have been discharged. The illustrations of reflex action most often chosen are those in which an immediate, even abrupt, response is seen. Yet it is quite easy to find examples of gradual adjustment to the new external condition. Changes of color, the outward sign of changes in the blood-supply of the skin, when they occur on account of warming or cooling of the surface, are reflexes of this prolonged and gentle order.

If there is any doubt as to whether a certain action is to be classed as a reflex, it may be tested according to the foregoing analysis. There must be an assignable stimulus, external at least as regards the central nervous system, there must be an afferent flow of the impulses resulting from the stimulation, a process within the bounds of the central axis, a return flow of impulses in multiplied volume, and the action itself. The more one thinks of the common course of events, the larger the number of actions which he finds he can place in this class. It becomes appropriate to ask what kinds of bodily activity are outside this department. To this question it can be replied that *automatic* actions, such as the beating of the heart, are to be distinguished from reflexes. The nervous system is not required to maintain the heart-beat. There are cases also in which the chemical composition of the blood reaching the centers modifies their behavior and causes them to send out certain impulses. Such cases do not fit our descrip-

tion of the reflex, since in them the stimulation is applied centrally and no afferent nervous mechanism is needed. Our breathing movements are determined to a great extent by such chemical conditions, but it is a fact that reflex disturbances of the breathing are so prevalent that it is often difficult to give just recognition to the two factors.

We are accustomed to contrast sharply actions which are reflex with those which we regard as strictly voluntary or deliberate. The distinction is a convenient one and not generally productive of confusion, but sometimes it becomes quite difficult to draw the line. It may be urged that all our conscious, intentional acts are performed in answer to external conditions which have risen to make an occasion for such new adjustments. So it might be argued that the writing of a word from a copy should be considered a reflex in which the retinal image of the copy furnished the external stimulus. Such images printed upon the retina of the trained pianist by the notes that are before him cause his fingers to drop upon the corresponding keys of the instrument. It may be claimed that this is a reflex action. Without denying the force of such reasoning, we shall do well to restrict the term to the class of responses for which we are quite sure that attention is unnecessary, and usually to those for which we have an inborn or at least a very early developed capacity. When we ask ourselves whether any act is really other than the result of external circumstances affecting an organism with its own past history registered in its structure, we find, almost with a shock, that we are face to face with philosophic and ethical problems, responsibility and free will. Most of us like to believe that a place is to be reserved for a type of action, even though it may be rare and slight, which is not externally caused.

The great difficulty encountered by the beginner in physiology lies in the attempt to realize the inevitable character of reflexes and their structural basis. He finds it hard not to read conscious purpose into acts which so constantly prove advantageous to the individual. When a

frog adroitly catches a fly it is natural to assume a desire and a design on the part of the frog. Scientific analysis nevertheless makes it appear far more probable that the fly is entrapped because the frog is a mechanical device adapted to do this thing over and over again. The eye receives the flitting shadow of the insect, the stimulus excites the brain, and the well-directed fling of the tongue follows. The reflex is not done away with when the part of the brain most likely to stand in relation to consciousness has been destroyed. We have to remember that much of the service of the eye is subconscious, as when it makes us turn aside from obstacles in our path. It is in this way that the eyes of the somnambulist assist in guiding his movements. Conscious attention is no more essential to such a use of the eyes in the waking than in the abnormal sleeping state. In fact, close attention to the balancing of the body is quite as likely to derange as to promote the reflex adjustment.

Central Resistance.—Reflexes are not obtainable with the same ease at all times. We express this fact by saying that there are variations of resistance in the central nervous system. If reflexes are hard to bring about, we say that the resistance is high; if they occur with unusual freedom and seem disproportionate to the exciting stimuli, we say that the resistance is low. Narcotics and anesthetics are said to raise the resistance, and their effect can be gaged by observing the degree of difficulty with which certain reflexes can be produced, or whether, indeed, they can be produced at all. Drugs of an opposite order, the true stimulants, make it easy to call out most reflexes. When one is distinctly under the influence of coffee, a noise may cause one to start, with a sharp contraction of many muscles. The auditory stimulus has an undue effect, and it is natural to assume that the conditions in the brain and cord are uncommonly favorable to the penetration and to the multiplication of nervous impulses. In poisoning by strychnin such an extension of conduction may exist that some trifling cause may precipitate a terrific and exhaust-

ing convulsion. Clearly, then, a certain degree of central resistance is the most favorable condition for the activities of life. Any increase will tend to prevent needed adaptations to external changes, and any great decrease will make the reflex responses exaggerated, disorderly, and ill suited to their object. There is reason to suppose that the more frequently occurring reflexes become progressively easier to induce through a lowering of resistance in their particular pathways. This brings us close to the subject of habit formation.

Our emphasis has been constantly upon the advantage derived by the animal (or by man) from the possession of reflex capacities. When the environment is the accustomed one and the changes taking place are such as the species has often experienced, we find that almost every reflex is obviously beneficial. The reactions are such as maintain bodily equilibrium, secure nutriment, evade or defeat enemies, resist changes of temperature, all making for self-preservation. But it must be noted that an unintelligent mechanism will act amiss in any environment which is sufficiently unlike the accustomed one. It will hardly be claimed that the reflexes exhibited by the novice on first going to sea help him in the struggle for existence. A number of reflex effects can be thought of which can scarcely be of value. Sneezing when going out into bright sunlight is one of these. Hiccups following immoderate laughter do not seem to be of any service, nor does laughter itself when induced by tickling. These instances, which on the whole have little importance, are mentioned simply to enforce the contention that the reflex mechanism, however refined, is not directed in its routine performances by intelligence. Its structure determines its conduct. The finger laid upon hot iron is twitched away before the situation is reasoned out, in fact, before pain is felt. Central connections exist which make the movement sure to occur. If we could rearrange those central connections we might conceive of a luckless subject who would not remove his finger from the stove, but would stand violently coughing while the injury proceeded.

CHAPTER VI

THE ALIMENTARY CANAL

The single-celled animal digests its food within its own protoplasm, sometimes holding it for a while in a temporary cavity filled with fluid, the so-called food vacuole. In such intracellular cavities true digestive secretions containing enzymes are doubtless at work. It is probable that single-celled forms may also secrete enzymes to the exterior and so modify food material which is near-by, but not yet enclosed. This appears to be the case with bacteria when they dissolve the solid gelatin in which they are growing.

Among many-celled animals digestion of this second type, that is, external to the cells, becomes more conspicuous. Their bodies are so formed as to contain spaces in which food may undergo digestion and from which the hydrolyzed products may be absorbed. In the sea-anemone a round opening or mouth leads to a cavity which is very large in proportion to the size of the animal. This primitive alimentary tract has no other opening. In the earthworm, a somewhat more highly developed form, a straight canal in the axis of the body leads from a mouth near the anterior end to an anus at the posterior. However much the alimentary systems of the higher animals may be elaborated, each still represents a more or less winding passage between a mouth through which food is received and a vent or anus for the discharge of residues and excretions. The canal may be greatly lengthened through coiling. Some sections may be widened and others narrowed; the walls in some places may be thick and elsewhere thin. Local differentiation of this kind causes us to distinguish in the human subject the familiar divisions of the

tract, as the esophagus, the stomach, the small and the large intestines. The lengthening of the system, it should be noted, does not merely increase its capacity, but multiplies the surface available for the processes of absorption.

A few anatomic expressions may well be defined at this time. *Anterior*, as we shall use the word, means toward

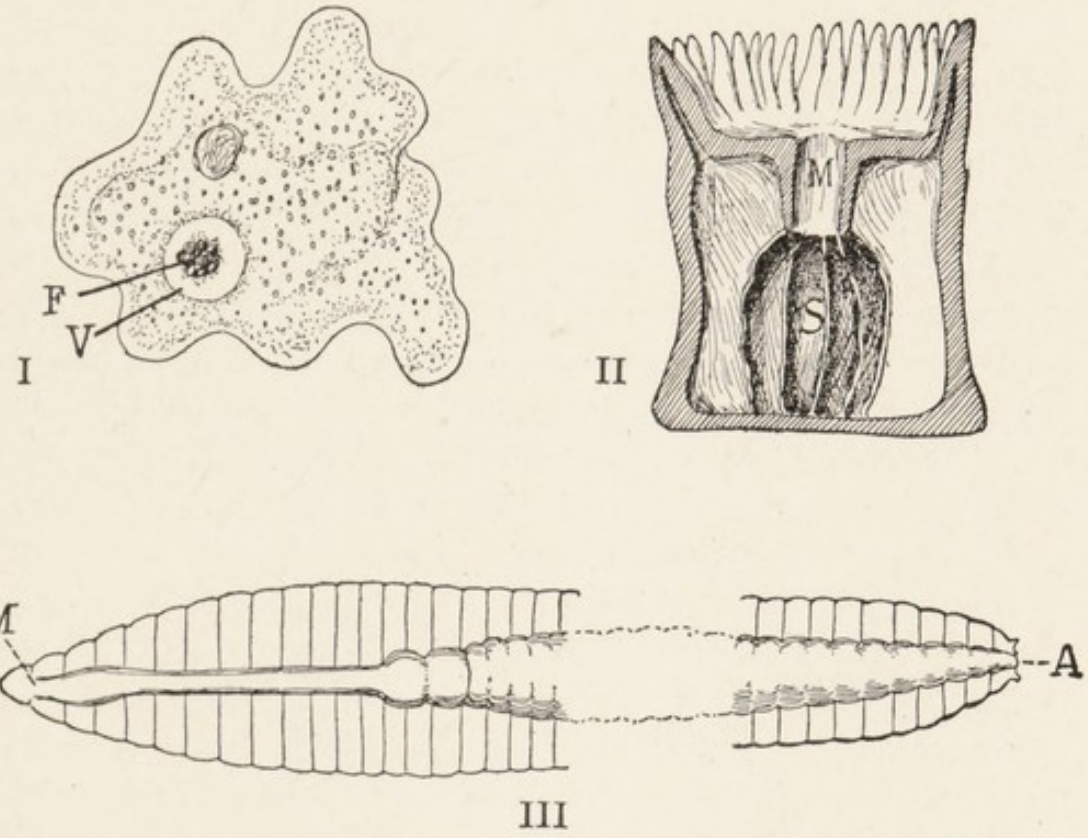


Fig. 7.—I represents a protozoan cell—an ameba—which has enclosed a particle available for food (*F*). The particle occupies the center of a clear space or vacuole (*V*). Undoubtedly it is surrounded by a fluid having digestive powers. II is a diagrammatic section through the familiar sea-anemone. There is a relatively huge digestive cavity (*S*) with a single opening to the exterior (*M*). III suggests the type of alimentary system found in the earthworm and in higher animals. Two openings exist, the mouth (*M*), definitely devoted to the reception of food, and the anus (*A*), used exclusively for the discharge of wastes.

the head; *posterior*, away from the head. *Dorsal* means toward the back; *ventral*, toward the front. Right and left have their ordinary use. (In most figures, the subject being viewed from in front, right and left are reversed.) Reference must often be made to the *body cavities*. These

are the thoracic cavity above the diaphragm and within the cage of the ribs, the abdominal cavity below the diaphragm, and the much smaller pelvic cavity bounded by the bones of the hip girdle. When we speak of these as cavities we do not mean that they contain any air-filled space. They are completely filled by the organs which they enclose plus a small quantity of fluid. Hence they are only potential cavities in life, becoming actual when their contents are removed in course of dissection. The thoracic cavity contains the lungs, nearly surrounding the heart, and is traversed by the esophagus. The abdominal cavity is filled almost entirely by the organs of digestion—the stomach, the small and large intestines, the liver, and the pancreas. The spleen at the left of the stomach is less certainly connected in its functions with the alimentary system. The kidneys lie in the dorsal body wall rather than in the abdomen. In the small pelvic cavity are the urinary bladder, the terminal part of the large intestine, and the reproductive organs.

The *mouth*, the first division of the alimentary canal, scarcely calls for detailed description. Above, a bony partition separates it from the intricate spaces of the nasal passages. At the back this "roof" is prolonged as a mobile, muscular curtain—the soft palate. Below the edge of the soft palate a region is reached which is common to the alimentary and respiratory systems. This segment of the canal is known as the *pharynx*, though the term is extended also to the space behind the soft palate, which is above the normal course of food. The teeth and the tongue with its wonderful muscular development are sufficiently obvious. Ducts from the *salivary glands* open into the mouth. We are rarely conscious of the situation of these openings, though in the dentist's chair we may notice the rapid flow of saliva from one which is opposite the upper molars. This is the place of entrance of the secretion of the *parotid gland*, situated before and below the ear, the gland usually affected in mumps. Under the tongue and within the sweep of the lower jaw-bone there

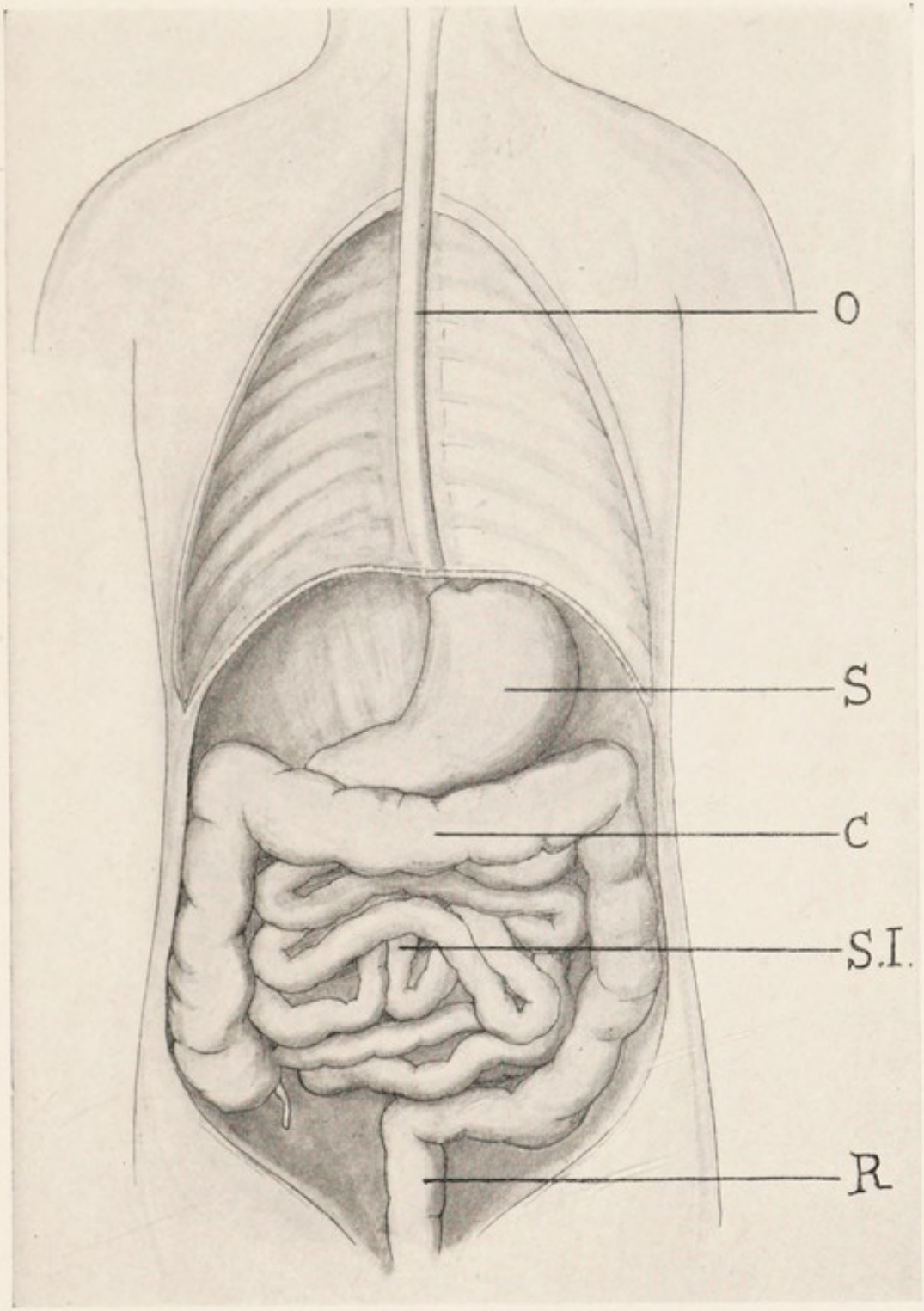


Fig. 8.—The human alimentary canal shown diagrammatically: *O* is the esophagus; *S* is the stomach; *S.I.* suggests the small intestine; *C* is the colon (see Fig. 14); *R* is the rectum. The connection between the stomach and the small intestine occurs behind the transverse colon, which also hides the pancreas.

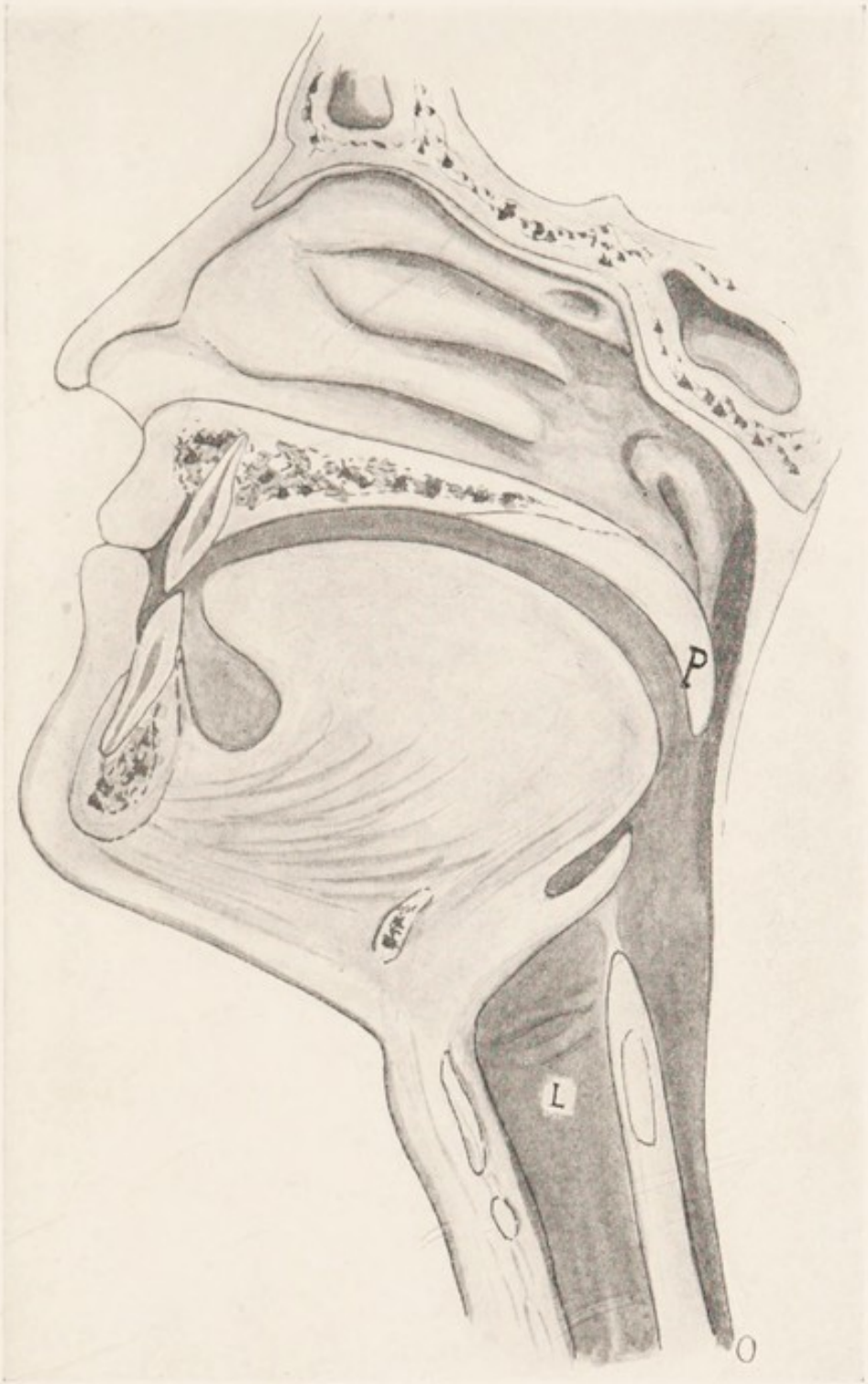


Fig. 9.—Relations of the mouth and nose. This is a vertical section through one nostril, and therefore slightly away from the midplane of the head. The convoluted character of the lateral wall of the nasal cavity is suggested. The connection between the nose and the throat will be seen behind the soft palate (*P*); *L* is placed in the larynx, above which is shown the spur of the epiglottis; *O* indicates the course of the esophagus. It will be noted that the course taken by the food crosses the route of the breathing in the pharynx.

are, on either side, two other glands, the *submaxillary* and the *sublingual*, with ducts opening in the floor of the mouth.

Below the root of the tongue there is a leaf-like projection, the epiglottis, which juts backward as though to guard the entrance to the *larynx*. Through the larynx a way is open to the trachea and the lungs. At this point, therefore, the courses taken by the food and by the breath part company. From here the esophagus extends through the neck and the thorax, lying at first behind the trachea, and lower down passing back of the heart. Perforating the diaphragm slightly to the left of the midline it opens into the stomach.

The stomach is the most expanded part of the alimentary canal. Its position is higher up than is generally assumed, so that it is well within the embrace of the lower ribs on the left side. It has a capacity varying greatly with the degree of its distention and with its variations of tone. After a full meal it may contain more than a quart. The form of the stomach also changes considerably from time to time, but we distinguish a large, rounded portion toward the left and a more conical region tapering off toward the right and joining the small intestine. The opening from the esophagus into the stomach is called the *cardia*, and that from the stomach to the small intestine is the *pylorus*. The pylorus is a trifle to the right of the midline. The upper border from the cardia to the pylorus is the "lesser curvature" of the stomach; a line drawn from the cardia around the convex left-hand side and thence along the lower margin to the pylorus is said to follow the "greater curvature."

Leading away from the pylorus the small intestine describes a short turn, within which is the *pancreas*. This first curve is called the *duodenum*. The remainder of the small intestine is a slender tube about 20 feet in length, coiled upon itself in a confusing manner. Two divisions are recognized, the *jejunum*, continuous with the duodenum and the *ileum*, extending onward to join the large in-

testine. No sharp line of demarcation exists between these sections, but the latter is regarded as constituting somewhat more than half the whole. The ileum finally arrives at a point not far from the crest of the right hip-bone and there enters the large intestine.

The large intestine is so called from its diameter, which is two or three times that of the small. It is quite as often

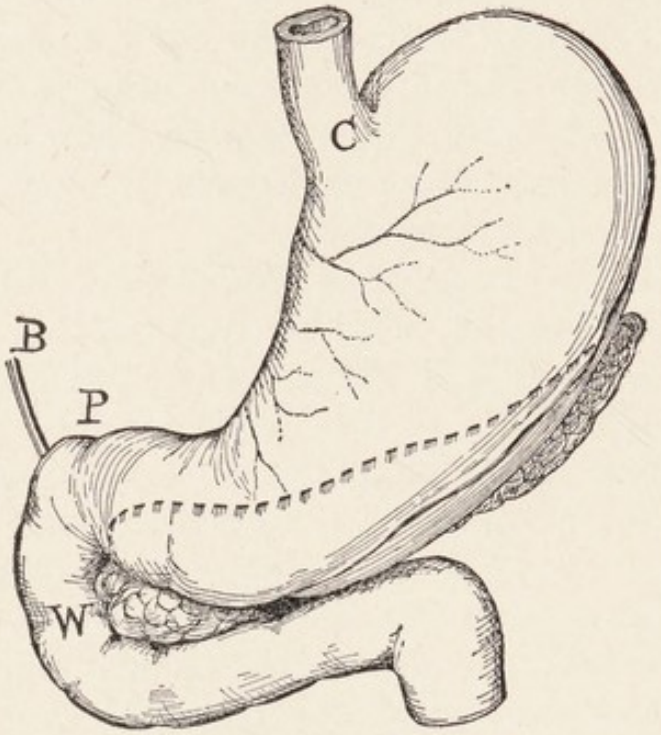


Fig. 10.—The stomach with the pancreas and duodenum: *C* is placed at the cardiac opening of the stomach, while *P* is at the pylorus. A dotted line is used to complete the form of the pancreas, which discharges to the intestine near *W*. The shape of the stomach is of one moderately filled; with further distention the lower border of the organ would sag and the pylorus would cease to be the lowest point. *B* is the common bile-duct, which reaches the intestine behind at the same point at which the pancreas delivers its secretion.

called the *colon*. Beginning with a small rounded pouch, the *cecum*, from which hangs the infamous *appendix vermiformis*, it may be followed upward on the right side of the body to the level of the lower ribs. This part is the ascending colon. From here it bends sharply to the left and crosses the full width of the abdominal cavity. This horizontal segment is known as the transverse colon and lies close to the ventral body wall. Thus it passes in front of the duodenum and is in practical contact with the

stomach. At the left side of the body and near the spleen the descending colon begins. Its course is downward and backward, so that it passes behind the coils of the small intestine. Following the dorsal boundary of the cavity around to the middle line, the colon forms the short, curved region called the sigmoid flexure. The remaining section is the *rectum*, situated directly in front of the lower extremity of the spinal column within the pelvis and terminating at the anus.

Almost everywhere the lining of the alimentary canal is pitted with microscopic glands. Those in the stomach furnish the gastric juice; those in the intestine, the intestinal juice. Besides these small glands and the salivary glands already mentioned, there are the pancreas and the liver, contributing secretions to the cavity of the digestive tract. The pancreas has been said to lie in the turn of the duodenum. It is thus under the pyloric portion of the stomach and behind the transverse colon. Its main duct discharges into the small intestine about 3 inches below the pylorus. A second, but very small, duct may open close by. The liver, which is the largest gland in the body, is fitted to the concave under surface of the diaphragm and is mainly to the right of the midplane. It is cleft into several lobes, from which ducts converge and unite as they approach the duodenum. A single duct is finally formed and it enters the intestine at the same point as the chief pancreatic duct. The arrangement serves to blend the two secretions, and is somewhat suggestive of the devices used with bath-tubs for mingling hot and cold water.

The liver produces bile, and its channel of discharge to the duodenum is accordingly known as the bile-duct. This duct has a side branch which leads to a contractile sac embedded in the under surface of the liver, this reservoir being the gall-bladder. Bile, as it flows down from the liver, may either find its way directly to the intestine or it may turn aside into the gall-bladder. The course taken will depend on the contraction and relaxation of the muscular walls of the ducts. Active contraction of the

gall-bladder when it is full may send a considerable amount of bile at one time into the intestine. The relation of the gall-bladder to the liver is like that of the urinary bladder to the kidneys, at least to the extent that its existence makes possible a continuous production of the secretion with an intermittent emptying. It has been shown, however, that the bile is concentrated and otherwise modified

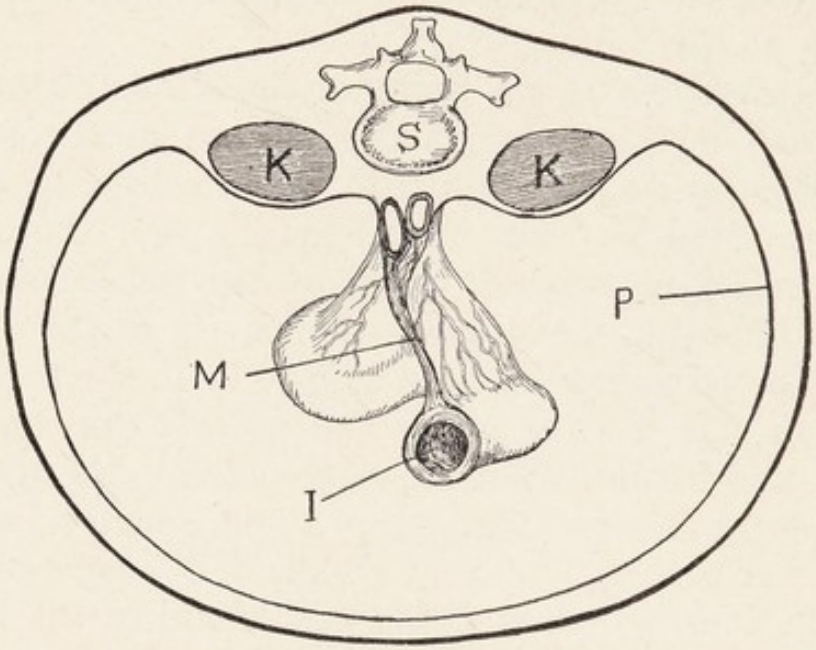


Fig. 11.—This is an entirely schematic section across the human body in the mid-abdominal region: *S* indicates the spine; *K*, the kidneys; *P* is the peritoneum, the lining of the abdominal wall. It is prolonged from the back to form the mesentery (*M*), which extends to and around the loop of intestine (*I*). The large unoccupied space shown does not really exist, for successive portions of the alimentary canal together with other organs completely fill the cavity.

during its stay in the gall-bladder. The urine does not change its character distinctly while it is in storage.

When the abdominal wall of an animal is cut through and laid back from the organs within, one's first impression is that the viscera are lying unattached in the cavity. They are, in fact, not adherent to the ventral or lateral portions of the wall. But if we take a loop of the small intestine at random and attempt to lift it from its resting-place, we find it attached to the middle of the back by a tough, transparent membrane, the *mesentery*. In the

mesentery can be seen blood-vessels, lymphatics, and nerves. This suspending sheet thus serves not merely for mechanical support, but also establishes connection between the intestine and the circulatory and nervous systems. The student is apt to find it hard to visualize the mesentery in its actual form; he is to imagine a membrane which at one edge extends to the entire length of the small intestine and to much of the large, while its other edge is condensed to be inserted into the space of a few inches before the spinal column. What results from these conditions has been described as "a ruffle or flounce." Although the mesentery is thin it is really a doubled sheet enveloping the intestine. This will be made clear by the diagram, which also shows how the mesentery is continuous with the exquisitely smooth, lustrous lining of the abdominal cavity, to which is given the name of *peritoneum*. Dissection of a small animal will give a comprehension of these anatomic facts which can scarcely be gained by reading.

The stomach has a supporting membrane attached to it along its lesser curvature and uniting it to the liver, which is, in turn, anchored to the dorsal body wall. This membrane is, in effect, a mesentery for the stomach, but is called the lesser omentum. An extension of similar tissue hangs from the greater curvature like an apron over the intestinal coils and is called the great omentum. It may become a ponderous appendage from the fat which it sometimes accumulates. The continuation of the mesentery over the external surface of the intestine and the identical covering of the stomach form for these organs what is spoken of as their *serous coat*.

The Finer Structure of the Alimentary Organs.—We have said that the internal surface of the stomach and of both intestines is provided with glands. The inner layer of the wall of the canal in which these glands occur is called the mucous coat or mucous membrane. This is in reference to the fact that its exposed cells produce the slimy substance, mucus, more familiarly associated with nasal

discharges. It probably acts as a lubricant in the digestive tract and also protects the lining cells from harsh contacts, both physical and chemical. The mucous membrane is depressed to form the recesses of the glands, and in the small intestine is raised into the microscopic prominences referred to as *villi*. Underlying it blood-vessels and nerve-fibers run thickly.

Between the mucous layer and the serous coat on the outside of the intestine there is a development of muscle of the order described in a previous chapter as characteristic of most internal organs, that is to say, slow acting, more or less automatic, and much given to tone changes. In the small intestine there are two distinct muscular coats: the inner and thicker has its fibers at right angles to the axis of the canal, while the outer has them set parallel to this axis. The inner coat is hence spoken of as circular and the outer as longitudinal. There is no doubt of the superior prominence of the circular coat in the production of intestinal movements. In the stomach the muscular organization is less simple and there are oblique elements in addition to those which can be classed as circular and longitudinal. The colon has the circular coat, but instead of a complete covering of longitudinal muscle it has three bands of contractile tissue extending along its wall.

At any point along the course of the intestine temporary closure may be effected by the contraction of the circular muscle. But there are certain places where such closure is far more frequent or, indeed, the usual condition. Where the esophagus joins the stomach an irritable band, the cardiac sphincter, is much of the time firmly contracted. There is, similarly, a pyloric sphincter guarding the opening between the stomach and the duodenum. Where the ileum enters the cecum a valve exists which is adapted to prevent the reflux of material from the colon to the small intestine. This, the ileocecal valve, is probably reinforced in its mechanical action by muscular support. Finally, the short anal canal is closed by an inner sphincter which is essentially a thickening of its own wall, and an external one composed of skeletal muscle.

CHAPTER VII

THE MOUTH—SWALLOWING; SALIVARY DIGESTION

Mastication.—The hygienic importance of thorough mastication is undoubted, but there is little occasion for any extended analysis of a process so obvious. It is to be observed that the lower jaw does not have merely an up-and-down movement, but that it glides backward and forward and has some lateral play at the same time. The teeth, therefore, do not simply chop the food, but rub and grind it. The direct pressure which sound teeth can apply is incredible. It may amount to 270 pounds.[1] Thus the morsel on which this force is brought to bear is dealt with more harshly than if a barrel of flour were set upon it! In the work of mechanical reduction a larger part is borne by the tongue than is commonly recognized. The little member seems to be everywhere at once, thrusting food between the teeth, withdrawing it again, bruising and rasping it against the roof of the mouth. While this action is going on an intimate mixture with the saliva is accomplished. We must now proceed to a discussion of this the first of the digestive secretions.

Mention has been made of the three pairs of glands which supply the saliva. Their united product is estimated to reach an amount of about 3 pints a day, equalling the volume of the urine. If one finds it hard to credit such a statement, attention may be called to the copious character of the flow which is noted when one is interrupted at the moment of taking food. There is little secretion apart

[1] Cannon, "The Mechanical Factors in Digestion," Longmans, New York, 1911.

from eating unless it is excited by chewing sundry things. At mealtime a large part of what is swallowed is saliva, and the proportion must be greatly raised by the practice of prolonged mastication, so-called Fletcherism. The formation of saliva is to be regarded as a reflex in which the primary stimulation is furnished by food in the mouth acting upon the endings of nerves excitable by its chemical ingredients and by its temperature more than by its mere contact. We have to do with something more than the typical reflex, however, because it is a familiar fact that the appeal to consciousness has much influence upon the flow of saliva. The "watering of the mouth" at the approach of acceptable food is a hard phenomenon to classify. It is a reflex, but it is one which would not occur in an unconscious subject. For such actions the term *psychoreflex* is often used.

The saliva is a bland fluid which one would hardly suppose to be endowed with active powers of digestion. In some animals it does not have any apparent chemical action. Still, it has valuable properties which we shall do well to recognize. Whether it is a digestive juice or not, its physical effect is useful in mastication, since it softens the food, makes it cohere into the pellets which are prepared for swallowing, and later lubricates their transit to the stomach. Moreover, it has a defensive use, protecting the mouth from injury when food or fluid is taken too hot or when some corrosive liquid calls for dilution. As it issues fresh from the glands it is slightly alkaline in reaction. If it stagnates for a long time in the by-places of the mouth, as happens during sleep, and if it contains at the same time traces of carbohydrate food in solution, bacterial fermentation may make it acid and the effect upon the teeth may be injurious. The value of an alkaline mouth-wash, like milk of magnesia, used at bedtime is evident.

Human saliva contains various salts. Attention need be called only to its lime compounds, which are always deposited more or less upon the back surfaces of the teeth, a process which reminds one of the formation of stalactites

and stalagmites in caverns. The hard crust that results is the tartar. It is not very unlike the original substance of the teeth in its chemical composition, and its occurrence might seem to indicate a mode of making good the wearing away of the teeth. Unfortunately we cannot regard it in this favorable light, for the lime salts are always contaminated with food particles and bacteria. The deposit should be removed by the dentist at regular intervals.

The three glands furnish slightly different varieties of saliva. *Mucin*, the essential compound in mucus, is present in the secretion of the two lower glands and not in that of the parotid. It gives to the saliva from the submaxillary and sublingual glands a ropy, mucilaginous character, which, of course, becomes more apparent when evaporation has concentrated the solution. This is illustrated when the mouth is dried by rapid breathing during exercise and becomes furred with the residue of salivary mucin. This constituent of the saliva probably makes it superior to water as an agent for molding the food into pellets. The most interesting property of the secretion, its power to hydrolyze starch, may be discussed to more advantage after we have followed the food to the stomach. Clearly, there is not time enough for much digestive change in the mouth of a person of average habits.

Swallowing.—The transfer to the stomach is a more complex matter than is likely to be realized. It involves an interruption of breathing and the protection of the nasal passages and the larynx against the intrusion of food. The first purpose is effected by the retraction of the soft palate against the back of the pharynx. The second is accomplished by the drawing forward of the larynx toward the chin, a movement which can be plainly felt. By it the larynx is tucked under the root of the tongue. The epiglottis was long supposed to bend down upon the larynx as a shield to ward off the food from this sensitive organ. Observation with the *x*-ray is said to show that it actually descends *after* the material has passed rather than in advance of it. The same motion which pulls forward

the larynx serves to widen the upper part of the esophagus, which is not at other times appreciably open. With the parts in this position the bolus of food is crowded back from its original seat upon the tongue and urged through the pharynx by the successive contraction of the bands of muscle which surround it. As soon as it is fairly within the esophagus the soft palate is lowered, the larynx is allowed to emerge from its covert, and the breathing can be resumed. Such quick and well-ordered adjustments give evidence of co-ordinated reflex action, the contact of

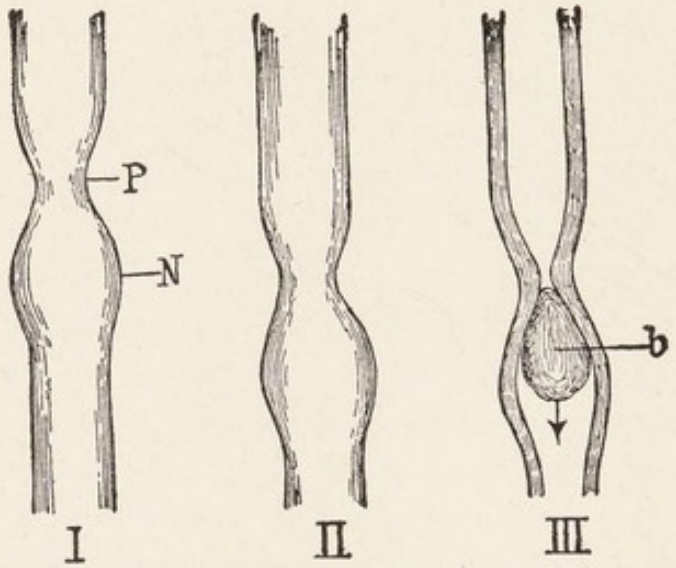


Fig. 12.—An exaggerated representation of peristalsis. I and II are successive views of the same portion of the alimentary tube: *P* is the zone of contraction shifting downward and always preceded by the zone of unusual relaxation (*N*). III is an imaginary section through II, showing the food bolus (*b*) slipping along in advance of the contracting region, its advance being facilitated by the relaxation below.

the food morsel with one spot after another furnishing the requisite stimuli. We cannot go through the series of movements unless there is at least a little saliva to be swallowed, and we cannot arrest the march of events when it is once begun.

The contractile tissue in the upper part of the esophagus is of the skeletal variety. Lower down this gives place to typical visceral muscle. Hence it is not strange to find that the advance of the bolus becomes progressively slower as it descends. The movement which is here taking place

is what is known as a *peristalsis*, and it is highly important that its principle should be understood. The most obvious feature is a ring of contraction setting in above the enclosed pellet, causing it to slide onward, and following it down by involving in succession each level of the tube. The mechanical application can be simply illustrated by propelling a glass bead through a soft-rubber tube by pinching repeatedly behind it with thumb and finger. A strict analysis of what occurs in the esophagus obliges us to recognize that the process is not so simple as it first appears. There seem to be two phases in what is called the peristaltic wave. The eye detects chiefly the traveling contraction, but this is apparently preceded by a zone of unusual relaxation, a region of inhibition.

The peristaltic wave which is necessary for the propulsion of solid food does not seem to be required to send liquid to the stomach. A swallow of water is shot swiftly from the mouth to the cardiac sphincter and arrives there distinctly in advance of the plodding peristalsis. When one drinks a glass of water, the swallows following in rapid succession, a single peristaltic wave ends the series. We shall find that the small intestine exhibits movements which are approximately the same in principle as those of the esophagus, but far slower and usually less energetic.

Sensibility of the Esophagus.—It may be laid down as a general principle that the sensory equipment of the alimentary tract is most complete for the mouth and less and less developed as the course of the canal is followed. The lining of the mouth is manifestly sensitive to contact, heat, and cold, besides possessing the particular sense organs for taste. When any point in the mouth is stimulated, we can localize it with great accuracy. Interesting observations, which have been made upon the esophagus, show that its mucous membrane is quite responsive to heat and cold, but indifferent to pressure unless it is of such a degree as to stretch the underlying muscular coat.[1]

[1] Carlson and Braafladt, Amer. Jour. Phys., 1915, xxxvi, 153; Boring, Amer. Jour. Psy., 1915, xxvi, 1.

Salivary Digestion.—Within the stomach the accumulated food with a large admixture of saliva lies for some time with little motion. Here then salivary digestion must take place. The statement has been made that in some animals the saliva has only mechanical and protective functions. More frequently, however, it has the power to hydrolyze starch, forming malt-sugar as the chief end-product. This seems to justify the assumption that an enzyme is present, and it is variously named *ptyalin, salivary amylase,* or *salivary diastase.* Such an enzyme probably plays an important part in the digestive processes of ruminants, animals which chew the cud. Human saliva acts upon cooked starch with surprising energy. A simple demonstration of the fact may be had by holding a bread-crumb in the mouth longer than is habitual, when it will gradually develop a mildly sweet taste.

The prevailing opinion in regard to the amount of digestion accomplished by the saliva in man has undergone a change during the last few years. It is allowed a larger place than was formerly granted to it. The enzyme is extremely sensitive to acid. Inasmuch as the gastric juice is decidedly acid, it used to be claimed that salivary digestion could not proceed in the stomach. But it has come to be recognized that when a large mass of food is introduced into the stomach within a short time the gastric juice penetrates it rather slowly. A few minutes after the completion of a meal we may picture the stomach-contents as being acidified near the surface, the acid slowly making its way inward, but having a neutral or even alkaline central portion. Salivary digestion will be continued in the steadily diminishing region not yet reached by the acid, and will cease only when the gastric secretion from one wall of the stomach meets that from the other. Any rotation of the contents would probably bring about an earlier distribution of the acid and arrest of starch digestion. No such rotation seems normally to occur. A factor which operates to postpone the destruction of ptyalin is the power of the proteins of the diet to engage hydrochloric acid in com-

bination. Since proteins are almost always present, the gastric glands must secrete acid enough to satisfy their capacity before there can be the excess of strictly free acid which will put an end to salivary digestion.

If the mixed food is quite acid at the outset, it is hard to see how there can be any hydrolysis of starch brought about by the saliva. Yet we constantly eat acid fruits before our breakfast cereal and notice no ill effects. Starch which escapes digestion at this stage is destined to be acted upon by the pancreatic juice, and the final result may be entirely satisfactory. Still it is reasonable to assume that the greater the work done by the saliva, the lighter will be the task remaining for the other secretions and the greater the probability of its complete accomplishment. The power of saliva to convert raw starch to sugar is almost incomparably smaller than its capacity to digest starch which has been cooked. Raw starch exists in very dense grains which have to be dissolved from the surface inward. Cooking, especially boiling, utterly destroys these grains, and permits a reaction between the enzyme and the separated molecules of the carbohydrate.

The change from starch to sugar seems not to be effected by a single reaction, but by stages. Physiologic chemists have studied extensively the numerous intermediate bodies which have a fugitive existence in the process. Most of these are covered by the term *dextrins*. It is sufficient for our present purpose to regard them as carbohydrates, simpler in their molecular structure than the original starch, but complex as compared with the familiar sugars. We have said that the chief product of salivary hydrolysis is malt-sugar or *maltose*. This is one of several sugars classed as disaccharids. By various means it can be hydrolyzed further to form *dextrose*, a sugar of the simplest type, and one which is ready to be absorbed and to minister to the living tissues. Some dextrose is said to be formed in prolonged salivary digestion, but the cleavage lags when the maltose stage has been reached.

CHAPTER VIII

THE MOVEMENTS OF THE STOMACH

It will be recalled (Chapter VI) that the stomach consists of a main rounded portion from which a much smaller conical segment extends to the right to join the duodenum at the pylorus. The larger part is called the *fundus*, the tapering region is the *antrum*. The muscular coats of the antrum are somewhat thicker than those of the fundus and show an especially conspicuous development of the circular elements. There is no such contrast between the two parts of the human stomach as between the thin-walled crop and massive gizzard of the bird, but there is a faint suggestion of an analogous difference. The fundus is, indeed, primarily a place for the storage of food; the antrum, while not a crushing mechanism, has distinctly greater motor properties.

The antrum is considered to be set off from the fundus by the so-called *transverse band*. This is an irritable ring of the circular muscle which is often contracted enough to indent the outline of the stomach at this point, and which may occasionally create a temporary division of the gastric cavity into two parts. It has been called the sphincter of the antrum, but it cannot fairly be compared with the cardiac and the pyloric sphincters, since these are habitually closed, while closure at the transverse band is rare.

Regulation of the Cardiac Sphincter.—Food and drink entering the stomach pass the cardiac sphincter. The guardian muscle is usually more or less contracted. It relaxes upon the arrival of the peristaltic wave in the esophagus. If it is recalled that the peristalsis consists of a wave of inhibition running before a contraction, it is

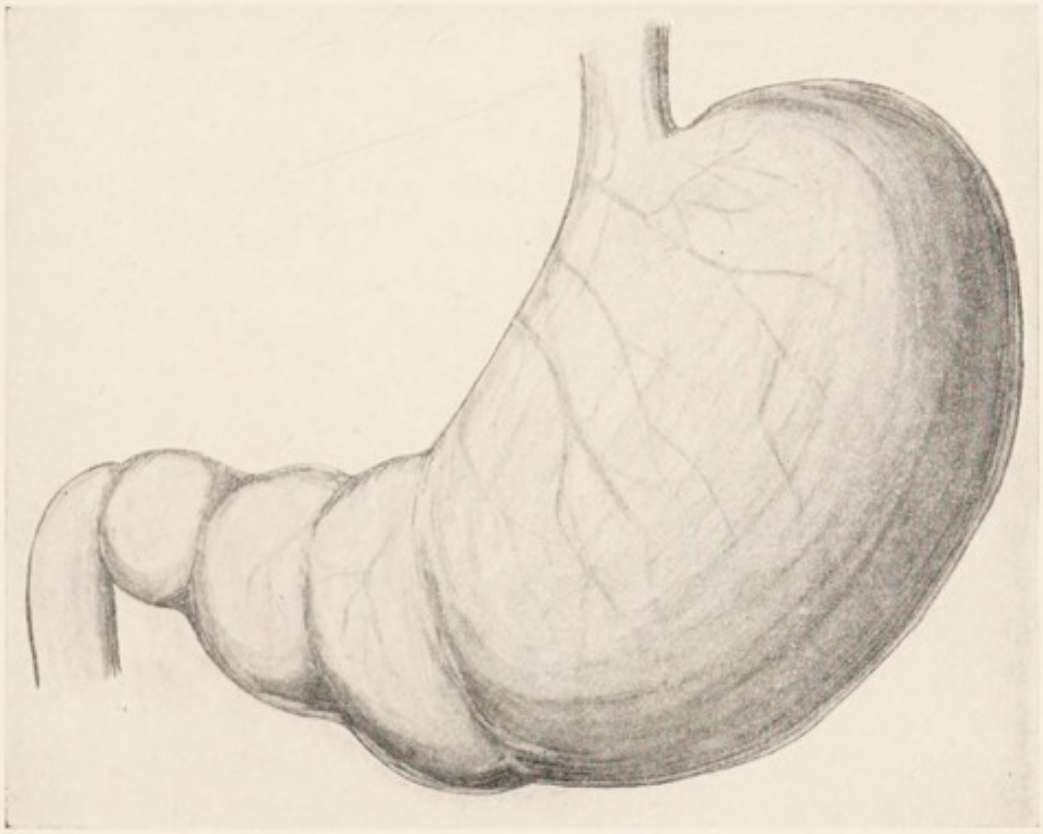


Fig. 13.—To suggest the probable appearance of the distended and active human stomach. Three marked waves of contraction are seen in the antral region. These are to be conceived of as passing onward toward the pylorus.

easy to see how the cardia may be opened at the moment when its muscular walls fall under the influence of the phase of relaxation. Closure will follow immediately, as the second or positive part of the peristalsis involves the sphincter. Attention has been called to the fact that liquids may outrun a pursuing peristalsis and arrive several seconds in advance of it at the cardiac opening. Under such circumstances it is said that the fluid remains at the bottom of the esophagus until overtaken by the wave, when the relaxation occurs which permits it to pass into the stomach. A person drinking with ill-advised haste may have the disagreeable experience of filling the esophagus enough to produce a painful distention. Relief comes abruptly when the peristalsis has made its way to the cardiac sphincter and secured an entrance for the liquid.

While this has been the generally accepted description of the facts, it has been shown recently that the cardia is not always so firmly contracted. Observations by *x*-ray methods, to be described presently, have shown that for some time after a meal there may be a reflux from the stomach of a cat into the esophagus. Each escape of food evokes a local peristaltic wave which returns it to the stomach. Such an incident does not entail any movement of the throat muscles and is probably subconscious. As the period of digestion continues the sphincter becomes more tightly set and no longer allows any such return of stomach-contents. The increased tension has a simple explanation, which, like many another point about the stomach, we owe to W. B. Cannon. He has shown that the tension is developed in response to the rise of acidity in the liquid just within the cardia. Since the acid appears normally after each filling of the stomach, we have here an automatic provision for the establishment of the requisite guard over this opening. The influence of the nervous system seems capable of nullifying the local effect of acid, since the sphincter may be relaxed to permit vomiting at times when the gastric contents are excessively acid.

The Fundus.—An important service of the stomach is to store food in relatively large quantities at mealtimes and to deliver it gradually to the intestine. A person who has been deprived of the stomach, or of most of it, by surgery is made aware of this when he finds it impossible to eat "a square meal," and is compelled to take small portions of food at short intervals. He is then serving his intestines somewhat as they are normally treated by the stomach. Storage is not the sole function of the stomach, but we do well to emphasize it. The fundus accommodates itself to its contents by tone changes, relaxing when food is being swallowed and afterward exerting a steady, moderate pressure which insures the filling of the antrum after every discharge at the pylorus. A lack of this tonic reaction may be a cause of serious disorders.

The earlier writers often claimed that they could observe a definite and regular overturning of the contents of the fundus. In the light of more recent observations this does not seem to be usual. A German investigator fed to a rat three courses of food of contrasted colors. The animal was then killed and frozen. A section made through the hardened mass within the stomach showed distinct stratification. The food first taken was in the antrum and the lower part of the fundus, the second instalment was above the first, and the third was just under the cardia. It seems hardly probable that entirely liquid food could remain thus stratified when one considers the extent to which the stomach is subjected to the influence of bodily movements.

Hunger.—It has been established that there is a connection between certain contractions of the stomach—particularly of the fundus—and the sensation of hunger. The experimenters who have demonstrated this fact point out that we must distinguish between hunger and appetite in all discussions of this kind. Hunger, as they intend to have the word understood, is a recurring pang readily referred to the gastric region. It is experienced alike by adults and infants, by human beings and

animals. Appetite, on the other hand, depends on psychologic factors (recollections of favorite foods, etc.).

It will be worth while to recount the ingenious experiment by which it was made clear that the intermittent hunger sensation corresponds with a motor process among the contractile elements of the stomach. Washburn,[1] working under the direction of Cannon, devised a way to record the contractions of his own stomach. For this purpose a stomach-tube, bearing a collapsed balloon at the lower end, was swallowed by the self-sacrificing investigator. The balloon could then be inflated, and the tube brought into connection with a gauge consisting of a water column carrying a float and writing-point. Thus, if the stomach squeezed the balloon the tracing showed an elevation; as the stomach relaxed the curve declined.

Washburn fasted until he could rely upon the occurrence of hunger pangs in spite of the discomfort to which he was subjected. The revolving drum which received the record was out of his sight. By pressing an electric key he could cause a mark to be made upon it at any time. He pressed this key whenever he experienced the sensation of hunger. The tracing showed that strong periodic contractions of the stomach coincided with the recorded gnawings. This result has been confirmed by Carlson,[2] who has made similar experiments upon a man with an opening through the body wall to the interior of the stomach.

It was observed in Washburn's experiments and in those of Carlson that the hunger contractions ceased when food was tasted and chewed. This indicates a reflex inhibition of the gastric musculature. It had already been noticed by Cannon that the tone of the fundus is temporarily lowered whenever food is swallowed. This constitutes what is called the "receptive relaxation," and it has an evident value since it facilitates the transfer of material from the esophagus to the stomach.

We are told that when a long fast is undertaken the

[1] American Journal of Physiology, 1912, xxx, 309.

[2] "The Control of Hunger in Health and Disease," University of Chicago Press, Chicago, 1916.

characteristic hunger pangs are not experienced after two or three days. It is probably true that insufficient feeding is more distressing than downright fasting. Such sufferings as those endured by the Greeley party at Cape Sabine afford a confirmation of this opinion.

Thirst.—When the body loses water at a rate which threatens to reduce the normal percentage in the system thirst is experienced and steadily gains in urgency. It may become one of the most grievous distresses known to man. The central fact in this condition seems to be the dryness of the mouth and throat. This is to be referred to a suspension of salivary secretion. The organism, deprived of its normal supply of water, is conserving its store so far as possible.[1]

Certain statements have previously been made concerning the sensibility of the esophagus to common forms of stimuli. Carlson and others have reported corresponding facts with reference to the mucosa of the stomach. They find that it is relatively difficult to evoke sensations from this surface. Pressure, to be effective, must be of such intensity that its transmission to deeper tissues has to be assumed. Heat and cold are productive of recognizable sensory impressions, but it has long been an unsettled question whether the mucous membrane itself is responsible for the effect or whether this depends on temperature changes in the skin. Carlson's subject gives such a prompt reaction when a small piece of ice is pressed against the lining of his stomach that the investigator believes there must be a true local sensitiveness to this kind of stimulation.[2]

***x*-Ray Studies of the Stomach.**—While much can be learned of the behavior of the stomach through experiments involving its exposure by surgical procedures, the ideal method is clearly one which leaves the animal in its normal condition. Such a method became available when

[1] Cannon, Proceedings of the Royal Society, B, xc, 1918, 283.

[2] See also Hertz, "The Sensibility of the Alimentary Canal," Oxford University Press, 1911.

the *x*-ray was first turned to account to observe visceral movements. The image of any part of the body projected by means of the *x*-ray shows the bones in clear contrast with the softer parts, but scarcely outlines the organs. If, however, any harmless substance opaque to the *x*-ray is introduced into the contents of the alimentary canal, it becomes possible to recognize the situation of this substance so long as it remains sufficiently concentrated. More than this, if the cavity is well filled its outline is, of course, identical with that of the included material. The *x*-ray picture will then show the changing contour of the organ in silhouette. The compounds most used to secure opacity to the *x*-ray are the salts of bismuth, generally the subnitrate or the subcarbonate.

The most numerous experiments of this sort are those of Cannon, and the cat has been the favorite subject. When the animal has had a full meal of bread-crumbs and milk with the bismuth salt evenly mixed in the mass the *x*-ray shows the entire form of the stomach. The fundus has an even outline and preserves it unchanged from hour to hour, except that a very gradual contraction takes place. The antrum is traversed by deep but slow-moving peristaltic waves, which originate near the transverse band and pass to the pylorus. The tendency of such waves must be to force successive portions of the food into the intestine, but in the great majority of cases the waves bear down upon a tightly closed pyloric sphincter. The only possible result is then an eddying movement, the contents advancing only to rebound from what is, for the time, a blind pouch. This favors the reduction of the larger morsels and helps to secure at length the formation of the smooth, creamy "chyme." But it is probable that most people have an exaggerated notion of the mechanical powers of the stomach.

The waves which pass over the antrum arise in the cat with strange regularity at intervals of ten seconds. Each wave takes about half a minute to make its way to the pylorus, so there are commonly three creases to be seen,

all shifting with a motion of clock-like slowness toward the outlet. During the prolonged period required for the emptying of the stomach of the cat—eight hours or more—it is evident that the total number of the waves may be over two thousand. When the pyloric sphincter momentarily relaxes, under influences to be discussed presently, the peristalsis of the antrum naturally drives more or less of its contents into the duodenum.

Nervous Control of the Gastric Movements.—Muscular elements of the order found in the stomach have been said to have an automatic property. We have insisted, however, that this fact does not exclude the influence of the central nervous system. There is abundant evidence so far as the stomach is concerned that the musculature of the organ is played upon by efferent impulses. If it is separated from the central nervous system many of its reactions take place in a nearly normal manner, but we cannot assume that its adjustments are as well timed and decisive as they were before. Laboratory trials show that the impulses which are sent to the stomach may either accentuate or abate its spontaneous movements. In other words, they may either excite or inhibit the contractile elements.

Of the two types of nervous control, the inhibitory seems to be of particular significance. Complete arrest of the peristalsis of the antrum may be brought about. This happens in the cat when the animal is enraged or terrified, and, indeed, when it seems merely to be restless. Cannon has again and again seen the peristaltic notches fading away from the *x*-ray profile of the antrum when the animal has wearied of being kept under restraint, and is manifesting its feeling by switching its tail and struggling. He has seen the regular activity resumed when the cat has been pacified. Similar facts have been demonstrated for the rabbit. Since we generally believe that the higher the grade of an animal's development, the more extensive the command of the nervous system over its organs, we have every reason to think that unpleasant emotions may be

accompanied in man also by inhibition of the gastric movements. We shall have occasion to enlarge upon this matter in connection with the Hygiene of Nutrition.

The Pyloric Sphincter.—The regulation of the escape of the stomach-contents to the intestine has long been a subject of interest. It was in 1833 that William Beaumont published his observations upon the stomach of Alexis St. Martin, a young Canadian trapper, who had suffered a gunshot wound in the left side, in consequence of which he had a permanent gastric fistula.[1] The impression which went abroad from this celebrated case has seemed to convey to the less scientific writers the idea that the pylorus has a power almost akin to intelligent inspection whereby it permits the passage of certain portions of the chyme and refuses egress to other portions. This notion recalls amusingly the teaching of Van Helmont, in the seventeenth century, that the soul of man resides in the pylorus. It cannot be said that all the conditions affecting the discharge from the stomach are entirely clear, but much progress has been made in this direction.

The sphincter is influenced both by the physical consistency and by the chemical reaction of the gastric contents. The contact of coarse, angular particles with the adjacent mucous membrane seems to reinforce its contraction, so that such material tends to be kept longer in the stomach. A more important factor with this sphincter, as with the cardiac, is the acidity of the chyme. It was stated above that when the stomach-contents becomes distinctly acidified, the tone of the cardiac sphincter is increased. The acid in this case is acting upon the lining *below* the irritable ring. Comparison of the two sphincters shows it to be a principle applicable to both—that acid acting immediately above favors their relaxation, while acid below causes them to tighten. If this is the main factor in regulating the

[1] See Osler, "An Alabama Student and Other Essays," Oxford University Press, American Branch, New York, 1909, 159–188. Beaumont's classic record of observations, introduced by Osler's essay, has been reprinted (XIIIth International Physiological Congress, 1929).

pylorus, the first opening will occur when the acidity in the antrum has reached a certain point. The next peristaltic wave will transfer a little chyme to the duodenum. At this instant there will be acid material both above and below the sphincter. The action from below appears to predominate, so that closure will be established and maintained until the acid in the duodenum is either neutralized or removed somewhat from the pylorus. When the stimulation from below is no longer effective the acid above will cause a second gaping of the sphincter, followed as before by prompt and decisive contraction. A more efficient mechanism to insure gradual delivery to the intestine without distending it locally can scarcely be conceived.[1] When the latest portions of a meal are leaving the stomach, the first which went out may have reached the colon, and intermediate fractions may be undergoing digestion in numerous loops of the intervening small intestine.

Our meals are usually of a mixed character, including proteins, fats, and carbohydrates. For purposes of experiment single food-stuffs may be fed to an animal and the rate of departure from the stomach noted for each. The *x*-ray has been employed for this purpose. Carbohydrates have a striking tendency to escape rapidly to the intestine. The discharge of proteins and of fats is relatively much delayed. The difference observed may be referred to the following facts. Proteins combine with acid and so delay the establishment of effective acidity at the pylorus. Carbohydrates do not have this power. Fats do not unite with the gastric acid, but they lower the rate of its production and hence retard the rate of discharge to the intestine. There is an increasing recognition of the possibility that after the stomach has been emptied some reflux into it from the intestine may occur.

Vomiting.—The occasional expulsion of the stomach-contents through the cardia and esophagus is accomplished

[1] Recent studies dispose us to give a larger recognition to regulatory factors other than acidity. An excellent summary is by Murlin, Journal of Nutrition, ii, 1930, 311.

as the result of a reflex movement in which the chief muscles involved are not the coats of the stomach, but the contractile tissue of the diaphragm and abdominal wall. When these contract simultaneously a high pressure is thrown upon the stomach. Such a pressure may accompany the act of straining or bracing the body for lifting, but does not ordinarily result in vomiting, it would appear, because of the resistance offered by the cardiac sphincter. In the crisis of nausea, however, convulsive movements of this kind take place with inhibition of the sphincter. With the passage open, each application of intense pressure to the stomach may drive a portion of its contents to the exterior. The palate meanwhile has assumed the same position as for swallowing; the larynx is drawn forward and is shielded by the root of the tongue, which is depressed and grooved. At every descent of the diaphragm the capacity of the thorax is increased, and as no air is permitted to enter the lungs the esophagus is dilated.

During the act of vomiting the fundus is said to contract steadily upon its diminishing contents. This is not a movement powerful enough to secure the emptying of the stomach, but adapts it to be gripped effectively by the muscles of the body wall. The transverse band is at the same time strongly contracted and the antrum has a very small volume. The pyloric sphincter is said to be closed, but it is a familiar fact that bile from the duodenum may be pressed backward into the stomach under the stress of violent vomiting. Profuse salivation precedes and accompanies the act. Such a reflex has a manifest value when it serves to remove from the stomach material which might prove poisonous. It occurs, however, under many circumstances when it seems not to have any advantageous result. Its apparent uselessness in seasickness has already been alluded to. It appears equally illogical when, in pregnancy, it is excited by irritation of the pelvic nerves.

A valuable aid to teaching in this connection is afforded by the "Class Room Films dealing with Physiology" prepared by the Eastman Teaching Films, Inc., of Rochester, N. Y. A complete list may be secured from The National Health Council, 370 Seventh Avenue, New York, N. Y.

CHAPTER IX

GASTRIC SECRETION AND DIGESTION

It was in the eighteenth century that the chemical factors in digestion were first clearly separated from the mechanical. The accounts which have been preserved of the experiments of Réaumur (1752) and of Spallanzani (1777) are of extraordinary interest. An entertaining summary is to be found in Foster's "Lectures on the History of Physiology," Chapter VIII. These ingenious investigators were the first to show that digestive changes may be caused to take place outside the body and in the absence of any mechanical process whatever. They obtained small quantities of gastric juice from various animals, mixed it with food in flasks and test-tubes, and watched for signs of alteration. Spallanzani, in particular, succeeded in bringing about considerable solution of his samples.

From that time to the present studies of digestion have continued. Where the pioneers were forced to be content with observing the dissolving of solid food, their successors are drawing inferences regarding the transformations of unseen molecules. A deeper insight into the meanings of digestion became possible as the new science of organic chemistry was swiftly advanced by the researches of Wöhler, Berzelius, and Liebig. As was pointed out in Chapter III, it is the molecular change which is significant and not the physical. Experiments in which material is introduced into the alimentary canals of animals and later withdrawn for analysis are constantly compared with trials in which the digestion takes place throughout in the thermostats of the laboratory.

The stomach is popularly supposed to have a very large share in the total work of digestion. It cannot, however, be claimed that it is indispensable to man. It forms, as already indicated, a convenient place of deposit for food and a gradual feeder of the small intestine, but it is mean-

while the seat of preliminary digestive changes which greatly facilitate the further advance of the process. Attention has been called to the fact that salivary digestion is continued for a time in the almost stationary contents of the fundus. When this is stopped by the penetration of the acid gastric juice it is superseded by a new type of digestion in which the proteins are the food-stuffs acted upon. The gastric hydrolysis of proteins is generally referred to as peptic digestion. Before we discuss it in detail we must consider the nature and the circumstances of formation of the gastric juice.

This secretion is the product of the numerous, relatively simple glands with which the mucous coat of the stomach is provided. Beaumont has vividly described the appearance presented by the lining of St. Martin's stomach directly after a meal. The surface, usually of a pale gray, flushed deeply, and the gastric juice welled up in glistening beads from the invisible mouths of the glands. Its manner of breaking out resembled the rising of perspiration from the pores of the skin. The empty[1] stomach may have a well-marked film of mucus upon its walls, but its active secretion is limpid and free flowing. The volume which the human stomach produces in twenty-four hours is apparently large; Carlson estimates it at 1500 c.c. (3 pints) in the case of his subject with a gastric fistula.

The Acid of the Gastric Juice.—Repeated reference has been made to the acidity of the stomach-contents. The early investigators were surprised and puzzled when they were forced to recognize that the acid in question is largely free hydrochloric. When we consider that this acid cannot be made industrially except by decomposing a chlorid with the still stronger and more corrosive sulphuric acid and in an earthen container, we can appreciate their feeling. For here is what we call a strong mineral acid proceeding from delicate living cells and from fluids of

[1] The "empty" stomach commonly contains air, saliva, an appreciable quantity of gastric juice, and frequently bile. The liquid contents may amount to one or two ounces.

neutral reaction. The formation of hydrochloric acid by the cells of the gastric glands has become much more intelligible in the light of modern chemical teachings. The current theories cannot be presented here. It is evident that when the elements of an acid are withdrawn from a neutral fluid it must, theoretically at least, be rendered alkaline. If we may accept a claim which has lately been denied we have a capital illustration of the refinement of the mechanism by which the body preserves uniform internal conditions in the fact that when gastric juice is being secreted, the urine, usually acid to common indicators, becomes alkaline. Thus the normal chemical equilibrium of the blood is maintained sacred from disturbance. The juice secreted into the antrum is said not to be acid.

Mention has been made of some ways in which the acid of the stomach modifies local conditions. We have seen that it gradually checks salivary digestion. It is the most important controlling factor for the two sphincters. Other features of its action must now be presented. Among these is its distinct antiseptic influence. Spallanzani noticed that pieces of meat undergoing digestion in gastric juice passed into solution without putrefying. Similar pieces kept for an equal time in water had radically spoiled. This was a significant observation at the time, because digestion and putrefaction had been regarded by many as identical. We know now that putrefactive decomposition of protein is due to the influence of swarming micro-organisms, and that hydrochloric acid in the concentration usual in the gastric juice restrains the development of such forms.

The average strength of the acid in man is given as 0.2 to 0.3 per cent., rising sometimes to 0.5.[1] Such a con-

[1] Dragstedt and Ellis have shown that the continued withdrawal of all the gastric secretion from a dog leads to death in five to eight days. In a single day the chlorid lost in this way may be two or three times the amount present at one time in all the blood of the animal. Other tissues are depleted and the rapidly fatal result is not surprising. (American Journal of Physiology, xc, 1929, 331.)

centration by no means suffices to sterilize the stomach-contents, but in all probability it destroys many kinds of bacteria, including some which might become the cause of disease. Others it undoubtedly weakens, so that they multiply less rapidly when the chyme passes on to the small intestine, where the conditions for bacterial growth are more favorable. It is not surprising to find that the species of organisms which thrive most in the stomach are those which themselves produce acid. The "sour stomach" commonly referred to is a stomach in which the generation of lactic acid from sugars is actively taking place. This is a process very like the familiar souring of milk. Indeed, milk is one source of such acid fermentation in the stomach. Excessive acidity, whether due to the native juice or to the activity of bacteria, may be a cause of discomfort and a hindrance to digestion. Cannon has lately shown that acidity above a certain degree delays the departure of food from the stomach, and this is easily comprehensible when it is recalled that after each brief relaxation the pylorus remains closed until the acid which has just passed has been neutralized or dispersed. Acidity within limits is a necessary condition of gastric digestion, and this will be discussed later.

The Secretion of the Gastric Juice.—The glands of the empty stomach seem to be quite inactive. The natural supposition that they begin to secrete when food comes in contact with the mucous membrane is not borne out by the results of experiments. It is most important to note that the juice may start somewhat in advance of the arrival of food. The stomach as well as the mouth may be said to water at the contemplation of a meal. Abundant evidence of this fact has been furnished by the extraordinary experiments of the Russian physiologist Pawlow upon dogs. When a permanent opening has been made to the interior of a dog's stomach a little gastric juice may issue when the dog is merely shown food which he likes.

That it is unnecessary to have actual contact with the stomach wall is still better shown in the case now to be described. A dog having a gastric fistula is subjected to a

second operation, by which the esophagus is severed and the portion connected with the pharynx made to open through the skin of the neck. Whatever is swallowed by the dog is now returned to the exterior. The pleasure of eating is not impaired. To maintain nutrition suitable food may be introduced directly into the stomach. When the dog chews and swallows a meal he is quaintly said to have a "Scheinfütterung"—a fictitious feeding. This proceeding is accompanied by a steady flow of the secretion from the gastric fistula.

The secretion obtained under circumstances like the above is called the psychic secretion. This term serves to emphasize the fact that a mental element is a necessary incident of the reaction. The conditions governing gastric secretion seem to be quite parallel with those which regulate the movements of the stomach, and their importance in hygiene is equally evident. There are a number of individuals who have in various ways lost the power to swallow food, commonly because of the closure of the esophagus. Their lives are preserved by feeding through gastric fistulas established by surgery. These unfortunates find it to their advantage to attend to the idea of eating, and to taste and chew portions of their food at the time when it is being introduced into their stomachs.

After a brief period of fictitious feeding the flow of gastric juice into the stomach of a dog may continue for two or three hours. In view of this we must conclude that, however important a favorable mental state may be for the initiation of the process, it need not be its accompaniment throughout. We cannot pretend that a meal receives our constant attention during any such interval. Nevertheless we are hardly likely to overestimate the necessity of securing a normal start. If the initial circumstances are not favorable the secretion may be long delayed or even lacking.

Now that we have reserved a due place for the psychic element, we must pass on to consider the other factors which modify the activity of the glands of the stomach. Much has been learned from the surprising operations of

Pawlow and others, who have succeeded in dividing the stomach of the dog into two parts without robbing either of its connection with the circulatory and nervous systems. When the dog has recovered from the immediate effects it may be said to have two stomachs. Either or both may communicate with the exterior by a fistula, while one still retains its normal relations with the esophagus and small intestine. This arrangement makes it possible to place food in one stomach and to obtain and measure the unmixed juice secreted into the other. The evidence goes to show that when the glands in the lining of one sac are active there is corresponding activity on the part of those in the other.

A most significant fact is at once noted when such a dog is under observation. There are kinds of food, perfectly appropriate for the animal's nutrition, which may lie in the stomach without exciting any flow of the juice. This is said to be true of bread, white of egg, starch, and some sugars. The same articles of diet would be met by an abundant gastric secretion if they had been eaten with enjoyment by the hungry dog. It makes a radical difference, then, whether these materials enter the stomach through the mouth and attract the favorable notice of the animal, or whether they are slipped through a fistula, a proceeding which would probably not be recognized by him as a mode of feeding.

On the other hand, there are some things which do cause an outbreak of gastric juice by their mere presence in the stomach and in the absence of any psychic factor. To a somewhat limited extent this is the case with water, though only, it appears, when there is enough of it to distend the stomach slightly. The best-known excitant of the secretion is meat, and the property is said to belong to the *extractives* or minor substances in this food, and not to the proteins of which it is chiefly composed. Meat causes a considerable flow of the juice, but there is a much longer initial delay than when the psychic element has its normal place. In fact, the total quantity produced when meat is introduced into a dog's stomach without attracting his

attention is decidedly less than when it is eaten in the natural way, and when the psychic and chemical agencies are combined.

It is unfortunate that our knowledge of this matter has been drawn so largely from a carnivorous animal. Meat might be expected to stimulate the stomach of the dog more surely than other foods. How far the secretion may be elicited by placing other compounds in the stomach is imperfectly known. Milk is credited with some power to call it forth, but its superiority to water seems doubtful. Alcohol is said to have a positive action of the same kind.

It is claimed that the dextrins, the intermediate bodies produced in salivary digestion of starch, have the property of starting the gastric flow. If this is true it is interesting as establishing a connecting link between the two successive processes, and making it apparent how one may tend to insure the setting in of the other in due time. A link of this sort exists between gastric digestion and pancreatic secretion, as we shall have occasion to point out. The condiments, such as pepper and spices, have a reputation for stimulating the discharge of gastric juice, and undoubtedly do so when they favorably affect the flavor of the food. They are known to increase the blood flow in the lining of the stomach, which would perhaps help to continue the secretion process when once under way, but whether they can actually initiate it apart from their psychic effect remains uncertain.

When gastric secretion is well started there is provision for its maintenance as long as the stomach contains food. It appears that some of the early products of digestion act after the manner of the extractive substances of meat and excite the glands to continued activity. The acid itself has been found to be absorbed by the cells lining the antrum and to set in motion a train of events leading to the same result. This form of stimulation will evidently cease only with the departure of the last portions of the acid chyme. The flow of gastric juice is retarded by fats.

Digestion in the Stomach.—The gastric juice is usually said to contain two enzymes. Recent work indicates the presence of a third. The two familiar ones are *pepsin* and *rennin*. The third is the gastric *lipase*. Certain writers have questioned whether we ought to speak of pepsin and rennin as distinct individuals, suggesting rather that there is in the secretion a single body having two sets of properties. We need not enter into such a discussion; we shall for the present continue the convenient usage of speaking of pepsin and rennin as two substances.

Rennin.—The fact that extracts of the stomach wall cause the curdling or coagulation of milk has been known from very early times. Such extracts, usually derived from the stomach of the calf, have long been in use in the manufacture of cheese. Rennet is the industrial term for an extract with this property; rennin is the scientific term for the supposed enzyme contained in it. Cheese curd consists of the bulk of the protein of milk which has undergone an obscure chemical change and has passed into an insoluble form. From a physical standpoint this is an anomaly among the digestive processes. We look to see solids becoming liquids, while in this curious instance a liquid becomes a solid. It may be suggested that this prevents an unduly rapid passage of milk to the small intestine. The curd when formed has to undergo solution like any other solid.

The action of rennin becomes the more enigmatic when it is noted that it is found in the stomachs of animals which do not have milk in their normal diets. Milk is curdled by extracts of various organs other than the digestive glands and by some vegetable juices. In the human stomach a very firm curd may be formed when a large quantity of cows' milk is taken at one time. The dense mass may be slow to digest. Human milk is said never to set into such a tenacious coagulum, and this is natural, since, regarded as a solution of proteins, it is much more dilute than the milk of the cow.

Peptic Digestion.—The chief enzyme of the gastric juice

is the one commonly called pepsin. Its relations with the acid of the stomach are so close that many writers urge that we should speak rather of "pepsin-hydrochloric acid," the term suggesting the existence of a compound of the two which is responsible for the action on the food. The power to digest proteins is manifested only with an acid reaction, and is permanently lost when the mixture is made distinctly alkaline. The conditions which permit peptic digestion to take place are, therefore, precisely those which exclude the action of the saliva.

When protein in solid form, such as boiled white of egg, is subjected to the influence of gastric juice the pieces swell and become softened. Later they are dissolved. When the trial is made with protein which is originally in solution, such as unboiled white of egg, there is no visible evidence of change. But there are physical and chemical tests which can be employed to show that digestion is as definite a change in this case as in the other. An early manifestation of this fact is the loss of the property of coagulation on heating. Later there are indications that the molecules are undergoing cleavage. At each successive stage there is a gain in the power of diffusion, a reduction of viscosity, and a diminution in the number of precipitants which can be employed to throw the protein out of solution.

Physiologic chemists have studied minutely the characteristics of the hydrolytic products during the advance of peptic digestion. They have attempted to identify numerous compounds, each of which has a transient existence and is then itself hydrolyzed. For our present purposes it would be unprofitable to dwell upon such questions of detail. Certain of the earlier cleavage products are included under the general name of *proteoses* or *albumoses;* others, arising later and of a simpler character, are called *peptones.* Roughly speaking, there is a parallel between salivary and peptic digestion. In either case, molecules of great size—of starch and protein respectively—are subdivided progressively, first with the formation of somewhat complex bodies—dextrins and proteoses—later to form maltose in

the first instance and peptones in the second. The correspondence is imperfect in several ways; for example, maltose is a single substance, while there appear to be a number of peptones. It will be remembered that maltose itself is slowly transformed by long-continued action of saliva. Quite similarly, the gastric juice will in time effect a further digestion of the peptones, but this advanced digestion seems normally to be postponed until the intestine is reached.

Gastric Lipase.—Down to a recent time it was held that fat underwent no true digestion in the stomach. It was recognized that some forms of fat, butter, for example, must be melted, and that the fat in the adipose tissue of meat might be released from the enclosing cells when their protein portion was dissolved. These, however, are mere physical changes. Attentive study has brought out the fact that there is, after all, some hydrolysis of fat in the stomach, though it is probably slight. An enzyme with this action is accordingly assumed and is spoken of as *gastric lipase*. It is only the most finely divided (emulsified) fats which seem to be appreciably affected. The products of this decomposition as well as of the later fat digestion in the intestine are *glycerin* and free *fatty acids*.

Summary.—The material passing the pylorus is comparatively dilute and normally free from coarse particles. It is acid in reaction, both the native hydrochloric acid and the acids formed by fermentation contributing. Much of the food is as yet practically undigested. On the other hand, some progress has been made in the transformation of cooked starch into sugar. The proteins are partially peptonized. If milk has formed a part of the diet, it will have been curdled and redissolved. Fats may have been liquefied and scattered, but are not likely to have been extensively hydrolyzed. On the whole, gastric digestion may fairly be described as preliminary in character.

CHAPTER X

THE SMALL INTESTINE: ITS MOVEMENTS, SECRETIONS, AND DIGESTIVE PROCESSES

THE intestinal content is propelled on its winding way by peristaltic movements. These are similar in their mechanical principle to the waves of muscular contraction passing down the esophagus in the act of swallowing. They are, however, much slower and gentler in character. As a rule they do not run an uninterrupted course from the pylorus to the ileocecal valve, though such a phenomenon is an occasional possibility. More commonly a wave will travel a limited distance and then fade out, leaving the material which it was moving to rest for a time in some depending loop. If this is true, the progress of the food is intermittent; *x*-ray observations upon human subjects have led to the estimate that it takes four or five hours for the passage through the whole length of the small intestine. This time may be assumed to vary widely with the individual and the diet. Reduced to an average rate the data quoted above give us about one inch per minute.

Intestinal peristalsis, like the movements of the stomach, is governed mainly by local mechanisms. Yet in this case as in the other the central nervous system may exert an influence tending to accelerate or to suppress the activity of the muscular coats. The second or inhibitory action is the more marked. A question much discussed is whether the direction of peristalsis in the small intestine is at all subject to reversal. The sum of the evidence at present supports the view that such a reversal (antiperistalsis) is possible, but only under conditions which are clearly abnormal. The circumstances tending to bring it about have been fully discussed by Alvarez.[1] Ordinarily

[1] "The Mechanics of the Digestive Tract," Hoeber, New York, 1922.

it is plain that the intestine is distinctly specialized to act in one way rather than the other.

Not all the muscular contractions exhibited by the small intestine have a progressive character. Frequently a loop which contains food will become creased at short intervals by rings of constriction which do not shift their position, but remain stationary for a little. The internal effect is to create a series of small pouches holding separate portions of the chyme. After this condition has persisted for a moment the regions originally contracted become relaxed, and new contractions set in at points midway between them. Under the influence of such movements the food is constantly shifted about and subdivided, but it is not driven steadily in one direction. This "marking time" on the part of the small intestine is referred to as *rhythmic segmentation*. Inasmuch as it serves to alter the contact relations between the intestinal contents and the lining, it probably favors absorption. Some writers have made much of the effect which these contractions may be assumed to have upon the flow of blood and lymph in the walls of the canal. When pressure is applied at brief intervals to tissue containing these fluids the result may be described as a massaging action, hastening the circulation and crowding out some of the lymph. This again must tend to promote the absorption process.

A longitudinal movement of individual loops is often described. Two neighboring turns of the intestine may be seen to glide the one upon the other, coming to rest after slipping a short distance, and presently reversing the direction of their travel. This form of activity cannot definitely further the progress of the contents, but when it affects segments enclosing liquid material we may suppose that the food and juices are tilted about and brought into relation with the largest possible area of absorbing surface. The upper part of the small intestine appears to be more active than the lower. Consequently it tends to free itself rather promptly of contained food. The name jeju-

num, meaning empty, reminds us that this behavior must have been noted centuries ago.

The Secretions Entering the Small Intestine.—In Chapter VI it was stated that this part of the canal receives the contributions of the liver and the pancreas, as well as of the microscopic glands in its own mucous membrane. The bile and the pancreatic juice, it will be remembered, enter just below the pylorus. The intestinal juice is produced by all parts of the extensive lining, but more abundantly in the upper than in the lower segments. The three secretions have some characters in common. They are all alkaline in reaction, owing to the presence in them of sodium carbonate. This confers upon them in a considerable degree the power to neutralize acids. As the acid chyme from the stomach meets the alkaline secretions in the duodenum there must be more or less carbonic acid gas evolved. This may be helpful to the digestive process, since the tendency will be to lighten the texture of the food particles, much as dough is lightened by the agency of yeast.

It is not merely the acid from the stomach which may be combated by the alkali of the juices below; there are two other sources of acid to be taken into account. One of these is found in the bacterial fermentation, chiefly of sugars, which goes on in the intestine. The second is the entirely normal formation of free acids occurring in the course of fat digestion. So far as the first class of acids are neutralized the products are mainly lactates and butyrates; the fatty acids may be converted into *soaps*. There is no guarantee of an exact proportionality between the acids and the alkali, and it is impossible to say which will be in excess in a particular part of the canal. Generally, however, the resulting reaction of the mixture is not far from the neutral point.

The united volume of the three secretions is held to be very large, but any estimate tends to mislead, since throughout the length of the intestine we have the withdrawal of water keeping pace approximately with its in-

flow. In a certain section selected for observation the bulk of the contents may show little change during a long period, and yet there may have been profuse secretion entirely disguised by counterbalancing absorption. In this consideration we see indicated an important service shared by all the digestive secretions, that of supplying liberal quantities of water to act as the solvent and carrier of food-stuffs destined for absorption. If absorption were to continue without compensatory secretion, a final stage might be reached in which the cavity of the intestine would be drained of all fluid, while the walls would be crusted with a dry residue suggestive of boiler scale.

The Pancreatic Juice.—In considering the causes of gastric secretion the importance of the central nervous system called for emphasis. This is not true to the same extent of the government of the pancreas, though here also it is held that the nervous system plays a part. A chemical means of control is better known. As has been hinted before, there is an intimate relation between the gastric activity and the later awakening of the pancreas from its state of repose. The arrival of acid from the stomach in the duodenum causes a timely outflow of pancreatic juice.

This might be supposed to be an instance of reflex action, like the production of saliva when acid is taken into the mouth. It has been shown, however, that it has another explanation. The acid, striking into the lining membrane of the duodenum, initiates a series of reactions which have been studied in detail, and which lead at last to the formation of a substance of quite definite chemical properties called *secretin*. This finds its way into the circulation, and, like a drug, is swept far and wide. It stimulates the pancreas to produce its secretion, augments the formation of bile by the liver, and probably excites the glands in the wall of the intestine to greater activity. In the light of these facts it becomes clear that a vigorous gastric digestion with the strongly acid chyme which results goes far to insure a normal intestinal process.

The pancreatic juice in man is an abundant secretion—a pint or more daily—and, in marked contrast with the saliva and the gastric juice, it has relations with all three principal classes of food-stuffs. It contains an enzyme which some have thought to be identical with the ptyalin of the saliva, but generally called *amylopsin* or *pancreatic amylase*. Thus the progress of starch digestion, interrupted for a time in the stomach, is now renewed. The slight acidity which may exist in the intestine is not likely to prevent this type of digestion from going on to completion.

Beside acting on starches, the pancreatic juice continues and greatly accelerates the hydrolysis of fats which has been barely begun in the stomach. The enzyme concerned is called *steapsin* in the older books, but by more recent writers *lipase*. The immediate products are glycerin and fatty acids. A secondary formation of soaps is a possibility already indicated. When an oil undergoes digestion it breaks up at an early stage into microscopic drops and is said to be emulsified. This subdivision clearly multiplies the surface of contact between the food and the digestive juice, and has an effect corresponding to that of mastication upon solids. It is, therefore, most helpful to digestion, but it is not to be confused with digestion itself.

The statement is commonly made that the pancreatic juice continues the work of pepsin upon proteins by virtue of an enzyme called *trypsin*. While this is approximately true, it calls for a certain qualification. If the juice is carefully collected as it comes from the main duct of the pancreas without being allowed to mingle with other secretions or even to touch the lining of the intestine, it is reported that it is usually incapable of hydrolyzing proteins. This power it gains in a striking degree when it has been mixed with ever so little of the intestinal juice, the *succus entericus*, as it is sometimes called. The interaction of the two secretions is described as resulting in the "activating" of the pancreatic juice. The natural inference is that the inactive fluid contains in solution a body, not yet deserving the name of enzyme, but ready to be-

come one by a quick transformation. An inactive antecedent body of this kind is termed a *zymogen;* in this specific instance, *trypsinogen.* Acting on the assumption that there is a definite substance in the intestinal juice capable of changing trypsinogen to trypsin, physiologists have given the name of *enterokinase* to the agent concerned. Bile, also, is capable of activating pancreatic juice.

Tryptic digestion differs in characteristic ways from the peptic process which has been described. Acid which is essential to digestion in the stomach is antagonistic to the pancreatic type. Trypsin does its work best in a nearly neutral mixture. In the normal course of events it acts upon material already partly hydrolyzed, but it has the power to carry through all its stages the digestion of native protein. If the food is a solid, mere inspection reveals a difference between peptic and tryptic solution. In the former case there is marked swelling, as previously stated; in the latter there is progressive corrosion, a shredding or honeycombing of the specimen.

When chemical methods are employed in the study of tryptic digestion, it is found to run a course roughly parallel with that of the gastric digestion of proteins. Corresponding intermediate bodies—proteoses—are described in both instances, though it is said that some stages in the tryptic process are passed so rapidly as to seem almost to be omitted. What distinguishes the pancreatic proteolysis most radically from the peptic is the facility with which the peptones are broken down into still simpler bodies. We have made the statement that these late cleavages take place only very slowly under the influence of gastric juice. So it becomes clear that trypsin is distinctly adapted to follow after pepsin in the accomplishment of protein digestion.

Peptones are compounds which are simple by comparison with standard proteins, but which are still too complex to be given precise chemical formulas. When they are hydrolyzed, most of the products come within the knowledge of the organic chemist so definitely that their molecular structure can be confidently expressed. To the student

it must be admitted that such formulas do not appear simple, but if he is disposed to resent the use of the word he is to reflect that these molecules stand in some such relation to the original protein complex as the bits of the mosaic bear to the whole design. It is with some such an idea that the Germans have called them *Bausteine*, that is, the building-stones, from which a new architecture can be constructed. The simplest products of the tryptic process are conveniently called amino-acids.

The Intestinal Juice.—This copious secretion was formerly regarded as having little to do with digestion. The present disposition is to credit it with a very considerable share. When the pancreatic juice is prevented from entering the intestine it remains possible to keep up the nutrition of the animal, and one must conclude that the intestinal juice is successfully preparing more than one kind of food for absorption. Samples of the secretion have often been obtained from loops of the intestine disconnected from the remainder of the canal. Different workers give varying accounts of its properties.

The feature of its digestive action concerning which there is the most general agreement is the hydrolysis of the more complex sugars, the disaccharids. Of these sugars, three are commonly present, and there appear to be three enzymes adapted to act upon them. Maltose arises principally from the salivary and pancreatic digestion of starch. It is hydrolyzed to dextrose by an enzyme, which is best called *maltase*. Lactose, or milk-sugar, is similarly converted into equal parts of dextrose, and the less familiar sugar galactose by the enzyme *lactase*. Saccharose, or cane-sugar, gives rise to dextrose, and a sugar of different properties, levulose (fructose), under the influence of the enzyme, *invertase*.

When an extract is prepared from the thoroughly minced lining of the small intestine it can be shown to have the power to cause proteoses and peptones to undergo hydrolysis, though it is said not to act upon the original unmodified protein. This is equivalent to saying that such an

extract can parallel the later work of trypsin, though lacking its power to initiate digestion. The enzyme implied has been named *erepsin*. It is regarded as an open question whether this enzyme normally enters the cavity of the intestine or does its work within the confines of the cells from which it can be extracted. We may conceive that when an animal is deprived of its pancreatic secretion it is still able to digest proteins, pepsin beginning the digestion and carrying it to a stage at which the products are susceptible to the action of erepsin. The presence of enterokinase in the intestinal juice has just been noted.

The Bile.—The secretion of the liver cannot be regarded in the same light as the digestive juices mentioned heretofore. It is not secreted merely after meals, but is always flowing through the ducts which converge from the several lobes of the liver. It is not necessarily entering the intestine at all times, since the gall-bladder provides a place for its temporary storage, as described in Chapter VI. While the production of bile never ceases, it does show an acceleration during the digestive periods, and this is believed to be in response to the stimulating effect of secretin.

Bile attracted the attention of physicians in very early times, its conspicuous color and intensely bitter taste giving it a certain distinction. It entered largely into ancient theories of disease and of medicine. We have traces of these facts in the root-meaning of such words as bilious, choleric, and melancholy. In popular estimation bile is a poison arising now and then in the system and causing digestive disturbances. Patient study has shown that the bile is a complex mixture, and that it numbers among its constituents some which are waste-products and others which have a favorable effect upon the progress of digestion and absorption. It stands, therefore, in a position intermediate between that of the gastric juice, which is formed solely to advance digestion, and that of the urine, which is composed of material useless to the body.

The pigments of the bile are counted as waste substances. A red one predominates in carnivorous animals. The bile

of the herbivora is green; human bile may be green, yellow, or orange. These pigments show in their chemical nature a close relationship with the red coloring-matter of the blood, the important compound *hemoglobin*. All the evidence goes to show that the bile-pigments are modified fractions of the great hemoglobin molecule, and that their abundance is an indication of the amount of destruction suffered by the red corpuscles of the blood. They do not contain the iron previously present in the hemoglobin; this element seems to be conserved. These pigments are relatively insoluble and are not always successfully carried to the intestine by the bile. When they deposit in solid form in the gall-bladder they contribute to the formation of "gall-stones," aggregations in which another compound, the waxy *cholesterin*, may be included. The pigments are usually more or less altered by bacterial action in the course of their journey through the canal, and eventually become the chief coloring-matter of the feces.

The bitter taste of bile is due to two organic salts of high molecular weight. These seem to have a totally different significance from that of the pigments. They are not lost to the body, but are absorbed from the lower part of the small intestine and are presumably secreted again and again. This phenomenon has been spoken of as the "circulation of the bile-salts." The withholding of these bodies from the alimentary tract tends to derange digestion and, in particular, to diminish the absorption of fats. When bile is tested by itself it shows only the feeblest digestive powers, yet pancreatic digestion is greatly promoted by its presence, and it may be likewise an ally of the intestinal juice.

Light is thrown on the properties of the bile by observing the condition of jaundice. This disorder is commonly caused by the more or less general plugging of the bile-ducts with mucus. The secretion cannot make its escape from the liver in the normal way and some of it enters the circulation. Bile-pigments make their appearance in the white of the eye and in the skin. The urinary pigment,

which is always closely related to the pigments of the bile, is much increased. The ill feeling which usually attends the condition may be due in part to the mildly poisonous effect of the abnormally retained bile constituents. It is likely to be aggravated by indigestion. The bile-salts are lacking and the capacity to digest the food and promptly absorb the end-products is greatly reduced. Bacterial action in the intestine may become pronounced. This last fact has suggested that the bile may be an antiseptic. It cannot be shown to have anything like a universal action of this kind, but it is very probable that it has a selective one, favoring one type of organism and restraining another. Even though it had no such influence, the intestinal bacteria might be expected to multiply in its absence, for the simple fact of delayed absorption would suffice to bring this about. Our best defense against excessive fermentation and putrefaction is in the early and complete removal of the food from the sphere of action of micro-organisms.

Summary.—The secretions flowing into the small intestine supply enzymes in sufficient number and variety to accomplish the digestion of all common foods. The transformation of starch to maltose begun in the stomach is completed by the pancreatic amylase. The resolution of proteins into the simple structural units from which their molecules are built is carried out under the influence of trypsin and perhaps of erepsin. The last-named enzyme is supposed by many to work upon the tryptic products as they pass through the lining cells on their way to the blood. Fats are hydrolyzed by the pancreatic lipase, with the formation of glycerin and fatty acids, the latter being in some measure converted to soaps. The disaccharids are changed to monosaccharids, a work attributed to the intestinal juice. Fermentation caused by bacteria has been taking place along with the strictly normal processes. The most evident products are organic acids, which may or may not be fully neutralized by the alkaline secretions.

Protection Against Self-digestion.—There has been much discussion of the fact that the proteolytic enzymes

in the digestive tract do not ordinarily attack its mucous membrane. They may do so after death and when the tissues are in an abnormal condition, as in case of gastric ulcer, the juices may strongly antagonize the healing process. It is often asserted that there is a definite chemical difference between the proteins of living and of lifeless matter. A recent explanation of the resistance which living cells offer to digestion is based on the apparent fact that such cells form bodies which have the capacity to neutralize enzymes in fixed proportions. The name of *anti-enzymes* has been applied to such protective substances. The ability of the tissues to withstand digestive agents is thus made closely comparable with immunity to the toxins of diseases.

CHAPTER XI

THE LARGE INTESTINE

The material passing into the colon is dilute and much reduced in volume as compared with the chyme passing out of the stomach. In the lower part of the small intestine the absorption of water more than counterbalances the secretion, hence the shrinkage of the contents. But since the end-products of digestion are being absorbed also, there is no tendency toward extreme concentration. In the large intestine there is but little secretion, and the continuation of the absorption of water reduces the contents at last to a nearly solid consistency.

The colon appears to be of very unequal value to animals of different classes. In the carnivora the work of digestion and absorption is so nearly finished by the small intestine that very little remains to be done. The small quantity of matter having a potential food value may be accompanied into the large intestine by enzymes, which may there carry further their digestive action. Such food, however, is likely to be a negligible amount, and the digestive powers of the mixture at this point are unreliable. In the herbivora, the food being bulky and refractory, a considerable portion may arrive undigested in the colon. These animals have very capacious ceca, in which great masses of contents seem to be held for long intervals. The digestion occurring there may be partly effected by the native secretions, but it is believed to be largely the work of bacteria.

The average human being resembles the carnivorous type rather than the other. Numerous cases have been observed in which no use was made of the colon, and it was never difficult to maintain nutrition. When the large intestine is no longer traversed the discharges are watery and rather voluminous, but they contain only small percentages

of valuable nutriment. The fluid escaping from the end of the small intestine or the beginning of the large is described as entirely inoffensive, which indicates that putrefactive

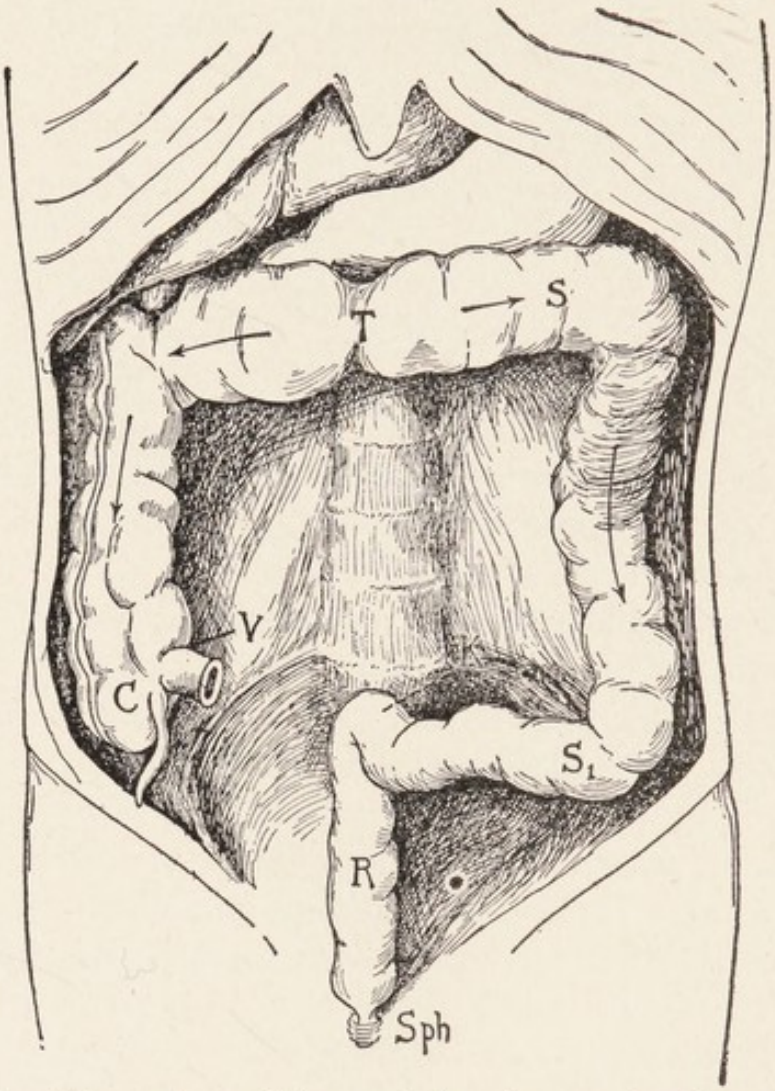


Fig. 14.—The colon with special reference to its movements: *T* is placed near the seat of frequent sustained or tonic contraction. From here backward to the cecum (*C*) antiperistalsis is of common occurrence, but this segment is swept also by occasional waves in the opposite direction; *V* indicates the position of the ileocecal valve, which prevents reflux to the small intestine under the influence of antiperistalsis; beyond *T* the infrequent movements which take place have always a progressive character; *S* and S_1 are regions often found to contain stationary contents; *K* is the kink referred to in the text; *R* is the rectum, and *Sph* is the double sphincter at the anus.

decomposition of protein is usually confined to the colon. Protein putrefaction has sometimes been held accountable for many ailments, and from this view has arisen the common teaching that man would be better off without a

large intestine. Comment upon this opinion may well be reserved for the chapter on the Hygiene of Nutrition.

The Movements of the Colon.—The average rate of progress in the large intestine is low. A factor tending to make it so has recently been brought to notice through the studies of Cannon and others. The ascending colon has a property not duplicated elsewhere in the canal, that of habitual antiperistalsis. As repeated instalments pass the ileocecal valve the cecum is filled and the accumulating contents reach higher and higher levels, but instead of thrusting onward this gathering mass, the circular muscular coat most of the time urges it backward. The result is said to be much like what is seen in the antrum of the stomach, although here the direction of the movement is reversed, that is, the waves of contraction press the mixture downward into a pouch, from which the only escape is by an eddying reflux through the crawling ring. It is assumed that the ileocecal valve prevents any return to the small intestine. A deliberate hindrance to progress at this point may be of service so far as it secures a more perfect absorption of digestive products and the retrieving of surplus water. The antiperistaltic waves are described as starting from a zone in the transverse colon near the midline of the body.

Another type of movement often witnessed is exhibited by the little pouches or sacculations which are characteristic features of the large intestine. These undergo distention as the fecal matter is pressed into them and from time to time they react and empty themselves by contracting. This is called "haustral churning"; it occurs in such a localized but irregular fashion that it has been likened to the dropping of piano keys under invisible fingers.

An interesting description of the behavior of the human colon has been furnished by Hertz. He has made use of food impregnated with bismuth salts, and has employed the *x*-ray to follow its progress. Earlier accounts left somewhat in doubt the means of transferring the contents

of the ascending colon to the transverse. It now appears that this is effected not so much by a peristalsis as by the vigorous contraction of the entire ascending colon, with the result that its cavity is almost abolished and the enclosed material decisively driven toward the spleen. Such marked contractions occur only at long intervals and, as Hertz believes, most commonly after a meal. At such a time the distal as well as the proximal portions of the colon are especially subject to agitation. This seems to indicate that the outpouring of nerve impulses upon one part of the tract is likely to be extended to other segments.[1]

Beyond the midpoint referred to above those movements which occur are invariably progressive, but are separated by long periods of repose. If we adopt a recent estimate we can make the following general statement: The foremost portion of a meal, that which was first to pass the pylorus and the ileocecal valve, may be expected to be near the spleen at the end of the ninth hour. When defecation occurs all the colon beyond this point may be freed of its contents. If this happens once in twenty-four hours, the age of the food residues discharged will evidently vary from thirty-three hours, for the matter longest retained, down to nine hours, in the case of that which barely came within the section evacuated. There must be extremely wide departures from these figures in individual subjects.[2]

The descending colon is reported to be found empty, as a rule, when observed with the *x*-ray. This is taken to mean that it is an irritable segment which is stimulated to advance all that enters it to the sigmoid flexure without delay. The sigmoid flexure, on the contrary, permits a relatively large accumulation before it is excited to contract.

[1] Hertz and Newton, Journal of Physiology, 1913, xlvii, 57.

[2] It is the claim of Burnett that the hygienic ideal calls for the retention of food remains for three or four days. The feces at the conclusion of this interval are in the form of compact pellets. Without conceding that this is the best condition possible we cannot deny that it is compatible with health. Burnett, Journal of the American Medical Association, 1925, lxxxv, 1777.

This region of the colon is interesting from a biologic standpoint, because it seems to be an adaptation to the erect position of the body. Quadrupeds hold the large intestine, roughly speaking, in a horizontal plane, and with them the effect of gravity on the contents is immaterial. These animals have no sigmoid flexure, the descending colon inclining toward the midline, and joining the rectum without the S-shaped connection. When the erect position is assumed there will naturally be a tendency on the part of the fecal material to settle toward the anus. The development of the sigmoid in the apes and in man provides a place of lodgment for the burden and spares the rectum from a constant distention.

The sharp bend between the sigmoid and the rectum, amounting almost to a kink, such as one may see in a rubber tube that has been doubled, is not easily passed by the feces. It is only when the quantity has become considerable that a vigorous peristalsis overcomes the resistance and fills the rectum. Here for the first time the pressure arouses distinct sensations. If defecation is postponed the tone of the rectum may be lowered and these sensations cease to be felt. If the occasion favors, the anal sphincters are inhibited and the rectum is emptied by its own peristalsis, reinforced by external pressure developed through contractions of the abdominal muscles and the diaphragm. The action of the skeletal muscles at this time resembles that in vomiting, but is, of course, much more largely voluntary and more sustained in character. When defecation takes place peristalsis may not be limited to the rectum. Material is commonly brought down from the region of the splenic flexure and forms the latest part of the evacuation.

The Feces.—Two classes of material may be mingled in the contents of the colon: the residues of the diet and the excretions of the alimentary tract including its glands. The proportion existing between these two is a variable one. Physiologists have lately come to regard the food residues in the feces, under average conditions, as forming

a less prominent element than was formerly supposed. A correspondingly increased importance is assumed by the excretions. The feces passed during long fasting are evidently made up exclusively of bodies of the second class. Such feces, while small in amount, may have practically the same composition as those formed upon a moderate and digestible diet. This suggests that the increased quantity which results from eating does not imply a greater residue so much as a greater production of secretions along the active canal. A mass very much like normal feces may gather in an isolated loop of the intestine to which no food is admitted. Among the substances originating from the tract rather than from the food are the modified bile-pigments, cholesterin or its derivatives, mucus, and detached cells.

Bacteria, living and dead, intimately mixed with the numerous products of their own life activity, are prominent in the bowel discharges. These organisms can in one sense be said to have their origin in the diet, since that was the source of the primary seeding or infection. From another point of view they are largely developed at the expense of the body itself, for they have multiplied in the intestine and may have lived in part upon its secretions as well as upon the food. The gases of the colon, other than air which has been swallowed, are due to their activities.

True food residues include the indigestible matter of the diet and some undigested food—normally but little of the latter. Absorption is strikingly efficient with most subjects and reasonable diets. Not more than 10 per cent. of most foods goes to waste. (The solids of an average daily ration amount to about 500 grams. The dry material in the day's feces is not usually more than 40 grams. Even if it were all derived from the diet this would represent a waste of only 8 per cent.) The principal indigestible component is the *cellulose* of vegetable tissues. When it is abundant, as in a diet containing coarse, woody matter, such as is eaten by the rabbit, the feces are given an immense bulk. The same result is secured in a measure

when man adopts a ration in which fruits and vegetables enter freely. Much cellulose is an impediment to complete digestion and absorption of the proteins and carbohydrates which it envelops, but the foods in which it occurs are cheap and the waste involved does not open an economic question of moment. Some bacterial decomposition of cellulose is said to take place in the colon and may be of slight advantage to us, not that we profit by the products of such fermentation, but that a freer exposure of proteins and starch may be insured.

Most writers have held that a moderate amount of indigestible material is a desirable feature of the diet. This teaching was emphasized by the celebrated Sylvester Graham early in the last century. Lowell has referred to him as an "apostle of bran." Later authorities have not recommended such wholesale loading of the tract with husks and fibers, but an admixture of such elements has been generally advocated. The favorable effects include the well-recognized stimulation of peristalsis and probably a better distribution of food along the canal. The indigestible fraction of the food has been spoken of as ballast and also by the expressive name of "roughage."

Under abnormal circumstances the loss of valuable food through the stools may become extensive. This will be the case when absorption is interfered with either by an acceleration of peristalsis or in other ways. Different cathartics bring this about in a varying manner, some by hastening the rate of propulsion, and others, especially the salines, giving the intestinal contents a concentration and a chemical character which forbids absorption. A mild disturbance of this nature is more apt to result in a waste of fats and fatty acids than of other forms of food.

Rectal Feeding.—While the large intestine of man is not called upon in normal conditions to absorb much nutriment, it has some reserve power to do so. This is often of a certain value in sickness, when it may be possible to tide over a critical time and to keep up a measure of strength by introducing suitable foods into the colon.

Fluid mixtures used in this way must be of low osmotic pressure, a fact which, unfortunately, rules out the sugars excepting in small amounts. Milk and eggs are much employed. Experience has shown that the body makes a partial use of the proteins offered, even though they have not undergone digestion. The results are better when artificial digestion has been brought about in advance. So far as we know there is no flow of efficient digestive secretions in response to the introduction of food through the rectum. It is believed that nutritive enemata may in part at least enter the region of prevailing antiperistalsis, and that this must favor their long retention and better utilization. It is fair to say that less reliance is placed upon rectal feeding than was the case a few years ago. Stimulants may be given through the large intestine and water to allay thirst.

CHAPTER XII

THE BLOOD

The intestinal lining is a barrier between the mixture of food and secretions within the canal and the blood which flows through the neighboring vessels. The main problem to be dealt with in treating of absorption is the transfer of portions of the intestinal contents to the blood. We shall find that a certain fraction of the incoming nutriment is carried for a time in the lymph, but this is destined before long to blend with the main current of the circulation. It will be for our advantage to become somewhat familiar with the make-up and service of the blood before we discuss the entrance into it of the products of digestion.

Blood is a carrier. Regarding it as such, we can conveniently subdivide its functions according to the classes of material which it conveys. Most people will think of it as, first of all, the bearer of food to the tissues. This is, indeed, a matter of prime importance. The food, during periods of digestion, is added to the blood mainly as it flows through the capillaries of the wall of the alimentary canal, and taken from it by the various parts of the living body in proportions corresponding with the degree of the local activity. The largest tax is that levied by the skeletal muscles. During fasting food for current needs is added to the blood from various reserve stores. An unfailing supply of oxygen is a need even more urgent from moment to moment than the presentation of food. Oxygen is added to the blood in the lungs, and is withdrawn from it as it makes its round through the body, the quantity consumed in different organs being an even better measure of their individual metabolism than is their appropriation of food. Where oxygen is taken from the blood, carbon dioxid is returned to it. This indicates that the blood is a bearer of wastes. The excess of carbon dioxid makes its escape during the next transit of the

blood through the lungs. Other waste substances are gathered by the blood as it flows near the active cells. The major part of these is destined for excretion by the kidneys, and these organs receive so large a share of blood that the entire volume must come under their influence within a short space of time. A minor fraction of the waste finds an outlet in the bile, the sweat, and through the intestinal wall.

It has already been pointed out that every organ has a chemical constitution and a metabolism peculiar to itself. Therefore each organ must make certain demands upon the blood not exactly duplicated elsewhere. What is more important, each organ gives rise to products unlike those formed by any other part. In a number of cases these products can be shown to have far-reaching effects. Their existence has been mentioned in Chapter IV. Recognizing the large part which they play in the economy of the organism, we may state at this point that an essential service of the blood is the transportation of internal secretions.

Another function of the blood, and one often overlooked, is that of equalizing the temperature of different regions. One is reminded of the arrangement of a heating system in a house where a fire burns in a furnace and a circulation of air, hot water, or steam disperses the heat through the rooms above. Interruption of this circulation will allow the upper stories of the house to cool off, while the basement is overheated. In the living body heat production is a function of all active tissues. The ancients believed that it was the particular duty of the heart. This organ is, in fact, distinguished for its rapid evolution of energy, but it must be remembered that it is of small bulk. A much larger share of the aggregate heat production is borne by the skeletal muscles. These are supplemented to some extent by the liver and the other great glands of the body. Blood passing through a tissue which is undergoing lively metabolism will have a higher temperature as it leaves than it had when it entered. As it flows on it will communicate some of this surplus heat to resting structures in which little or no heat production is going on. This is the case with the connective tissues and with the skin.

At the surface the blood loses heat, at least under all conditions which can be called normal. The cooler blood then returns to the large vessels, merges with the heated blood from the muscles and glands, and brings the temperature of the mixture to an average which seldom varies materially. The means by which this standard temperature is maintained will be discussed at length in a later chapter. It will be well to point out even at this time that the skin is subject to considerable changes of temperature, and that our sense of being warm or cold depends entirely on the condition prevailing at the surface. If we turn again to our illustration of a house heated by a "circulation" of hot air or water, we shall recognize that here, as in the living body, there is a constant escape of heat to the environment. The temperature of a pane of glass in a window of the house will be influenced both by the internal and the external state of affairs. The glass may be warmed as hot air is wafted against it from within or cooled by a gust from without. So the skin may be warmed by a waxing of the blood-current close beneath it or chilled by a passing draft.

Blood may be described as a red fluid, but inspection with the microscope shows at a glance that its redness is not due to a coloring-matter in solution and uniformly distributed, but to the presence of minute solid bodies in suspension. These are the *red corpuscles.* The liquid in which they are swept about is the *plasma.* The corpuscles make up something less than one-half the total volume. In view of this, it is surprising that the blood can have such a free-flowing character and find its way through the capillaries so readily. One would anticipate that such a mingling of solid particles with fluid would result in the formation of a highly viscid mass. That the actual condition is so different must be due to the absolute smoothness and the great pliability of the corpuscles.

The Red Corpuscles.—The individual corpuscle is usually seen in the form of a disk slightly hollowed on its surfaces. It is about five times as wide as it is thick. A very slight unbalanced pressure acting from one side will con-

vert it into a saucer- or even a cup-shaped form, but it is remarkably elastic, and springs back into its original shape as soon as there is no longer a force acting to distort it. Most cells of the body are variable in outline and in size, but one red corpuscle is as much like another as though all had been made in the same mold. The diameter does not vary perceptibly from $\frac{1}{3200}$ inch. This is the figure for human blood; there is a standard size of corpuscle for each animal species. As the corpuscles are very minute so they are almost inconceivably numerous. The total number in the blood of a man must be reckoned in trillions.

The red corpuscles are often spoken of as cells, but their claim to rank as such is questionable. Regarding them

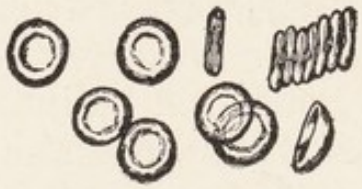


Fig. 15.—Red blood-corpuscles. Several are shown in different positions. The hollow centers are evident. In one case two corpuscles are overlapped to show that they are transparent. They tend to run into piles, as shown at the right. A saucer-shaped form is represented.

from an anatomic standpoint, they lack a feature which is reckoned an essential of the cell; namely, the nucleus. On the physiologic side there is little reason for supposing them to be alive. The fairest view, probably, is to look upon each red corpuscle as a modified and, in a sense, degenerate cell. A single substance has come to constitute a very large percentage of its make-up. This is the peculiar, iron-containing protein, *hemoglobin*. We shall not be far wrong if we consider the corpuscle to be a packet of hemoglobin moving passively at the mercy of the current. Its function is clear and definite. Hemoglobin has the property of combining with oxygen whenever the gas is freely present in the surrounding medium. It has also the property of releasing this oxygen when it comes into a situation where there is a relative scarcity of the element.

The hemoglobin of the blood, as can be seen from what has been said, is ever passing from one state to another, as

it alternately adds oxygen to itself and parts with it. Evidently it can be described as existing in two varieties: a form fully charged with detachable oxygen (oxyhemoglobin), and a form from which this loosely engaged oxygen has been removed (reduced hemoglobin). The first is the prevailing variety in *arterial* blood fresh from the lungs, and it gives to such blood a bright scarlet color. The *venous* blood, returning from the tissues, still contains a goodly proportion of oxyhemoglobin, but mingled with it there is now a variable amount of the reduced compound. Reduced hemoglobin is of a dark color, and venous blood, in consequence, inclines toward a purple. The sharply contrasting red and blue so commonly used in diagrams to distinguish arteries from veins greatly exaggerate the actual difference.

The red corpuscle, it will now be clear, is a bearer of oxygen. A service like this must be dependent on the extent of surface exposed for the absorption and the discharge of the gas. The disk is obviously more efficient than a sphere would be, for it has more surface in proportion to its mass. Small corpuscles likewise must be quicker to load and to unload than large ones, and this helps us to understand why the largest corpuscles in nature are not found in large animals, but in those like the frog and the fish, which do not have a very intense metabolism. There is an additional reason why small corpuscles are better fitted to meet the demand for a great oxygen supply: the capillaries must be of a size to admit the corpuscles, and an animal with large corpuscles cannot have the closely woven capillary net which becomes a possibility when the diameter of the corpuscles is reduced and which brings the oxygen into closer relations with the cells which require it.

The red corpuscles originate, generally speaking, by the transformation of cells in an unexpected locality. This is the so-called "red marrow" which fills the small spaces that abound in the enlarged extremities of the long bones. Here there is always going on a progressive change in the composition of the cells, in course of which hemoglobin

replaces most of their original substance. The cell nuclei are eventually lost and the newly formed corpuscles detach themselves and drift away in the blood-stream. Their hollow centers strongly suggest the deficiency due to the loss of the nuclei. It is an interesting fact that when recovery is taking place after hemorrhage, red corpuscles containing nuclei or presenting other signs of immaturity are often to be found in samples of the blood. This makes it seem as though in meeting the emergency corpuscles in an incomplete stage of their development had been pressed into service.

A marked reduction in the number of the red corpuscles constitutes an *anemia*. Such a condition naturally limits activity and, if extreme, threatens life itself. The loss of half the corpuscles may be fairly well borne. Many cases of anemia have proved very resistant to treatment. Certain ones have recently responded in a striking way to liberal feeding with liver. It is evident that the cells of this organ normally furnish something essential to the formation of perfect corpuscles. Their contribution appears not to be a compound of iron. Concentrated preparations of the liver are now available for patients, obviating the necessity of eating the tissue in distasteful quantities.[1]

The first glance at a specimen of blood under the microscope leaves the impression that the corpuscles are all of one unvarying type. Closer observation shows here and there among the host of colored elements bodies of another order, the white or colorless corpuscles. There is but one of these to 500 or 1000 red. The white corpuscles are not flattened, but more nearly spheric. They are, however, of no fixed form, and many of them have the property of ameboid movement. This is good evidence that they are to be considered living, and it can be shown further that they have nuclei and conform to our conception of complete cells. Much that is of interest is known of them, and the relation which they bear to the checking of bacterial infection is of the utmost importance. We shall not enter upon a discussion of this fascinating subject.

[1] Cohn, et al., Journal of Biological Chemistry, 1927, lxxiv, lxix.

The Plasma.—Aside from the transportation of oxygen, all the chief functions of the blood could apparently be fulfilled by the plasma. The standard foods of the tissues are here. So also in much smaller amounts are the non-gaseous wastes. Carbon dioxid, the most abundant of all waste-products, is carried jointly by the plasma and the corpuscles. It is evident that we must expect a solution meeting such manifold requirements to be of a highly complex nature. This is eminently the case.

More than nine-tenths of the plasma is water. The proportion is little increased by drinking and little reduced by thirst. Its constancy is secured by kidney activity coupled with rapid exchanges of fluid which take place between the blood and the lymph and tissues. When a great draft is made upon the water of the blood, as is the case in profuse sweating, the volume is restored by taking in water from outside the vessels, and this may mean a marked loss of body weight. The blood itself shares less than might be anticipated in such a loss.[1] Its total volume in the adult of average build has been variously estimated at from 3 to 5 quarts. The earlier calculations led to the higher figures; 4 quarts (8 to 9 pounds or $\frac{1}{16}$ of the weight) is a reasonable standard for us to adopt.

Among the substances in the plasma which can be classed under the general head of foods, proteins take the first place. They form about four-fifths of the total solids. This high proportion does not correspond at all with the make-up of an average diet, in which, as we have seen, proteins take the second or even the third place. It is usual to distinguish three varieties of protein in the plasma, serum-albumin, serum-globulin, and fibrinogen, but indications are multiplying which support the belief that the actual number of proteins with clearly individual characters is much greater. Our knowledge of these bodies, their mode of origin, place of formation,

[1] Haldane and Priestley found that the drinking of 5 liters of water in two hours and fifteen minutes did not produce any distinct dilution of the blood as judged by the percentage of hemoglobin. The urinary output reached more than 5 liters in eight hours. Journal of Physiology, l, 1916, 296.

and the particular value of each one in the system, is in a highly unsatisfactory state. The impression prevails that the proteins of the plasma constitute a relatively stable and permanent mass not subject to depletion and, accordingly, not actively produced under ordinary conditions.

Carbohydrates, which occupy the leading position in the rations ordinarily chosen by civilized man, are very scantily represented in the plasma. The principal one present is the monosaccharid, dextrose, known also as glucose, or grape-sugar. The percentage of dextrose figured for the whole blood is usually near 0.1. This means about 1 gram of sugar in a liter of blood, and limits the total amount in circulation to something like 5 grams. Such a quantity seems insignificant when it is remembered that 100 grams of sugar may easily be formed in the digestion of a moderate meal. The sugar is not readily increased by free feeding of carbohydrates, nor does it noticeably diminish during long fasting. The explanation of this singular constancy will be given later.

Fat, or its derivatives, is found in the plasma in a proportion of a similar order to that of sugar. It is much more subject to variation, rising notably after a meal in which there was much fat. Plasma obtained from a dog at such a time may exhibit the phenomenon of developing a true cream, the fat gathering at the surface. During starvation the blood is not necessarily poor in fat, since it is likely to be engaged in carrying this form of food from places of storage—the adipose tissue—to the muscles and elsewhere to be oxidized.

Those compounds in the plasma which we can confidently designate as waste-products occur only in the smallest quantities. Carbon dioxid is, of course, an exception, being very abundant. Among the non-gaseous wastes destined to be dealt with by the kidneys, *urea* is the only one which is easily detected. This is the compound in which seven-eighths of the nitrogen is carried from the body. The fact that the waste substances are kept down to such a low level in the blood is evidence of the remarkable efficiency of the kidneys and the supplementary or-

gans of excretion. It is also a reminder of how rapid and copious is the circulation. No portion of the blood can long escape passage through the glands which have this striking power to hold it to a standard composition.

If the mixed solids from a sample of plasma are incinerated, we have left a small mass of ash or mineral matter amounting to about 1 per cent. of the whole blood. By far the largest component is sodium chlorid, the chief salt of the diet, and the only one which we deliberately add to our food. Other bases represented are potassium, calcium, and magnesium. Besides chlorids, we find carbonates and phosphates, the former having greatly involved relations with the carbon dioxid of the blood.[1] To the list of components native to the blood might be added many minor constituents, some of which are judged to be present because of certain properties displayed by the blood rather than because they can be chemically identified. Illustrations of such are afforded by the internal secretions, enzymes, and the immune bodies. Individual peculiarities of metabolism, susceptibility, and resistance must depend on substances of this obscure class.

Coagulation.—Blood when shed shows the familiar property of clotting. This is a most valuable quality, since it provides for the automatic checking of ordinary bleeding and also forms a protective shield, the scab, beneath which the healing process may go on. The importance of coagulability is emphasized by the rather frequent observation of cases in which it is lacking, and in which serious or even fatal hemorrhages follow trifling injuries. The essence of the process is a chemical change affecting one of the minor proteins of the plasma in such a way that it passes into a solid form and cements together the red corpuscles. The original protein is the one already named as fibrinogen. The modified form after coagulation is called *fibrin*. The actual amount of fibrin is extremely small (perhaps 2 to 4 parts in 1000 of blood), but it is not

[1] Sulphates will also be found in such a sample of ash. They are scarcely to be discovered in normal blood, but arise from the burning of proteins.

difficult, when we consider its gummy character, to understand how it can convert a liquid medium into a stiff jelly by knitting together the suspended corpuscles.

The entirely natural impression that coagulation is the result of exposure to the air is erroneous. The matter has been the subject of the most painstaking studies, of which we can give only the briefest summary. The formation of fibrin is an instance of enzyme action, and forcibly recalls the curdling of milk in the stomach under the influence of rennin. The resemblance is not complete in every respect, but is still suggestive. If we are to assume that an enzyme exists in the blood at the time of clotting and not before, we must establish its origin. Reducing the facts to the barest essentials, we may make the following statement: normal blood contains in great numbers minute and extremely perishable bodies known as the blood-plates. These are much smaller than the red corpuscles. When

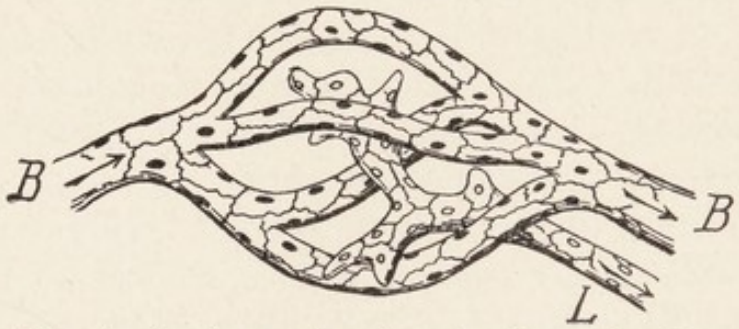


Fig. 16.—The beginnings of a lymphatic. Blood capillaries are suggested (*B–B*). Associated with them is the supplementary channel (*L*) through which surplus fluid may pass away. To complete the picture these vessels must be conceived to be embedded in a mass of cells.

the surroundings are normal, as is presumably the case within the vessels, they keep their integrity, or at least do not disintegrate *en masse*. When they are brought in contact with foreign surfaces they do undergo prompt decomposition and, of course, their constituent material is dissolved in the plasma. Something derived from the blood-plates sets in motion the series of chemical reactions which leads at last to the perfecting of an enzyme, *thrombin*, capable of transforming the soluble fibrinogen into the insoluble fibrin.

Lymph.—This term is usually made to stand for the

fluid outside the blood-vessels. Used in this way, it includes the liquid filling the microscopic intervals between neighboring cells, the larger spaces which often occur in the loosely woven connective tissues, and also the contents of an inconspicuous system of tubular channels known as lymphatics. A recent writer, Starling, has suggested that a distinction should be made between the fluid in the lymphatics and that which is not enclosed in vessels of any sort. He would restrict the term lymph to the first application, and would speak of the other as tissue-fluid. This usage appears highly desirable and is increasingly current.

Lymph, in the sense of tissue-fluid, cannot be collected for analysis. Considering the delicacy of the capillary wall and the probable freedom with which exchanges take place through it, there is reason to believe that this fluid must closely resemble the blood-plasma. When a tissue is the seat of an active metabolism the income and outgo of its cells must tend to alter the composition of the adjacent lymph and to make it less like the plasma. The general effect will be to reduce the oxygen to a low level, to raise the carbon dioxid content correspondingly, to consume a fraction of the organic food, and to add miscellaneous waste-products. The lymph which can be obtained by cutting one of the larger lymphatics of the body has these characters. This lymph may not be precisely like the mixture which exists in close contact with the living cells, but it is probable that the differences are not great. According to a view formerly universal lymph can work its way from any interstice of an organ into the branches of the lymphatics, and so to larger vessels of the same class. Most authorities now hold that there is a definite separation between the unwalled spaces of the tissues and the interior of the true lymphatic system. If this is the correct conception, we have good reason to differentiate lymph from tissue-fluid. We may adopt either view provisionally without being seriously misled. Lymph contains white corpuscles and blood-plates. Since it has in it some fibrinogen it may coagulate, but owing to the absence of red corpuscles the clot is frail and tremulous.

CHAPTER XIII

THE CIRCULATION

We must postpone still further our account of the absorption of the products of digestion until we shall have made clear the general course followed by the circulating blood. We have quoted the estimate that the body contains 8 or 10 pounds of blood. At a given moment about one-fourth of this may be assumed to be in the thorax (the heart, the lungs, and the great blood-vessels), a fourth in the skeletal muscles, a fourth in the liver, and the remaining fourth elsewhere. The ceaseless movement of this large volume of liquid is maintained by the beating of the heart.

This organ consists of two halves, right and left, completely separated, so far as their cavities are concerned, by a middle partition. Regarded as a mass of muscle, the heart is single; considered as a pump, it is double. Each half is, in a literal sense, a force-pump. Each side shows us two communicating chambers, an auricle above and a ventricle below. The auricles *receive* the blood, which the corresponding ventricles will shortly *discharge*. The vessels leading to the auricles are called veins; those which convey the blood from the ventricles are called arteries. The auricles have thin walls, while the ventricles are fitted for their task by heavy muscular development. The left ventricle has much more power than its fellow, and the necessity for this will soon be evident.

A single great artery, the aorta, springs from the left ventricle. Its branches reach all parts of the body. Subdividing repeatedly, they introduce the blood at last into the *capillaries*, the innumerable vessels of the smallest order through whose exquisitely thin walls take place the

exchanges with the lymph already described. The word "capillary" means hair-like, but the description falls far short of indicating the actual slenderness of these microscopic tubes. They are so narrow that the corpuscles pass through them practically in single file. The capillar-

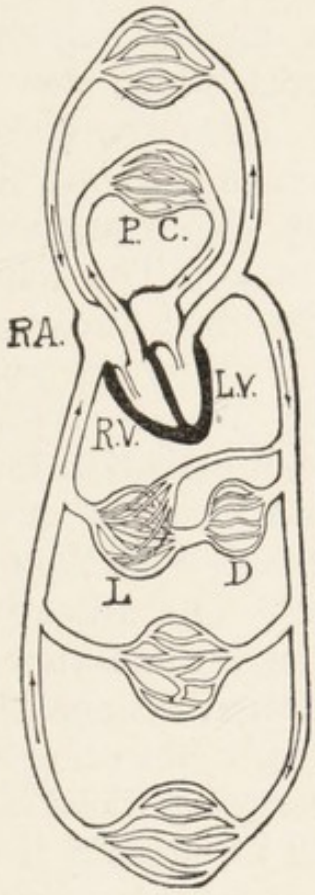


Fig. 17.—In this diagram, as is usual in such cases, right and left are reversed. This is as though the observer were looking at another subject. The short pulmonary path is to be traced from the right ventricle to the left auricle (*P. C.*). Alternative routes are suggested for the passage of the blood through the greater circulation from the left ventricle to the right auricle. The blood which traverses the digestive tract (*D*) passes through a second set of capillaries in the liver (*L*) before it can return to the heart. Note that the liver has in addition a separate arterial supply of blood.

ies are short and soon unite to form the smallest veins. These lead the blood back toward the heart, joining as they go to form larger and less numerous channels, until at the last there are but two great veins. These enter the right auricle, one from above and one from below. The sweep of the blood from the left ventricle through the body

at large and back to the right auricle is called the *systemic* circulation.

From the right auricle the blood descends to the ventricle of the same side, and is sent forth again, this time through the vessel known as the pulmonary artery. This immediately forks into branches which plunge into the two lungs. The smaller pulmonary arteries lead to rich capillary networks which are wrapped around the numberless air-sacs. Here the corpuscles are recharged with oxygen and the carbon dioxid of the blood is reduced to a standard amount. Four pulmonary veins return the blood to the left auricle. The relatively short journey of the blood from the right ventricle to the left auricle by way of the lungs is called the *pulmonary* or lesser circulation.

It is necessary to call attention to the fact that the adjectives "arterial" and "venous" are not used in a sense which exactly corresponds with the meanings of the nouns "artery" and "vein." The adjectives have a chemical significance; the nouns, an anatomic one. Arterial blood is blood fully oxygenated; venous blood is blood more or less deficient in oxygen. But an artery, as has been said, is merely a vessel carrying blood away from the heart. The blood within will be arterial if we are observing the systemic circulation, and venous if it is in the pulmonary. So the systemic veins are filled with venous blood, while the pulmonary veins carry that which has just been brought up to the arterial standard through coming into relation with the air in the lungs.

From what was stated above with respect to the distribution of the blood, it is evident that less than one-fourth of the whole volume is in the pulmonary circulation at one time, but the student must be cautioned against the conclusion that the pulmonary circuit is traversed by less blood than passes through the systemic pathways. The quantities passing along the two routes are inevitably equal, for it is, after all, the same blood which runs through each in turn. If a slack chain is traveling over two wheels,

as shown in the diagram (Fig. 18), the links pass the two in equal numbers, and yet there are constantly more links on their way from *L* to *R* than from *R* to *L*.

When we speak of a heart-beat we mean a co-ordinated contraction of the heart's peculiar muscle. The phenomenon includes two phases: a brief and not forcible contraction of the auricles followed by a longer and much more powerful closing in of the ventricles upon their cavities. The ventricular contraction is the essential factor in propelling the blood. Valves between the auricles and the ventricles permit the latter to fill during their period of

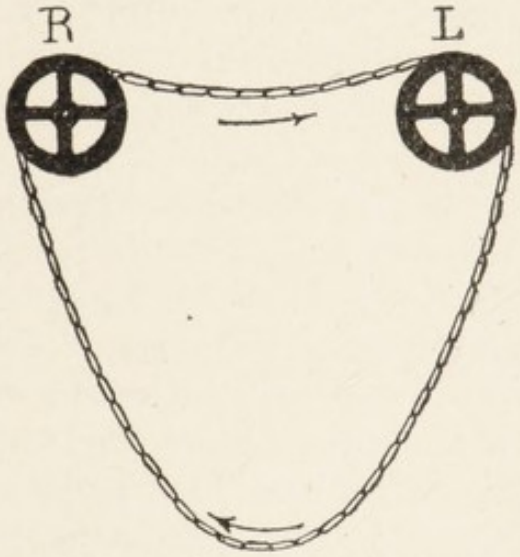


Fig. 18.—For explanation of figure see text.

relaxation, and forbid the backward flow from the ventricles when they are emptying themselves. Other valves at the commencement of the aorta and the pulmonary artery allow blood to pass out during each contraction of the ventricles, but not to return from either artery into the heart when the resting phase ensues. The action of the two sets of valves is precisely on the principle of the two which make a syringe-bulb an effective force-pump. The right and left halves of the heart act practically at the same time.

Either ventricle when full may contain 5 or 6 fluidounces of blood. As it contracts it reduces its capacity and dis-

charges blood in like measure. At the conclusion of the active period it may have nearly obliterated its cavity, or the effort may fail while there is still considerable blood within. Estimating an average output from one ventricle to be about 4 ounces, or 100 c.c., it is apparent that forty beats will suffice to discharge from one side of the heart an amount of blood equivalent to the entire quantity of circulation (40 x 100 = 4000 c.c., or 4 liters). In other words, it will require less than one minute for all the blood to pass successively through both sides of the heart. When this statement is made it should be remembered that certain routes in the systemic circuit are many times longer than others (compare the path to and from the feet with that to and from the esophagus), and some corpuscles may revisit the heart two or three times while others are making one prolonged journey.

It would be out of place to enter here upon a discussion of the value of the auricles. From a mechanical point of view they contribute but little of the energy required for driving the blood. They serve to accommodate the gathering volume of blood which the veins bring in during the rather prolonged contraction of the ventricles, and they secure a more efficient filling of the lower chambers of the heart. While their muscular development is slight, their automatic power is peculiarly marked, and it is a fair statement that the ventricle, under normal conditions, is stimulated to perform each beat by an influence radiating to it from the auricle. If there is an interruption of certain strands of tissue which normally unite the two, they cease to maintain the same rhythm, the auricle continuing at the accustomed rate, while the ventricle beats much less frequently. When the heart is dying the last signs of pulsation are in the auricles.

The Portal Circulation.—In our general description of the course followed by the blood on its way through the body it was stated that when it has passed through a set of capillaries it is gathered up into veins to be returned to the right auricle. An important departure from this

order is now to be indicated. The blood which has traversed the small vessels of the digestive tract (including the stomach, both intestines, the pancreas, and the spleen) would be expected to make its way back to the heart through branches of the systemic veins. The actual arrangement is as follows: A large vessel receives all the blood from this region and carries it into the liver, where a second set of capillaries is entered. When these unite it is to form short veins discharging into the chief vein of the body, just below the diaphragm and practically within the boundaries of the liver. The channel leading from the organs of digestion to the liver occupies a unique position. Inasmuch as it is formed from a capillary system it seems to be a vein, but since it also supplies a capillary system it may be contended that it is an artery. Its structure favors the view that it is a vein and it is so called. The vessels which gather the blood from the digestive tract and distribute it inside the liver are said to form the portal system; the chief conductor described above is called the portal vein. An important consequence of this arrangement is that the absorbed products of digestion, so far as they are in the blood rather than the lymph, are brought under the influence of the liver before they go elsewhere.

The question will naturally be raised whether the liver is supplied exclusively with venous blood. Provision is made for a supplementary supply through what is known as the hepatic artery, a vessel which is an offshoot of the general arterial system, and which, of course, introduces into the liver blood rich in oxygen. An analogous condition may be noted in the lungs, where the main currents are the venous streams coming from the right side of the heart, but where there are also interwoven in the tissue much smaller vessels which take their rise in the arterial tree springing from the left ventricle.

The problems of the circulation fall into two classes: There are those which are purely physical and which can be approximately reproduced and more or less successfully studied in lifeless models. There are also those which have

to do with the behavior of the organs concerned when they are viewed as living structures. Under the first class are included the facts of blood-pressure, velocity of flow, the resistance overcome, etc. The interpretation of such data is almost a science in itself and is known as hemodynamics. Among the questions of the second sort are the mysterious automaticity of the heart and the nervous government of the quantity and the distribution of blood flow. These difficult matters may well be left to be briefly dealt with toward the end of the book, when the general work of the central nervous system will be presented. We must, however, devote some space at this time to the fundamentals of hemodynamics.

The Character of the Blood Flow in Vessels of Different Classes.—When an artery is cut the blood escapes in a forcible jet which may spring to a distance of several feet. The stream is not steady, but mounts and declines in a rhythm corresponding with the heart-beat. A good deal of pressure must be applied to restrain the bleeding. If a vein is severed the flow of blood is rapid and copious, but easily repressed. It is uniform so far as can be judged. These observations lead to the conclusion that the blood in the arteries is under a high average pressure, with large fluctuations from moment to moment. The pressure in the veins is evidently very low.

The diminution of pressure between the arteries and the veins can be simply explained. When the blood is started on its course through the systemic circulation the high pressure which it exerts against the elastic wall may be regarded as a measure of the energy which the ventricle has impressed upon it. When it draws near the right side of the heart, the goal of its journey, its abated pressure is the sign that the initial energy has been spent. How has it been consumed? There is but one possible answer: It has been transformed into heat in overcoming the friction encountered in the vessels. Analogous conditions can be demonstrated for any tubular system through which liquid is driven. In the mains which carry a city water-supply

from a pumping-station to distant points there is a similar decline in pressure along each line as it is followed farther from the fountain head. (The assumption is made that we have to do with pipes which are on the same level throughout.)

In any such system the cutting down of the pressure will be abrupt at any point on the route where there is an unusual impediment to the flow. This is the case in the body where the blood-steam is so extensively subdivided to enter the smallest vessels. Subdivision of channel means multiplied surface for friction. Thus there occurs a radical drop in pressure between the smallest arteries in which we can measure it and the veins of similar size. The highest pressure developed anywhere must be in the left ventricle when it is discharging the blood, for it is then to be regarded as the starting-point of the circulation. The lowest pressure which is ever registered is probably in the same ventricle when it is beginning to fill, for now it is the terminus of one of the two circuits.

The swelling of the arteries which promptly follows each ventricular contraction is what we recognize as the pulse. It is the sign of a newly introduced portion of blood distributing itself in the vessels. We have said that the veins show no such rhythmic enlargement. We have, therefore, to account for the conversion of the intermittent flow in the arteries into the constant flow in the veins. The principal factor concerned is the marked elasticity of the arterial trunks. It will be helpful to refer to the artificial devices which serve the same purpose in connection with force-pumps. A familiar one is the air-chamber. This is a large container communicating with the outflow-pipe. Whenever a stroke of the pump drives water along this pipe a certain share proceeds directly toward the outlet, while another fraction turns aside into the air-chamber. During the return stroke when no water is issuing from the pump barrel the air which a moment before underwent compression in the chamber tends to regain its original volume, and in so doing forces water through the lateral

branch and thence along the main pipe. The intermittent delivery through the valve is transformed more or less successfully into a continuous flow through the remote outlet.

The neutralizing of intermittency in the blood system is referable to the same principle, but the elastic compensator is not to be found as a single localized feature; it is discovered in the universal capacity of the arteries to stretch and to regain their former size. At the beginning of the aorta or of the pulmonary artery we have complete intermittency, the blood alternately forging ahead and halting. But each portion of blood ejected from the heart finds room for itself partly by distending the arteries and not altogether by driving forward the blood which is before it. Hence, when the ventricles relax and the outpouring of blood ceases there is still an onward movement in the smaller and more distant arteries, because the larger ones, which were momentarily overdistended, are now contracting and sending along part of their accumulation. The farther we go from the heart the more largely the driving of the blood is to be attributed to the reaction of the stretched arterial walls and the more nearly uniform it becomes. This does not mean that the whole power keeping up the circulation is not to be sought in the heart-beat; it merely means that this energy may be stored temporarily by these elastic structures and rendered back again.

The facts we have been treating may be expressed in another way. The arterial tree forms a reservoir of considerable capacity. Within it is an amount of blood so large that the single contribution of the ventricle makes a rather small addition to it. The escape of the blood through the terminal twigs cannot cease while there is so much stored under a high pressure in the aorta and its branches. The heart may omit or "drop" a beat without noticeably diminishing the flow through the capillaries. A standstill will be reached only when the arteries have attained a degree of contraction such that the internal pressure is no higher than that in the veins. The homely

illustration (Fig. 19) which accompanies this may be helpful. The pump delivers water intermittently to the leaky trough, keeping it filled to a level which is nearly constant, though fluctuating a little in the rhythm of the strokes. Meanwhile the escape of water through the cracks is all but uniform in its rate. One important difference between the pump and trough, on the one hand, and the circulatory system, on the other, lies in the fact that in the

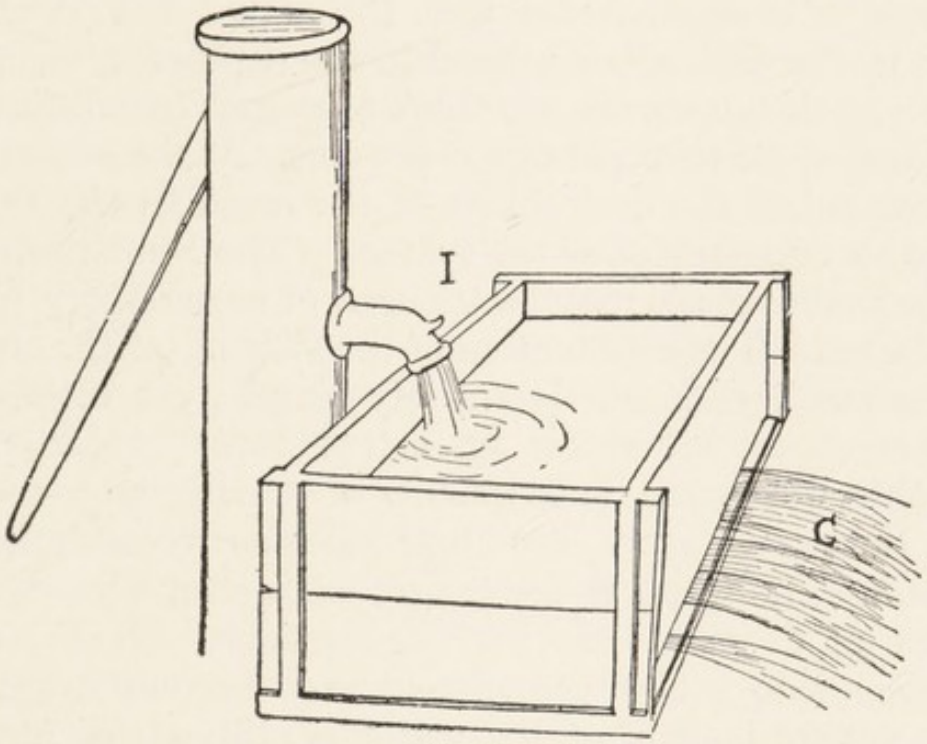


Fig. 19.—At *I* the discharge is in gushes with pauses between—the type of the expulsion of blood from the heart At *C* the escape through the cracks is at a practically constant rate; this is true of the blood flow through the capillaries.

first case the driving force is gravity; in the second, it is the reaction of the enclosing elastic walls.

A set of facts which it is well to separate in one's thought as completely as possible from considerations of pressure is the body of data respecting the linear velocity of the blood. By this is meant the rate of advance of the average corpuscle. In any vessel the stream runs more swiftly in the central axis and lags along the walls. The velocity in the arteries rises and falls as does the pressure, but, on

the whole, is relatively high. The aorta is passed at a speed of at least a foot in a second. The veins also are traversed at a high velocity, though the figures are somewhat lower than for the arteries. The movement in the capillaries is in sharp contrast to that in both arteries and veins, being exceedingly slow, perhaps $\frac{1}{2\frac{1}{5}}$ inch in a second. It appears that a corpuscle may take as long to go through a capillary link which would scarcely span the breadth of a pin-head as to travel from the heart to the brain.

When it is remembered that the actual service of the blood to the tissues is rendered in the capillaries (since all other vessels have walls too thick to permit free diffusion), the value of the slow passage is obvious. At the same time, one recognizes the desirability of the rapid transit to and from this department of the system. The heart itself and all the main vessels may be thought of as accessory to the capillaries. The explanation of the slowing of the stream in the small channels is entirely simple, yet often misapprehended. Whenever an artery forks to form two branches, these are individually of smaller cross-section than the parent stem, but their *combined* cross-section is greater. The result is the same that is seen when a river widens or deepens—the current slackens. If the river broadens into a lake the current may become imperceptible, yet we know that the water is still setting forward toward the outlet.

Are we then to believe that the capillary system is many times wider than the aorta or the great veins? There is no escape from this conclusion: their number is so vast that, despite their infinitesimal size as single conveyors of the blood, collectively they form the broadest division of the entire path. If they fail to suggest a lake, an analogy may be found in the tangled swamp in which a stream loses itself, breaking into many sluggish arms, from which at last the waters converge to resume a rapid course over a narrow bed. The acceleration noticed as the veins are followed toward the heart is merely a sign that as their number grows less their combined cross-section also contracts.

The Movement of the Lymph.—Just as we find veins returning from every part of the body, we can make out, though with much greater difficulty, small vessels bringing lymph in the same general direction, that is, toward the thorax. Like the veins, they unite as they draw near the heart, and the great majority eventually contribute to a trunk known as the *thoracic duct*. This springs from the union of many branches in the abdominal cavity, pierces the diaphragm, and can be traced upward in front of the spinal column until it empties into a great vein which is bringing the blood from the left shoulder toward the right auricle. A comparatively insignificant group of lymphatics centers at an outlet in the corresponding position on the right.

The onward movement of the lymph in its channels is parallel with that of the venous blood, but is incomparably slower. It is sometimes almost entirely arrested. The lymphatics bear away a certain overflow of fluid and may be regarded as supplementing the service of the veins. As to the cause of the halting movement of their contents, the simplest statement that can be made is somewhat as follows: The formation of new lymph in all the organs crowds away the lymph previously in the beginnings of the lymphatics; this is the central fact to be considered. The energy required is derived partly from the heart, since liquid may be forced out of the capillaries by its transmitted pressure, and partly from other sources too obscure to be discussed. The lymph is generally referred to as a carrier of waste, but a partial exception must be made in favor of the lymph coming from the intestinal area during digestion. This lymph may contain absorbed food, principally fat. It was in the mesentery that lymphatics distended with milky liquid were first seen. They were called *lacteals* because of their appearance, and this term is still used in a local sense.

CHAPTER XIV

THE ABSORPTION OF THE FOOD-STUFFS

If two unlike solutions are separated by a membrane, such as a sheet of parchment or some artificial substitute, they will usually tend to equalize both in composition and concentration. When, for example, potassium chlorid and sodium chlorid solutions are placed on opposite sides of such a partition, each salt proves its ability to pass through the barrier, and in the course of time there will be uniform mixtures in both compartments. This is said to show that the salts are *diffusible* and that the membrane is *permeable*. Different membranes are permeable in very different degrees, and the freedom with which various salts pass through a particular membrane is also far from constant. Some substances may appear freely soluble and may go readily through ordinary filters, but may hardly diffuse at all. This, as a rule, is the case with the proteins. If a mixture of unboiled white of egg and sodium chlorid is on one side of a membrane and the other side is washed with running water, nearly all the salt will escape, leaving the protein practically undiminished. The process by which diffusible salts are encouraged to separate themselves from substances which cannot accompany them through the membrane into the water beyond it is called *dialysis*.

The products of digestion are, in general, much more diffusible than the food-stuffs from which they are derived. Starch, even when boiled for a long time, does not make its way through ordinary membranes; the sugars do so with relative ease. Fats are not even soluble in water; soaps and glycerin are diffusible compounds. Peptones arising from the hydrolysis of proteins have some power to penetrate membranes, and the simpler amino-acids pass

still more freely. We might picture the situation in the intestine somewhat as follows: The blood flows steadily beneath a rather complex cellular wall, the other surface of which is bathed by the mixed products of digestion and the digestive secretions. Peptones and amino-acids, sugars, soaps, and glycerin, being formed in relative abundance in the intestine, diffuse into the blood, which contains little of these bodies. If the blood were to stand still the small volume in direct relation with the absorbing surface would accumulate digestive products until it held them in the same concentration in which they exist in the canal. Then a state of equilibrium would be established and no further transfer to the blood would occur.

Detailed observation shows that the facts of absorption cannot be expressed in this simple manner. It has already been hinted that large allowance must be made in such a case for the fact that the membrane under examination is alive. Its cells may discharge material at one surface quite unlike that which they receive at the other. They probably have a considerable metabolism. This means that energy is set free within their borders and a share of it may be applied to the moving of the absorbed food. We have previously called attention to the parallelism between secretion and absorption.

Before we can go further with this discussion something must be said concerning the place of absorption and the minute anatomy of the structures involved. There is a measure of absorption from the stomach. Until rather recently this organ was not credited with any marked powers of this kind, unless it were in the case of *alcohol.* This is a highly diffusible compound and its prompt entrance into the circulation is noteworthy. When one says of a glass of wine, "This goes to my head," the statement is literally true. The alcohol strikes through the walls of the stomach at once and is borne to all parts of the body, including the brain. On the other hand, water is not at all freely absorbed when it is taken into an empty stomach. It is known to pass the pylorus in practically

unchanged volume. Some poisons produce no positive effects while in the stomach, but exert their action promptly when they pass to the small intestine.

As regards the sugars and the products of peptic digestion, it is now believed that there is a considerable absorption of these substances from the stomach. They disappear most rapidly when they are present in high concentration, and the process is promoted by condiments which increase the blood flow under the gastric mucous membrane. When all reasonable allowance is made for the part played by the stomach in absorption, the fact remains undisputed that the major part of the work is done below the pylorus. Furthermore, since, as has been said, there is usually little valuable material left to be recovered by the colon, it becomes evident that the small intestine is of central importance.[1]

A striking peculiarity of the small intestine is the extension of its internal surface. This is effected, first, by the numerous cross-folds which cut into its cavity, and, second, by the microscopic projections which stud its lining. These are the *villi*. An individual villus may be described as a minute finger-shaped process. It rises above the general surface in a contrast to the glands, which sink below; the villus is a peg, as the gland is a pit. Obviously the existence of the villi increases many times over the number of cells in contact with the intestinal contents. These cells are described as columnar; they are prisms standing side by side, with their larger surfaces in contact and their smaller ends presented to the interior of the intestine and to the loose internal tissue of the villi. A certain share of absorption may take place through the crevices between the cells, but the main transfer of material seems to be through their own protoplasmic bodies.

[1] The provision made for absorption is strikingly liberal. Much of the small intestine may be removed and the remainder still prove adequate. Tuomikoski reports the extreme case of a patient who lived seven years with only 80 to 90 cm. of small intestine—less than 3 feet of the normal 20. (Acta Chirurgica Skandinavica, lxv, 1929, 375.)

The interior of a villus is filled by a confusing assortment of cells. There is evidence that some of these are contractile. Microscopic examination of the living intestinal lining is reported to show villi alternately extending and

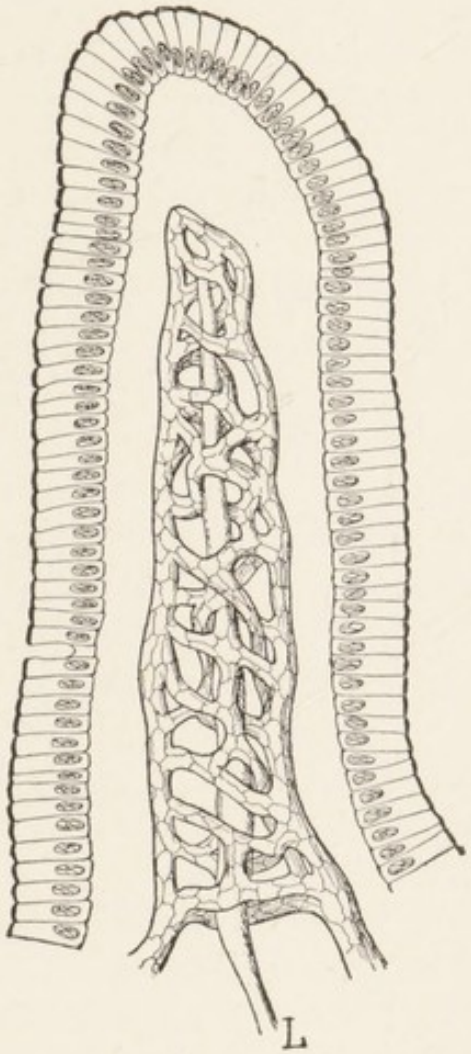


Fig. 20.—This is a conventionalized drawing to show the essentials in the structure of a villus. The lining cells of the intestine are shown as in section. Within is seen a tangle of capillaries, and at the very core of the villus a lymphatic (*L*). The loose tissue, which in reality exists inside the villus, has been ignored for the sake of simplicity.

retracting like marine organisms on the bottom of an aquarium. Between the internal cells there are probably intervals containing lymph, and near the central axis of the villus is a rather definite *lymphatic* channel. It is a small branch of the general lymphatic system and opens one

way by which food can pass from the seat of absorption to the veins in the thorax, there to mingle with the blood. Between the exposed cells of the villus and the lymphatic at its core is interposed a net of capillaries carrying blood which has come from the neighboring aorta, and which will flow through the liver before it returns to the heart. It may be said at once that, of the two possible routes for absorption, the portal system is the more important. Such food as enters the lymphatics will not have to run the gauntlet of the liver on its way to the general circulation.

The statement has been made that the cells lining the intestine do not act in a way that can be imitated by lifeless models. The fact is covered by the expression that they exercise selective powers. Too much might easily be inferred from this phrase; there is the same danger which was pointed out in connection with the pyloric sphincter, the inclination to credit the cells with something more like intelligence than it is right to assume for them. It is reasonable to believe that however complex and unexpected may be the behavior of the cells concerned, a mechanistic explanation would be apparent if our knowledge were sufficiently full. What is meant by selective action can be readily illustrated.

If a comparison is made in the laboratory to determine the relative rates at which dextrose and magnesium sulphate make their way through an ordinary membrane, the sugar will lag behind the salt, although both pass with relative freedom. If a mixture of the two is introduced into the living intestine the impression is totally different. The sugar is absorbed, while the magnesium sulphate is kept back. We say that the mucous membrane is impermeable to this salt, though we can hardly picture the peculiarity of structure which makes it so. A salt which is refused absorption by the intestinal wall will act as a laxative, for it will hold back from absorption a large quantity of water and this will be swept through by the peristalsis. An investigator has called attention to the fact

that all the common precipitants of calcium are denied passage into the blood, and may, therefore, be reckoned as cathartics. These include, beside the sulphates, the phosphates, the citrates, and the tartrates.

Again and again we find as we pursue the subject that laboratory tests give us little indication of what may be expected of the intestine as an absorbing mechanism. Some substances usually held to be indiffusible pass into the circulation with comparative readiness. Even egg-albumin, a protein of enormous molecule, may enter the blood. This was recently proved by the observation that after eating a number of raw eggs the albumin may be found in the urine. It evidently reaches the capillaries to some extent before it can be hydrolyzed by the digestive enzymes, even at a time when these are presumably present and active. The application of mild poisons to the lining of the intestine causes it to behave much more like the typical indifferent membrane. Thus a weak solution of sodium fluorid (which does not visibly disorganize the cells) wipes out the selective properties which have been instanced. This makes it seem the more probable that the normal processes require the application of energy, and that accordingly they cannot continue after the death of the cells.

A mosaic surface formed of cells, each one of which is a living body, is far from comparable with a homogeneous partition. Even if we leave out of account the crevices between the cells which may bear a part in absorption, as already noted, we must consider the individual cell to be an elaborate structure. Its surface layer is undoubtedly different in its chemical nature from its interior. There is good reason to believe that the exposed border differs entirely from the end which abuts on the connective tissue. A result of this complex organization is the existence of a property that might be called "polarity," that is, a capacity to act in one direction rather than the other. A somewhat ponderous expression for the same idea is found in the phrase "irreciprocal permeability." This means special-

ization for absorption, and strongly suggests that if the cells could be reversed in their relation to the interior of the intestine they would begin to absorb from the lymph and secrete into the canal. Gland-cells may be said to have irreciprocal permeability in this reversed sense.

The departure of the intestinal lining from the behavior of a common membrane is still more obvious when we note that absorption may be accompanied by chemical transformation. The food-stuffs which leave the interior of the canal do not of necessity reappear in the circulation in the same form. Two possibilities exist: either the process of digestive cleavage may be continued during the passage through the wall, or a recombining of the products of digestion may be accomplished. The first action is thought to occur to some extent when the peptones formed in the cleavage of proteins are moving toward the blood. It will be recalled that the enzyme erepsin, having the power to decompose peptones still farther, is obtainable from these cells, and it is quite possible that its action is intracellular.

The opposite property, that of synthesizing, is illustrated by the behavior of the products of fat digestion. We have seen that the pancreatic enzyme hydrolyzes fats, with the formation of fatty acids and glycerin as the first result of the cleavage, and that the fatty acid may be changed to soaps, though we do not know how extensively they undergo this second change. It follows that it is these bodies which disappear from the intestine, but they are not to be found at all freely in the contents of the lymphatics. In their place we have neutral fat evidently reconstructed during the transfer. Microscopic study of the cells through which the material has been passing shows that the border adjoining the cavity of the intestine is without fat droplets, but that these occur deeper down, increasing in size toward the other border. The appearance strongly indicates that some compounds other than neutral fats entered the cells and underwent a transformation while progressing through the protoplasm.

CHAPTER XV

THE METABOLISM OF FATS AND CARBOHYDRATES

It was pointed out early in our treatment of the subject that foods serve a twofold purpose: to some extent they are built into the body as relatively permanent parts of its structure, while in a much larger degree they are steadily oxidized, yielding their energy to maintain its activities. The proportion between the two divisions of the supply cannot be constant. Clearly, the fraction of the diet devoted to construction must be larger in childhood than in adult life. There may be other periods during which the constructive work is notably prominent, for example, recovery from illness or from fasting, pregnancy, and perhaps athletic training. Apart from these times we must assume that the actual building of tissue is a very small item. In other words, the living matter of the body is comparatively stable and needs only slight though perfectly definite contributions to insure its up-keep from day to day.

The food-stuffs entering the circulation may be destined for immediate destruction or for storage. Throughout long terms of our lives a fair balance is preserved between the income and the consumption of these compounds. If we receive in one day certain quantities of proteins, fats, and carbohydrates, and there is evidence of an exactly equal decomposition of the three classes of material, we cannot say with precision whether the oxidation affected the particular food eaten or corresponding matter stored previously, but in either case the condition of the system at the beginning and at the end of the twenty-four hours is the same. We must now proceed to discuss the possibilities of transformation and retention of the different food-stuffs, and we shall find that the story is most simple in the case of the fats.

Fat Metabolism.—It has been customary to say that fat never becomes anything else until it is decomposed with release of energy. This statement may be too sweeping to cover all the conditions which arise in disease and has come to be questioned even for health. We have traced the fat from the walls of the intestine into the lymphatics. From the smaller branches it must find its way to the thoracic duct, and through this vessel it goes to merge with the general blood-stream. In the blood, the lymph, and the tissues at large fat is present in a small percentage. We must now give attention to the special provision made for the storage of fat in what is called *adipose tissue.*

The word "fat" is used in two senses. In its strict chemical meaning it describes a certain type of compound, and it is this usage which we have thus far employed. But when we speak of the fat of meat we include something more. We mean a form of connective tissue in which the cells hold a large accumulation of fat in the chemical sense. Under the microscope this tissue is seen to be composed of a fibrous network holding within its meshes these distended cells. The fat which they contain is in drops of such a size that the protoplasmic portion of each cell seems a mere envelope, while the nucleus is crowded to one side. So it happens that while the fat is really an inclusion, it forms a very large percentage of the whole mass. When a piece of adipose tissue is subjected to the action of gastric juice the protein of the cells and fibers is rapidly digested, and the actual fat, being liberated, rises to the top and floats as a clear layer of oil.

Of course, the amount of adipose tissue varies widely with the individual. Still it is more abundant in subjects of spare build than is usually supposed. The hollow shafts of the long bones, such as those of the arms and legs, contain what is called the white marrow. This is typical adipose tissue. A large deposit is to be found at the back of the abdominal cavity, where it closes round the upper parts of the kidneys. Flakes of it occur in the mesentery and on the surface of the heart. It is developed in the

deep eye-sockets. In subjects better nourished there will be more or less of this tissue widely distributed over the body occupying a position between the skin and the underlying muscles—the so-called subcutaneous fat. This may be indefinitely increased in the obese. Another characteristic of obesity is the gathering of adipose tissue in the great omentum, the sheet of membrane hanging from the lower border of the stomach. When much fat is present in this situation the ventral wall of the body has a double burden, one layer of this reserve material outside and a second within the abdominal muscles.

We shall postpone to a later time any discussion of the factors which influence the accumulation of fat in the system. A point previously made is to be insisted upon, that the fat of the body is not derived solely, nor, indeed, chiefly, from the fat of the food. We shall presently consider to what extent it is formed from the other food-stuffs. Whether there is a great or only a moderate amount, it will serve to maintain the activities of the muscles during periods of insufficient feeding or absolute fasting. When an animal has died from starvation but little fat can be found in its tissues. The reduction of the fat presumably present at the beginning of inanition has been estimated to have reached 97 per cent. of the supply when death finally supervenes. The power to endure starvation is naturally greater for an animal or a man having a large initial store.

For each species the body fat has a nearly constant character. There is a certain ratio maintained between the several fatty acids, and, as a result of this, a definite melting-point. There cannot be such a diversity here, as is the case with the proteins of different animals, but there is a similar appearance of individuality. Accordingly, when one animal preys upon another of a different species and is nourished at the expense of its victim, it does not store precisely the form of fat which it has eaten, but modifies it to conform to its own standard. The making over is a still more marked phenomenon when a vegetable oil is eaten and transformed into animal fat.

The question whether the body can under any circumstances transform fat to sugar has been much discussed. For a long time the weight of evidence seemed to be decidedly against such a change. Many physiologists are now convinced that the glycerin fraction of fat can be worked over to form dextrose. This represents only about one-ninth of the molecular mass of fat. Whether the fatty acids can possibly yield sugar is still a matter of controversy. When an isolated muscle is made to work to exhaustion its content of carbohydrate is greatly decreased. Its fat is reported to remain undiminished. This shows that the muscle deprived of the coöperation of other tissues cannot use fat for fuel. When the system is intact it can undoubtedly do this. Just what organs make the fat available, and whether through a transformation to sugar remains to be discovered.[1] (See p. 38.)

The Metabolism of Carbohydrates.—The sugar of the blood is usually called dextrose or glucose.[2] As a matter of fact, it cannot be strictly correct to speak of a single sugar in the plasma, for there are probably three at least. Glucose, however, is undoubtedly the principal one, and so far as we know the possible services to the body are practically the same for all. Reference has already been made to the fact that the quantity of sugar in the blood is small, but singularly constant. It is now time to explain how this constancy is maintained.

It has been stated that the body contains relatively little carbohydrate in spite of its large supply. When it is considered that the entire volume of blood contains less than 10 grams of sugar, though the amount absorbed after a single meal may be as much as 100 grams, it appears strange that there should be, as a rule, no significant increase in the percentage circulating during the period of digestion. The solution of this problem was achieved in

[1] The evidence for transformation of fatty acids to sugar may be found in "The Fuel of Life," Macleod, Princeton University Press, 1928.

[2] The word glucose has a commercial use which does not correspond closely with its strict scientific meaning. (See page 253.)

great measure by the French physiologist Bernard, near the middle of the last century. Knowing that the incoming sugar passes to the liver, he anticipated that this organ might have the power to take the surplus from the passing stream and store it temporarily in some form.

Glycogen.—Investigation showed that there could be obtained from the liver of a well-fed animal (rabbit) considerable quantities of a carbohydrate resembling starch. This substance is called glycogen. Its presence within the cells of the liver can be demonstrated in microscopic preparations. Its molecule is of unknown size, and it is capable of undergoing digestion in the same manner as vegetable starch with the formation of sugar. The amount may be strikingly large, reaching, in the rabbit, one-fourth the total weight of the liver, deducting the weight of the blood usually contained in it. In the human liver it does not attain to such a high percentage, but may still equal something like 10 per cent. of the net weight of the organ. This means that a full-sized liver may hold 150 grams of glycogen.

Bernard's interpretation of his discovery was somewhat as follows: The liver is the carbohydrate bank of the body. Like any bank, it is subject by turns to deposit and withdrawal. Its hoard is increasing when much sugar is arriving from the intestine, for it is then diverting the surplus from the blood of the portal circulation. The change by which sugar is made into glycogen is clearly just the reverse of the digestive process, a dehydration and a condensation to form larger molecules as contrasted with the familiar hydrolytic cleavage. The liver cells seem to be stimulated to make this change by the rise of the percentage of sugar in the portal blood. When absorption ceases it may be assumed that the sugar of the blood in general sinks slightly in amount. This condition appears to cause a reversal of the prevailing reaction in the liver, the stored glycogen is gradually transformed to sugar, and this passes out to renew the supply in the circulation. The approximate constancy of the sugar in the blood is thus

accounted for in the main by the power which the liver possesses to remove or return it, according to the shifting conditions.[1]

The making of glycogen from sugars occurs only during life. The converse change from glycogen to sugar takes place freely after death, and is doubtless due to an enzyme. It might be anticipated that a comparatively short period of fasting would suffice to exhaust the glycogen of the liver. As a matter of fact, there is a large reduction in the first day, but the removal then proceeds slowly and is scarcely ever completed. The disappearance is greatly hastened by muscular activity, most effectually by the intense convulsions produced by strychnin-poisoning. For human subjects it has been shown that glycogen is consumed rapidly under the influence of iced baths. (How we are able to judge of the abundance or scarcity of glycogen in living men will be explained in another connection, p. 188.)

For some time after Bernard first called attention to the "glycogenic function" of the liver, the fact that glycogen is deposited also in the skeletal muscles was overlooked. In these tissues it does not reach any such percentage as may be found in the liver, but inasmuch as the muscles form nearly half the entire mass of the body, a small percentage means a large aggregate. Collectively, the muscles have commonly been estimated to hold an amount equal to that in the liver, and there is a growing impression that they contain even more. The total glycogen in the system may probably be as much as 400 grams, or nearly a pound. The question which now calls for consideration concerns the importance of maintaining such a strict constancy in the sugar-content of the blood.

Some light is thrown on this matter when we observe the result of artificial increase of sugar concentration. This may be brought about by injecting sugar solution

[1] An animal deprived of the liver cannot be kept alive much beyond twenty-four hours. During the limited period of its survival it has been shown that the sugar of the blood falls to an exceedingly low level and that a transient improvement in general condition follows the injection of dextrose into the circulation.

into the blood-vessels. If this is done freely there is excessive lymph-formation and other evidence of deranged conditions in the circulatory system. A symptom to which especial attention must be called is the appearance of sugar in the urine under such circumstances. The kidneys are so organized that any distinct rise of sugar in the blood leads to the excretion of the excess. Thus the composition of the blood is restored to the standard, while potential food is lost to the tissues. Such a waste of sugar is less likely to follow abundant feeding of foods rich in it than to occur after the experimental procedure just described, but it may nevertheless result from the selection of peculiar diets. It is then called *alimentary glycosuria* and it is induced somewhat readily in some persons by eating sugar, but hardly ever in wholly normal subjects by eating starch. The differing reaction is presumably explained by the fact that sugar requires a brief digestive treatment and is then rapidly absorbed. Starch, on the other hand, has to pass through serial stages of digestion, and the absorption of the resulting sugar is extended over a longer period. In the first case we may suppose that the inrush of sugar overwhelms the liver, which is unable to arrest all of it. That which goes by raises the sugar content of the blood above the level at which it begins to pass into the urine.[1]

If for any reason much of the glycogen in the liver or the muscles is quickly resolved into sugar the blood must be affected quite as though the added sugar had come from the intestine. Glycosuria will ensue. Certain bodily changes are known to cause such a flooding of the system with sugar and the appearance of a part of it in the urine. A most interesting instance of such glycosuria is that following an experience of strong emotion. It seems that one of the results of the disturbance in the central nervous system is the conversion of a large amount of glycogen into dextrose. With acute insight a physiologist

[1] The critical level or so-called "threshold" is not far from 0.17 per cent.

has pointed out that this release of sugar is a helpful reaction under the circumstances. The occasion of emotion is usually an occasion for strenuous action, perhaps for flight or for giving battle, and the muscles may be reinforced by the increased supply of their preferred fuel brought to them.[1]

The regulating action of the liver and the muscles upon the carbohydrate distribution may be paralleled, in part at least, by an analogy. Let us compare the active tissues to a mill turned by the waters of a stream. The water-supply to the mill is to be compared with the sugar-supply to the cells which derive their energy from it. A meal is to the body as a storm is to the mill-stream—it adds to the volume of the power-producing element. The dam by the mill is like the kidney in its relation to the accumulated store; if the water rises above the crest of the dam it flows over and passes on down the stream without having contributed its energy to the turning of the machinery; if the sugar rises above a certain level it begins to escape, with its potency for work lost to the organism. Moreover, the capacity of the liver and the muscles to hold back carbohydrate suggests the function of a broad mill-pond. The larger the pond above the dam the more successfully the irregularities due to alternating rain and drought will be offset and the less likely will be a wasteful overflow when a storm follows a term of low water. The conversion of an intermittent supply into a constant one is the function of the mill-pond, and it is equally the service of the tissues holding glycogen.

Severe and long-continued exertion may lower the sugar of the blood. If the reduction proceeds until the percentage is about half the normal, the subject is brought to the verge of collapse. The close relation between the blood-sugar level and endurance has been established by observations on Marathon runners. Those who finish in good condition are those whose sugar has not been seri-

[1] Cannon, "Bodily Changes in Pain, Hunger, Fear, and Rage," Appleton, New York, 1929.

ously depleted. In such trials it has often been found helpful to eat glucose in some form at intervals.[1]

While a relatively sudden rise of sugar in the circulation may produce glycosuria, a slight chronic excess over the normal may have an entirely different effect. If the diet is supplying day by day a little more carbohydrate than the body is oxidizing, the surplus may be transformed to fat. The opinion that starchy and saccharin foods are fattening has scientific support as well as common observation in its favor. Glycogen formation is limited and we may suppose that fat-building takes place when the glycogen reserve is at its maximum and still more sugar is offering. An important advance was made in physiologic knowledge when Liebig called attention to the fact that a cow's milk contains an amount of fat utterly out of proportion to the scanty supply furnished by the food of the animal. It had been believed that no such transformation could be accomplished by animal tissues, and that all fat found in the body or in the secretions must have been received as fat. Liebig fell into error when he stated that the milk-fat had been made solely from proteins and not at all from carbohydrates, but he had taken a notable step in recognizing the possibility of changing one food-stuff into another. Quantitative experiments soon showed that carbohydrates must be given a very prominent place among fat-forming materials.

The steps through which sugar is transformed into fat are little understood. A comparison of the composition of the two makes it evident that a great deal of oxygen has to be removed in the reactions. This element is never set free in animal metabolism; in the present instance it is separated in the form of carbon dioxid. This is not merely a theoretic consideration, but a condition which can be demonstrated by experiments upon an animal rapidly gaining fat. A wood-chuck, for example, when it is eating voraciously of starchy food and gaining steadily in fat,

[1] Gordon et al., Journal of the American Medical Association, 1925, lxxxv, 508.

breathes out more carbon dioxid than can be accounted for by the oxygen consumed. The excess is a by-product of the process in which sugar with its high percentage of oxygen is made over into fat with a much lower percentage.[1]

Recourse may be had once more to analogy. Bernard compared the liver to a bank, but we may extend the comparison to the whole body. The products of digestion are the daily deposits; the oxidations stand for the daily payments. The bank will have a convenient cash balance on hand from which to meet current demands. This is the function of glycogen. The cash in the bank will be but a small fraction of its total resources, and its variations from hour to hour will signify but little as regards the stability of the institution. So the glycogen of the body is a small reserve and may vary by 50 per cent. within twenty-four hours. The body-fat, like the securities held by the bank, is a large accumulation and less subject to change. If for some time the deposits are in excess of the withdrawals, the officials of the bank will, of course, make new investments. The parallel is clear: the body receiving more carbohydrate than it is expending will not allow it to go on increasing in the liver and muscles, but will begin to convert it to fat. Unhappily, the correspondence becomes uncertain at one point: a bank which is subject to a "run" may sell its bonds and other holdings that it may have cash to pay its depositors. The obvious suggestion is that the fat of the body will be reconverted to sugar when there are demands to be met and no incoming food. We have pointed out (p. 142) that this is not certainly known to occur; the oxidation of fat during starvation has been held to proceed without any such previous change.

[1] Without assuming that the process is fully understood, French authorities have suggested that the principles involved may be shown in the following equation:

$$13(C_6H_{12}O_6) = C_{55}H_{104}O_6 + 23(CO_2) + 26(H_2O).$$

(Shäfer, "Text-book of Physiology," vol. i, p. 933.)

Using another metaphor, though still a financial one, it may be said that the glycogen is like a checking account which a man uses to pay his routine expenses, drawing upon it often and recruiting it at longer intervals. Such an account is sometimes nearly wiped out and then at one stroke largely increased. The fat of the body is like a savings bank deposit, gathered slowly, drawn upon only in emergencies, and, it may be added, gaining by compound interest in many cases.

Two facts readily suggest themselves which may be used to explain the low limit of glycogen storage. For one thing, its physical properties would probably make a high percentage of it undesirable. In the second place, there is a distinct economy in substituting fat for glycogen because fat represents more energy in proportion to its mass. An individual who carries 20 pounds of fat in adipose tissue may wish to be rid of a part of it, but if he were compelled to bear a load of glycogen equivalent in energy his burden would amount to about 45 pounds.

The Pancreas and Carbohydrate Metabolism.—We have repeatedly compared the carbohydrate of the body to money. Just as it is the eventual function of money to be spent, so it is the destiny of carbohydrate to be oxidized that its latent energy may be turned to account. This oxidation takes place chiefly in the muscles, to some extent, doubtless, in the glands, the gray matter of the nervous system, and the absorbing cells of the intestine. The intensity of the local process will in every case be proportional to the heat and other forms of energy developed. Considering the wide distribution of this purposeful destruction of sugar it is surprising to find it all dependent upon an obscure action of the pancreas.

This organ has been dwelt upon previously as a most important contributor of digestive juice to the intestine. It would be anticipated that the removal of the pancreas from an animal would be followed by defects of digestion and assimilation. This is probably justified by the results of a trial, but the effect upon digestion is overshadowed by

a consequence hardly to be foreseen. This is the almost complete loss on the animal's part of the power to utilize dextrose. In other words, a process not occurring in the pancreas at all, but in the tissues at large, is arrested by the removal of this gland. What is the natural explanation of this condition? Evidently that something proceeds from the pancreas through the circulation to other parts of the body, without which the cells in general are incapable of decomposing the sugar.

The fact that some product of the pancreas is necessary to insure the oxidation of sugar has recently been confirmed by a remarkable observation.[1] Experimenters were engaged in recording the symptoms exhibited by one animal after another following the removal of the pancreas; diabetes set in with uniformity until, quite unexpectedly, a negative case appeared. Under scrutiny it turned out that the animal which escaped diabetes was a pregnant female. It was then surmised that the retention of the power to utilize sugar was due to the presence of pancreatic tissue in the embryos. The inference proved to be correct for, directly after the birth of the young, the mother developed diabetes with full intensity.

Diabetes.—If, owing to a lack of the pancreatic hormone, the ability to utilize sugar is lost, the continued absorption of carbohydrate will raise the percentage in the blood, with the result which always ensues under this condition. The kidneys will steadily excrete the surplus sugar. Unlike alimentary glycosuria, this overflow of sugar will not be limited to times of free feeding with carbohydrates, but will attend the ingestion of the most moderate amounts. (As a matter of fact, sugar will still be excreted when carbohydrates are excluded from the diet and in fasting. The explanation of this fact must be deferred to the next chapter.) The difficulty of keeping up nutrition when the cells can make no use of glucose will be evident in a measure even at this point, and we shall find additional reasons later.

[1] Carlson, Orr, and Jones, Journal of Biological Chemistry, xvii, 1914, 19.

The complications which set in when a case of diabetes approaches a fatal issue are of a nature not yet indicated. It is not the simple difficulty resulting from the loss of the power to oxidize sugar which is encountered; toward the last the metabolism of fat pursues an abnormal course. The fact seems to be that as soon as a stage is reached when dextrose can no longer be destroyed the clean and complete oxidation of fat likewise becomes impossible. The system begins to suffer from the accumulation of acid by-products originating from fat. An *acidosis* is said to exist. These are responsible for the coma and, to a great extent, for other symptoms which signify that the end is near. The curious dependence of proper fat metabolism upon the simultaneous destruction of sugar has been picturesquely described by saying that "fat has to be burned in the flame of carbohydrate."

The attempt to exclude carbohydrates from the diet and to live chiefly on fats with a moderate protein allowance results in a serious acidosis.[1] The subjects of such experiments become miserable in the extreme and soon loathe the carefully prepared dishes (bacon, eggs, creamed chicken, etc.) which are set before them. Analysis of the urine shows the presence of the toxic substances.

We have seen that in fasting there is at first a free use of glycogen and then a substitution of fat for carbohydrate in the metabolism. When the replacement has become nearly complete there may be difficulty in oxidizing so large a quantity of fat and symptoms of acidosis may become more or less marked. This is largely an individual matter and accounts in part for the fact that some people find fasting highly disagreeable while others do not mind it. When fasting is enforced by an attack of indigestion the same metabolic derangement may be induced, prolonging the nausea and malaise. These are the familiar cases which terminate so happily as soon as food can be taken.

It is difficult to draw a line between diabetic and non-

[1] Higgins, Peabody, and Fitz, Journal of Medical Research, xxxiv, 1916, 263.

diabetic human beings. We have at one extreme those whose power to store and utilize carbohydrate is never demonstrably overtaxed, at the other those who cannot oxidize any sugar. All gradations between are represented. In a doubtful intermediate class are those subjects who have glycosuria when they indulge at all freely in carbohydrates. They are said to have a low tolerance for sugar. There is reason to think that they can neither oxidize it rapidly nor turn it readily to glycogen. The two capabilities are strangely linked.

The fact is now well established that persons with a low sugar tolerance invite the development of grave diabetes if they allow themselves diets productive of glycosuria. The pancreatic function seems to fail progressively under such treatment. Apparently this organ, unlike some others, cannot be strengthened by systematic demands upon it; if it is weak there is no advisable course but to spare it.[1]

Insulin.—As soon as the responsibility for diabetes was definitely fixed upon the pancreas physicians began a series of attempts to treat the disease by the use of variously prepared extracts of the organ. For many years their efforts were fruitless. We can now account for the repeated failures in a simple way. In ordinary preparations of pancreatic material the enzyme trypsin is activated, and it destroys at once the internal secretion which it has been desired to obtain. A special technic is requisite to avoid this untoward result.

There are in the pancreas certain cell-groups which do not contribute to the digestive juice discharged through the ducts of the gland. These are known as the Islands of Langerhans, and it has long been assumed that it is their function to manufacture the hormone which regulates carbohydrate metabolism. They have frequently been found degenerated in postmortem studies made upon victims of diabetes. We now have proof that the

[1] Joslin, "The Treatment of Diabetes Mellitus," Lea & Febiger, Philadelphia, 1923. Also Williamson, "The Practitioner," cv, 1920, 233.

view generally held is correct. A principle of the utmost value in the control of diabetes can be derived from these cells. Because of its source it is called Insulin or Iletin.

The first successful quest of such an agent was achieved by Banting, Macleod, and Best of Toronto. It had been suggested that the product might be secured from a pancreas in which the part originating the juice had been caused to atrophy. If this condition could be brought about the interference from trypsin would be avoided. The desired degeneration was induced by tying the ducts of the pancreas and keeping the animal alive for some weeks. The islands remained normal and yielded an extract having remarkable properties. It has since been found possible to prepare Insulin from glands fresh from the slaughter-house. Alcoholic extracts are used.

The internal secretion of the pancreas is ineffective when taken by mouth because it is decomposed in the digestive tract. When it is injected under the skin and thus introduced into the circulation it promptly lowers the concentration of the blood-sugar. If the dose is rightly measured this will prevent the excretion of sugar in the urine. More important than this is the fact that the tissues begin to utilize dextrose in the normal way. The liver regains the power to store glycogen. The tendency to acidosis is counteracted. The reduction of blood-sugar by insulin does not necessarily stop at the normal level; if it proceeds farther marked prostration results. In the course of Insulin treatment for diabetes such reactions are warded off by eating oranges or glucose when the sensation of weakness is experienced. There is clear evidence that the cells producing insulin are under nervous government. Stimulation of the vagus nerve under carefully controlled conditions causes a drop in blood-sugar, which must be attributed to the release of the pancreatic hormone.

Reference may be made to a case of extraordinary interest. (Wilder et al., Journal of the American Medical Association, lxxxix, 1927, 348.) A man became increas-

ingly subject to onsets of faintness and trembling. Restoration could always be had by eating carbohydrate food. It was inferred that he was suffering from cancer of the island tissue of the pancreas; with the unrestrained multiplication of the cells his system was flooded with insulin and his blood-sugar depressed below the normal. Toward the last this tendency could only be combated by steady injection of glucose into a vein or by inordinate feeding with sugar—about 2 pounds a day. Fat was added to his body even while his strength ebbed away. Post-mortem examination confirmed the early diagnosis: there was a great increase of the insulin-producing tissue.

The improvement of diabetic patients receiving insulin has been extraordinary and it is clear that we have here one of the greatest of medical discoveries.[1] At the same time it should be stated that the treatment does not cure diabetes; it is palliative in character. By its help life is made comfortable and efficient, but the dependence on the injections must probably continue. However, the alternative is semi-starvation, greatly restricted activity, and uncertainty as to the future. All clinicians emphasize the fact that diabetes attacks chiefly individuals who have allowed themselves to become overweight.[2] In later life at least the spare subject is practically insured against it. Among the underfed populations of Central Europe diabetes is one of the few diseases which has definitely decreased.

[1] Macleod, Physiological Reviews, iv, 1924, 21.

[2] Adams (Journal of Nutrition, i, 1929, 339) reports that of 673 diabetic patients (Mayo Clinic) 91 per cent. were overweight—82.9 per cent. by more than 10 per cent.

CHAPTER XVI

NITROGENOUS METABOLISM

Our knowledge of the history of the products of protein digestion has been much extended in the past few years, but there are still many uncertain passages. Any account which can be given must be held subject to revision. Nevertheless the course of nitrogenous metabolism, in its broader aspects, is tolerably clear. The present interpretation is most easily appreciated when earlier conceptions have been briefly reviewed.

Not long ago it was held that the earlier products of tryptic digestion were promptly absorbed, and that the formation of the late products, the amino-acids, was rather an accidental and, possibly, an unfortunate occurrence. It was believed that the simplest bodies could not serve all the purposes of nutrition. Such compounds were known to arise in the laboratory experiments, but their formation in the intestine under strictly normal conditions was questioned. The opinion prevailed also that the peptones which disappeared from the canal were reconstructed at the time of absorption and represented thereafter by the protein of the blood. The old impression that but little in the line of synthesis could be expected of the animal tissues was distinctly influential.

About 1901 it was shown that a dog can be nourished when the nitrogenous food which it receives is in the form of the most advanced products of tryptic hydrolysis. A quantity of lean meat had been digesting with pancreatic juice for a period of months. The resulting mixture contained only bodies of a simpler order than the ones on which nutrition had hitherto been supposed to depend. Food so prepared is not attractive, but it can maintain an

animal in fair condition. Physiologists accepted the evidence and granted that the proteins of the organism could be synthesized—sometimes at least—from amino-acids. Shortly after this change in our conceptions the discovery of erepsin was announced. It was recognized that the existence of this enzyme made it more probable that digestion should normally run its full course rather than be terminated at an early stage by the intervention of the absorbing cells. It became apparent that even though the material leaving the intestine might have the relatively complex character which we associate with the peptone stage of digestion, the products delivered to the interior of the villi by the cells might have undergone further cleavage. The ability of the animal to turn to account such simple bodies in synthesizing its own proteins became clear.

In the chapter on Intestinal Digestion (Chapter X) the statement was made that the various amino-acids have been called the "building-stones" of metabolism. In the course of digestion they are separated, and after absorption or during the very act of absorption, they are to some extent assembled again. Many facts bearing upon this process have been brought to our attention by the recent studies of physiologic chemists concerning the constitution of protein molecules. All that has been done of late in this direction has served to emphasize the variety of individual structure comprehended under the term protein. When such compounds from various sources are subjected to decomposition, either by digestion or by other means, the assortment of amino-acids obtained differs with the particular protein under investigation.

Some, which one is tempted to regard as perfect proteins, yield the full list of amino-acids as at present known. Others, seemingly defective when judged by this rather arbitrary standard, fail to yield certain members of the series. This variation has an important bearing on matters of nutrition. It can no longer be maintained that all substances characterized as proteins are equivalent in

their power to minister to growth and repair. Among an increasing number of defective proteins now recognized gelatin is the best known. Its behavior in the system calls for exposition.

Gelatin.—This familiar compound belongs to the ill-defined group often spoken of as the albuminoids. These may fairly be regarded as proteins which have undergone a more or less definite degeneration both in function and in chemical structure. They are found as intercellular substance in the connective tissues and also in the dead and dry surface layer of the skin. They make the chief substance of the hair and nails. Gelatin itself is derived by boiling certain varieties of connective tissue, including bone and tendon. It gives nearly average percentages of the five elements present in ordinary proteins. When this fact was discovered in the early days of organic chemistry it was urged that gelatin must have a value in nutrition quite equal to that of any nitrogenous food.[1]

Trials were made on a large scale in the pauper institutions of France. It was found very definitely that the free use of gelatin led to indigestion and that it soon became repugnant to the subjects, however hungry they might be. These effects were later found to be correlated with inadequacy to maintain the weight and strength of animals. An animal cannot be said to be perfectly nourished if it is losing more of any element day by day than it is receiving. This is eminently true of the nitrogen in the income and the outgo. "Nitrogenous equilibrium," expressing the equality of the two, is a phrase we shall use freely. Now nitrogenous equilibrium cannot be established by feeding gelatin in place of all other protein, no matter how skilfully the experiment is conducted.

For many years the insufficiency of gelatin to make good the losses from the tissues remained a mystery. It has

[1] The early history of gelatin is related entertainingly by Lewes, "Physiology of Common Life," Edinburgh, 1859, vol. i, 129. The whole work is of interest as setting forth the prevailing opinions of the period.

been amply explained by the findings of chemists in our own time. Gelatin yields most of the building-stones required for the new construction, but it does not furnish them all. Therefore, it is impossible to make blood-proteins or the proteins of the living cells from its cleavage products. It is useless to increase the *quantity* of the amino-acids if the *variety* is not great enough to supply the details of the molecular pattern to be wrought. What is true of gelatin is true of a number of proteins from vegetable sources. They do not give all the groupings needed in the constitution of the more elaborate animal protoplasm.

In some cases a single protein may be adequate for nutrition, supplying a complete assortment of amino-acids. But it will be seen that successful nutrition is more certainly to be secured by using proteins from various foods. This is our practice, save in the important case of the milk-fed infant. Milk actually contains proteins of more than one order, so that the exclusive use of this food does not narrow the selection of building units so greatly as might be supposed. The chief protein of milk contains the element phosphorus and is perhaps of somewhat unusual complexity.

A very important body of work bearing upon this matter has been reported by Mendel and Osborne of the Sheffield Scientific School. They have conducted feeding experiments of the most elaborate character, in course of which small animals have been supplied with single proteins. Non-nitrogenous and mineral constituents have been liberally furnished. By this procedure individual proteins from various sources have been placed on trial. The investigators have shown that the proteins employed may be placed in three classes: those which suffice for all purposes of nutrition, including growth, those which can sustain life but not growth; and those which are quite inadequate for either purpose.[1]

[1] Lusk, "The Fundamental Basis of Nutrition," Yale University Press, 1914. This is a most valuable reference. See also Underhill, "The Physiology of the Amino-acids," Yale Press, 1915.

Interesting facts have appeared respecting the second class of proteins mentioned above. White rats limited to such forms of nitrogenous food may be kept alive for months during the period in which a normal animal makes a steady growth and yet remain stunted, their weight nearly constant throughout. When they are at length granted a more favorable diet growth may begin and continue until a full stature is attained. Mendel has pointed out that this postponement of growth and its subsequent accomplishment may be comparable with an arrest of development in man which should continue up to the age of forty and then be followed by full and normal growth. This statement is based on the ordinary longevity of the rat.

In an introductory chapter the protein molecule was likened to a watch with its many dissimilar parts associated in the one possible way to secure a desired result. One or more of these parts might be missing without their absence being apparent to the untrained person as he looked into the works. He could nevertheless observe the fact that the watch would not go. This is quite parallel with our progress toward an understanding of the failure of gelatin and other proteins to serve all purposes in nutrition. Just as the watch-maker, with his special knowledge, easily detects what is wanting, so the physiologic chemist is now able to say with much accuracy what particular amino-acids are lacking in his feeding experiments. As the defective watch may be made serviceable by the addition of certain bits of mechanism, so in a measure an insufficient diet may be made adequate when extra amino-acids are supplied.

Mendel has made it clear that we cannot control the supply of amino-acids, in the case of an experiment, so precisely as might be supposed. This is because of the micro-organisms which flourish in the canal. These simple plants take to themselves a share of the food and build it into their own substance. As they constantly die and are subjected to digestion they constitute a source of proteins, and so finally of amino-acids, which may be quite different from those which it was designed to furnish.

It is necessary now to approach a subject of some difficulty. We must attempt to show why a given quantity of protein fed—say 100 grams—cannot contribute an equal quantity to the protein supply of the body. When protein of one kind undergoes complete hydrolysis and protein of a new kind is to be made from the resulting cleavage products, certain of the building-stones will be needlessly plentiful, while others will be relatively scarce. We have seen that if a single one of these structural units is not furnished, there is complete failure to synthesize the new compound. Similarly, if the second body is to contain a large percentage of an amino-acid which is but scantily represented in the first, the possible formation is definitely limited. The principle is easily illustrated. Suppose that in a club of 100 members there are 25 Democrats. It is desired to elect for purposes of debate the largest possible body, consisting of Democrats and Republicans in equal numbers. Evidently, this body will comprise 25 men of each party. There will be 50 men unrelated to the new organization. We may change the comparison: A house is pulled down and another is to be erected from the timbers. If the second house is of an architecture entirely unlike that of the first, there will be many unavailable pieces to discard and the new building will be smaller than the old. It is not at all unlikely that the misfit fragments of building material will go into the cellar of the new house, later to be used as fuel. This is just what the body does with the misfit amino-acids. So far as they do not find place in the mosaic which is put together they serve as producers of energy.

Again, a better analogy suggests itself: The structure of a molecule of food-protein, previously compared with that of a watch or a house, may be likened to the type set up to print a page. The letters, some of which occur frequently and some rarely, stand for the amino-acids. The type is allowed to fall apart, the symbol of digestion. It is to be set up again to print different matter. If the language and vocabulary are much as at first, it may be possible to com-

pose nearly a whole page before the lack of some letter brings the proceeding to a standstill. But some shrinkage will be inevitable and when the type-setting has to halt there will be some unused letters. The shrinkage will be much greater if the second page is to be printed in a language other than the original. Suppose, for example, the type used in English composition is next devoted to German. The resulting difficulty is readily foreseen—the letter *z* is uncommon in English, but frequent in German. Hardly a line can be perfectly set up before this letter will be vainly sought. Almost the whole collection of type will be useless for composing. This is analogous to the attempt to minister to animal growth with some isolated vegetable protein of exceptional constitution. Offering the cleavage products of gelatin to the cells is like giving the compositor incomplete fonts of type. He cannot set up connected matter if some of the letters are not to be found.

The requirement of the body in the way of structural units is really less rigorous and exacting than this analogy suggests. While the number of the amino-acids approaches twenty and encourages the comparison with letters of the alphabet, it has been shown that they are not all indispensable. In fact, about half a dozen may serve all purposes of nutrition. Apparently the cells can work over the molecular groupings found in these essential members of the series and from them form certain others. A craftsman working with type could turn an L to an I or an R to a P by the touch of a tool. In a similar way the simpler amino-acids may be derived from the more complex. Perhaps the transformation sometimes is actually a synthetic one.

It seems natural to assume that the closer the structural resemblance between the proteins digested and those to be synthesized, the more economically the transformation can be accomplished. In fact, we have definite evidence that the quantity of protein required to maintain a balance may be very much greater for one type than for another from a different source. The reference is to the experiments of

Thomas. This investigator made a series of trials upon himself, making liberal use throughout of non-nitrogenous food and, combined with this, proteins of various kinds to ascertain the amount of each necessary to keep him in equilibrium. Some of his results are tabulated below[1]:

Meat protein	30 grams.
Milk protein	31 "
Rice protein	34 "
Potato protein	38 "
Bean protein	54 "
Bread protein	76 "
Indian corn protein	102 "

It is not strange that meat and milk should stand first when rated on a basis like this. Meat may be expected to have a constitution closely resembling that of the body which is to be nourished, while milk is nature's food for the growing animal. The good showing made by rice and potato is rather more surprising, and, when we consider what vast populations depend largely upon these staples, we must conclude that there could scarcely have been a better choice.

Our knowledge of the place and the manner of protein synthesis is incomplete. The cells which line the intestine and receive the digestive products were formerly held to bear a large part in the work. The fact that these cells may be made to yield erepsin, an enzyme capable of breaking down the more complex nitrogenous bodies, does not exclude the possibility that dehydrations and condensations may still take place within them. The enzyme may be modified under some conditions so as to be inactive. It is even conceivable that it may facilitate the combining of the building-stones. Some enzymes, like other catalysts, may favor the progress of reactions either in one direction or the reverse, according to the proportions of the substances present at the moment. There is an increasing body of evidence that the liver-cells play an important part in the manufacture and storage of proteins.

[1] Lusk, loc. cit.

Not long ago it was usual to make much of the blood proteins in outlining the probable course of nutrition. These are abundant constituents of the plasma and it was natural to conceive of them as being made in the intestinal wall from the products of protein digestion, offered to all the tissues, and locally digested to furnish the groupings needed for growth and repair. During fasting it was supposed that the cells imperatively requiring to be preserved still made a draft upon the proteins of the blood. At a time when these could not be produced by the intestine various reserve tissues were called upon to supply them.

The present way of picturing the process is different and distinctly more simple. The amino-acids from the intestine are believed to remain uncombined in the blood and to be appropriated by each tissue according to its need. When the intestine does not contribute the requisite material it is released to the blood by other organs in which reserve protein is being hydrolyzed. In this case as well as during feeding the amino-acids in transit are free rather than combined. The blood proteins accordingly cease to be emphasized as standard food-stuffs. It is no longer believed that they are continually consumed and replaced. The presence of amino-acids in the blood can be demonstrated by delicate tests. The amount is small, but we have only to recall the disproportion between the quantity of sugar in circulation and its importance in metabolism to realize that we need not make much of this fact. Money is vastly important to our comfort, but the currency of the nation seems insignificant in comparison with its total wealth.

It is not easy to estimate the extent of protein synthesis which normally takes place. Of course, it is more prominent during growth than during adult life. The present impression is to the effect that only a very small fraction of the usual protein income is thus used. Most people can materially reduce the quantity of protein in the diet and still remain in nitrogenous equilibrium. When the lowest level at which this is possible has been attained it

is still true, as we have just pointed out, that the amount of new protein constructed is but a fraction of that supplied. It is, therefore, certain that under average conditions by far the larger part of the nitrogenous food eaten never exists in the form of proteins after absorption. We must now consider the destiny and value of the uncombined building-stones.

The surplus amino-acids, either free or in simple combinations, are borne away from the intestine in the portal blood. Accordingly, these digestive products, like the sugars, are brought under the influence of the liver-cells. They undergo a transformation in this organ—and very probably elsewhere—which has important consequences. This is the process described as "deaminization." To deaminize an amino-acid is to remove from it the group to which it owes its name, the radicle NH_2. One of the products of this reaction will be non-nitrogenous, the other will contain nitrogen in a greatly increased percentage. We cannot claim to know all the steps which are gone through in this connection, and we shall not discuss those which are known. We shall emphasize simply the final results.

The chief nitrogenous compound which issues from the series of reactions affecting surplus amino-acids is *urea*. This is apparently of no further use in the system. It is destined to circulate until it shall find its way into the urine. The efficiency of the kidneys is so remarkable and the whole blood volume is carried through them at such short intervals that the percentage of urea in normal blood is kept very low. Urea seems to be a most convenient form for nitrogen elimination; it is highly soluble and diffusible, inert, and, comparatively speaking, non-poisonous. If a man eats 100 grams of protein in twenty-four hours he will excrete some 30 grams of urea, an amount which represents about seven-eighths of the total nitrogen passing into and out of the body. This urea is largely if not wholly produced in the liver. Most of the sulphur from those amino-acids which contain the element is oxidized and leaves the body as sulphates.

What is the principal non-nitrogenous compound produced from the amino-acids? There seems to be no doubt that it is *dextrose.* Evidence in support of this belief has been derived from the study of diabetes. Whether this condition is experimentally induced or develops spontaneously, it is found that, if the case is one of full severity, sugar excretion goes on even when no carbohydrate is fed, and, indeed, throughout long periods of fasting. This sugar might be assumed to have come from the fat of the body, but it can be more surely attributed to the protein which is being decomposed. The following consideration shows this: the nitrogen and the sugar in the urine of the fasting diabetic patient maintain, in many cases, a singularly constant ratio; 1 gram of nitrogen is accompanied by 3.6 grams of dextrose. They rise and fall together. This seems to prove that the two must have a common source, which can only be protein. Again, the feeding of amino-acids to the diabetic increases his loss of sugar; the feeding of fat does not have this effect. A simple calculation shows that 100 grams of protein fed may give rise within the body to about 58 grams of sugar. The seriousness of diabetes will now be better appreciated than has been possible up to this time. The organism loses not merely the support normally secured from the chief carbohydrates of the diet, but, in great part, that ordinarily furnished by protein food.

From all this it appears that much of the protein which we eat serves only to supply the tissues with carbohydrate. The impression is likely to be that this is a roundabout and not an economical way to provide sugar, which might have been taken as such at the outset. The facts may fairly be employed to support the modern teaching that excess of protein is to be avoided, but we have already shown the necessity for allowing more than is actually to be reconstructed after the digestive dismembering. Recognizing as inevitable the discarding of amino-acids, we can see the desirability of having them made to furnish a simple standard food like sugar, valuable for its store of

energy. The possibility of glycogen formation from protein naturally follows. The glycogen of carnivorous animals presumably has such an origin. The maintenance of the sugar of the blood during long fasting is also ascribed to the disintegrating protein of the tissues. Given dextrose in such quantities, the production of fat from protein becomes at least theoretically possible. Broadly speaking, we may claim for protein that it can do all that any form of organic food can do for the system. Yet this does not impair the statement, equally to be recognized, that carbohydrates and fats should form much the larger part of the income.

After the constructive requirement has been met, all additional protein seems to entail unprofitable labor on the part of the liver in deaminizing the cleavage products, the presence of various substances of a possibly detrimental nature in the circulation, and an activity on the part of the kidneys which may amount to an abuse of these important excretory organs. There is this general contrast between the behavior of proteins and non-proteins in the body: the former give rise to rather complex waste-products imposing a task upon the liver and kidneys; the latter are oxidized cleanly to carbon dioxid and water, two compounds which are eliminated with ease. A fuller discussion of these facts will be undertaken in the chapter on The Hygiene of Nutrition (Chapter XXII).

Folin, of the Harvard Medical School, has classified the facts of protein metabolism in a particularly clear and helpful form. He distinguishes two lines of transformation, the *endogenous* and the *exogenous*. Under the head of endogenous metabolism he traces the various steps in the history of those building-stones which are erected into the proteins of the blood and other tissues. The narrative is continued in the account of the rather gradual and steady crumbling which such tissue-proteins undergo. What is loosely called the wear and tear of the cells gives rise to definite end-products, one of which Folin holds to be of particular value in estimating the extent of such decompo-

sition. This is the substance *creatinin*, which accompanies urea out of the body and which is far less subject to fluctuation. The urea excreted rises and falls with the protein ration, but the creatinin is not markedly responsive to dietetic variations. It is believed, therefore, that endogenous metabolism, a necessary feature of animal life, is relatively independent of feeding, at least while nutrition is satisfactory.

Exogenous metabolism is an expression to cover all the reactions affecting the uncombined amino-acids. Hence it includes the formation of urea, dextrose, and whatever substances may be formed from the nitrogenous cleavage products in the liver. It may be extended to take in the secondary production of glycogen or of fat from surplus sugar originating in this way. In contrast with endogenous metabolism its amount varies widely. With a low protein diet the exogenous changes will be but a fraction of what they will become with abundant protein. One may be tempted to conclude that in fasting the metabolism will be wholly endogenous. The insight of a German writer has served to show us that this is not so. We have spoken at length of the assembling of amino-acids fresh from the intestine to form the standard proteins of the various tissues. Now there are differences of constitution between the proteins of the various organs. When a particular tissue, muscle, for example, is to be nourished at the expense of some other, a true local digestion is necessary, and once more there must be the selecting and rejecting of amino-acids. Those not available may be deaminized quite as if they had come from the seat of the original digestion. This type of activity whereby one kind of tissue is sacrificed to build up another is best illustrated in the case of the salmon before spawning. No food is taken; the muscles steadily waste and the roe increase at their expense.

While all proteins are complex in their molecular structure, there are some which are distinguished above the others by the intricacy of their organization. The presence

of phosphorus in certain proteins suggests such an eminence. This is a characteristic of the proteins in cell nuclei, though phosphorus is found in other compounds also, for example, in the casein of milk. When such proteins decompose in the body phosphates are among the metabolic products.

The same peculiar proteins of the nuclei which yield phosphates give rise to a number of closely related organic bodies known collectively as the *purins*. These undergo various transformations under the influence of enzymes and are very largely converted to a single end-product, *uric acid*. If we measure the output of uric acid we shall have an indication of the nuclear metabolism, provided that two conditions are fulfilled. These are, first, that excretion is keeping pace with production, and, second, that no purins are furnished by the diet. When the food includes much nuclear material (meat especially) the uric acid which the body has to eliminate is the sum of two fractions, one *endogenous*, an inevitable product of the life-processes, the other *exogenous*, derived from the current ration.

Vitamins.—We often need to remind ourselves that there is an important distinction between proteins and protoplasm. Living matter may fairly be considered to consist very largely of proteins—with much water, of course—but other components are doubtless necessary to its existence. That this is true of certain mineral compounds has become familiar (p. 255). There is increasing evidence that various organic bodies other than those produced by the digestion of proteins are also essential. It has been proposed to call such compounds vitamins. An amin is a nitrogenous body of a particular type, and the prefix conveys the idea that the one referred to is indispensable. The objection that the term is too narrow and specific seems to be well taken. We do not know that all such valuable bodies have the molecular structure of amins. To designate them as "accessory substances" would be better, but the other usage is rather firmly established.

The belief in vitamins has proceeded from the study of certain diseases. One of these, the best suited to our discussion, is beriberi. It is technically described as a multiple neuritis, that is to say, a wide-spread degeneration of the nerves. The great majority of cases have occurred among populations which subsist largely upon rice. Here and there the disease, or one much like it, has been recognized where rice has not figured prominently in the ration, but the diet has always been monotonous. Various theories have been advanced to account for the disorder, but the one most in favor is that it is a "deficiency disease," due to the lack of a particular nutritive substance. A compound, the want of which produces such disastrous effects, obviously deserves to be called a vitamin according to our previous description.

Some years ago it was shown that a decline with symptoms resembling those of beriberi could be induced in pigeons by limiting them to a diet of "polished" rice, that is, rice without the husk or pericarp. The inclusion of the pericarp in a ration otherwise similar would prevent the derangement or remedy if it had not gone too far. Employing our modern terminology, we shall be inclined to say that the pericarp in this case furnishes a vitamin absent from the enclosed kernel of the rice. A leading worker in this field believes that he has isolated the pure vitamin of beriberi and ascertained its chemical structure, which is not of high complexity. He identifies it with a body obtainable from meat and from yeast. It follows that either meat or yeast—and doubtless other materials—added to a diet of polished rice may be expected to render it adequate.

It will be well briefly to outline the supposed course of events when the supply of vitamin is cut off. The compound is assumed to be most urgently needed in the white matter of the nervous system. For a time the demand can be met by levying a tax upon other tissues, such as the muscles, but the withdrawal of a necessary component will result in the complete breakdown of such cells. The

consequence is a destruction of protoplasm, which appears to be utterly out of proportion to the minute quantity of the vitamin transferred to the nervous system. It is like the wrecking of complex machinery to secure a supply of bolts and rivets. While this stage continues the individual rapidly loses weight and strength, but does not manifest the acute nervous symptoms. These supervene when it is no longer possible to collect the vitamin even at such a ruinous cost.

Another disorder which apparently should be regarded as a "deficiency disease" is scurvy. The chronicles of explorers, especially of Arctic voyagers, are filled with accounts of this distressing malady. Many readers will recall the painful situation on board Dr. Kane's ship, when the majority of the party lay helpless in their bunks and their commander set up a mirror to cast into their midst the first beam of the returning sun. Among the symptoms of scurvy are prostration, intense soreness of the mouth with spongy swelling of the gums and loosening of the teeth, hemorrhages under the skin, and remarkable fragility of the bones. We readily recognize the signs of scurvy in Benvenuto Cellini's vivid narrative of his imprisonment in the Castle of St. Angelo. The disease, like beriberi, has occurred chiefly among those whose diet has been lacking in variety. Certain articles of food, such as fresh meat, potatoes, and lemons, have been reputed to ward off or cure scurvy, and have been described as "antiscorbutics."

It is commonly supposed that the want of a definite vitamin is responsible for scurvy. Analogous facts probably hold for other disorders. Pellagra may be one of these, though there was until recently no clear evidence of a single curative substance.[1] Malnutrition in infancy may often be referred to such deficiencies. There is interesting evidence that the fat of milk is superior to most other fats as a promoter of growth. This probably means that it

[1] U. S. Public Health Service, Hygienic Laboratory, Bulletin No. 120, 1920. McCollum and Simmonds, "Food, Nutrition, and Health," published by the Authors, Baltimore, 1928, Chap. VII.

carries in minute amount an admixture of some essential accessory. The same is believed to be true of orange-juice, long known to be beneficial to babies. We are brought to a new appreciation of the value of a varied diet. The more numerous the foods which we eat, the more certain we are to include all the minor compounds which we require. It is, furthermore, a question whether some of these essential bodies may not be decomposed by cooking or by prolonged preservation of food. This consideration gives at least a measure of support to the teaching that we should make a considerable use of uncooked articles and be chary of canned goods. Nevertheless, many writers have grossly exaggerated whatever dangers exist in this direction.[1]

In the opinion of many observers the vitamin question admits of a more specific enunciation. A condensed statement of the apparent facts, based on the valuable summary of McCollum and Simmonds, may be given. The vitamins are distinguished as water-soluble and fat-soluble.

Fat-soluble A.—Want of this accessory causes stunting, susceptibility to infection, and often an inflammation of the eyes (ophthalmia). It is believed that this local trouble is the result of a suppression of the tears. Lack of A may cause a corresponding reduction in the flow of saliva. This vitamin is furnished by milk and eggs, also by green and yellow vegetable foods.

Water-soluble B.—Failure to obtain this food constituent is the cause of beriberi. It is seldom wanting except in carefully refined articles—as white flour, polished rice, and sugar. It is not found in close association with fats. Recent study has indicated that what used to be called Vitamin B is probably a duplex affair. Foods which contain it lose their power to protect against beriberi when they have been quite strongly heated but still retain the property of correcting or preventing pellagra. The heat-

[1] Funk, Journal of State Medicine, xx, 1912, 341. Harrow, "Vitamines, Essential Food Factors," E. P. Dutton & Co., New York, 1921.

resistant substance has been called by some writers B_2, by others, including McCollum, Vitamin F.

Water-soluble C is the antiscorbutic vitamin. It is less stable than the others. When milk is pasteurized it may lose the virtue by which it guards the child against scurvy and the addition of fruit-juice becomes imperative.[1]

Fat-soluble D.—Rickets is a serious and frequent disorder of nutrition. The prominent feature is a failure of the skeleton to acquire the lime necessary to give it rigidity. The soft bones become bent under the weight placed upon them and deformities result. Analysis of the blood in such cases shows abnormal ratios between calcium and phosphoric acid. Foods containing vitamin A have generally been found to correct rickets and there was for a time a disposition to credit this accessory with the beneficial property. But there is ground for claiming that a specific "antirachitic vitamin"—called D—is required for development.[2] While rickets may be remedied by additions to the diet, we must give due recognition to the fact that it can, apparently, be cured by sunlight. The double possibility has doubtless been productive of confusion in the search for causes and preventives. Thus a child who is much in the open may escape the disorder while subsisting on a ration which would be inadequate for another less fortunately situated. Certain foods may be so altered by exposure to light as to acquire antirachitic properties. It seems well established that the beneficial rays are those in the ultra-violet region of the spectrum and it is most important to bear in mind that these cannot pass through ordinary window-glass. The brightest interior lacks something of the hygienic virtue of outdoors. It is not strange that rickets is for the most part a disease of the cold and dark months of the year. Cod-liver oil has long been relied upon as a remedy for rickets and it has been suggested that the power has been de-

[1] McCollum, "The Newer Knowledge of Nutrition," Macmillan, New York.

[2] Park, Physiological Reviews, iii, 1923, 106.

veloped by the fish because it frequents depths beyond the effective reach of the sunlight.

A Vitamin for Reproduction.—A fifth vitamin (E) seems clearly indicated by the investigations of Evans and others.[1] They have found that rats thrive individually upon certain diets, but are yet incapable of reproduction. They require something in addition to A, B, C, and D. Various supplementary foods make good the deficiency and enable the females to bring forth normal young. One of the best sources of Vitamin E is the oil from the germ of wheat, a most unsatisfactory dependence for the others. It is not held that human sterility is at all likely to depend on diet.

A SUMMARY OF METABOLISM

Fats are hydrolyzed in the alimentary canal to fatty acids and glycerin. To an uncertain extent there is soap formation. These products are largely combined to form fat during the passage through the lining cells of the intestine. Fat is stored chiefly in adipose tissue. Its eventual service is to be oxidized to carbon dioxid and water with release of its energy.

Carbohydrates enter the circulation in the form of simple sugars, mainly dextrose. There is little sugar in the blood at any one time. Much is dehydrated by the cells of the liver and muscles to make glycogen, subject to reconversion to sugar when required. A surplus may be converted to fat. The possibility of the converse change from fat to sugar is generally held to be unproved. The final value of carbohydrate is like that of fat; its energy is set free through the respiratory oxidation, and the end-products again are carbon dioxid and water. The internal secretion of the pancreas is necessary to bring about this destruction.

Proteins are hydrolyzed to simple compounds (amino-acids or combinations of these), and these are used for the synthesis of the new proteins—of types peculiar to the

[1] Evans in "Lectures on Nutrition," Mayo Foundation, Saunders, Philadelphia, 1925, p. 209.

species—which can be utilized for growth or repair. A large surplus of uncombined amino-acids is usual; these are dealt with by the liver and other tissues, and the best-known resulting products are urea—destined to be excreted—and dextrose, for which all the possibilities exist that have been mentioned above. The amount of wasting suffered by nitrogenous tissues as a part of their life process is believed to be indicated by the extent to which the product creatinin is eliminated. All proteins yield sulphur compounds among their decomposition products. Some yield phosphorus compounds also, and among them are the proteins which give rise to much of the uric acid which requires to be removed.

Finally, we have seen that successful nutrition requires supplies of various compounds both mineral and organic in addition to the chief foodstuffs. Long ago the gifted Sylvester Graham warned against the excessive refining of natural foods, pointing out that by this means valuable substances might be discarded. The flour which is known by his name was prepared in accordance with this advice. Scientific knowledge of beriberi acquired many years later demonstrates the soundness of his views. There is a real danger in a narrow selection of our articles of diet.

McCollum and Simmonds[1] have shown in a most interesting way how threatening deficiencies in the food supply of great populations have been avoided. In the Orient, where rice is the main source of energy and of protein, fish and poultry being consumed in relatively small amounts, people are found to eat largely of leafy vegetables. In the Near East the staple barley, dates, and meat are supplemented with milk and its derivatives. The carnivorous Eskimo consumes not only muscular and adipose tissue but the glands of his food animals. For us the inclusion of milk and greens goes far to insure the adequacy of the ration.

[1] Loc. cit., Chap. XI.

Reference: Mendel, "Nutrition: The Chemistry of Life," New Haven, Yale University Press, 1923.

CHAPTER XVII

THE REMOVAL OF THE END-PRODUCTS OF METABOLISM

THE statement has repeatedly been made in varying form that the bulk of the food is taken for the sake of its potential energy. Either at once or after storage it is oxidized, and the energy turned to account for temperature maintenance and for the performance of muscular work. The main products are carbon dioxid and water. These are likewise the chief products formed when familiar fuels are burned outside the body. Wood, coal, and gas yield the two in great quantity and only small amounts of other compounds. Hence the primary problems of excretion concern the manner of elimination of carbon dioxid and water.

The water leaving the body during twenty-four hours may be 2 or 3 kilograms. The carbon dioxid discharged in the same period is not commonly in excess of 1 kilogram. Nevertheless, we say that carbon dioxid is the leading waste-product of animal life. This is justified by the consideration that by far the larger part of the water which we measure is merely water previously received in the same state. To this large volume the tissues have added a moderate quantity of water—say 250 grams—which is a true metabolic product. This has been formed by the oxidation of compounds containing hydrogen. The water output of the body is inevitably greater in the long run than the water income. This fact may be disguised on single days by water retention.

Carbon Dioxid Elimination.—Respiration has been defined as the process within the living cells in course of which complex organic molecules are decomposed and

more or less completely oxidized. Carbon dioxid is the most conspicuous product. The respiratory exchanges occur in the different tissues in a measure corresponding with the extent to which they severally evolve energy. The skeletal muscles lead in amount of respiration (and of carbon dioxid set free), both because of their great mass and by reason of their activity. The glands, especially the liver and the kidneys, contribute largely to the total.

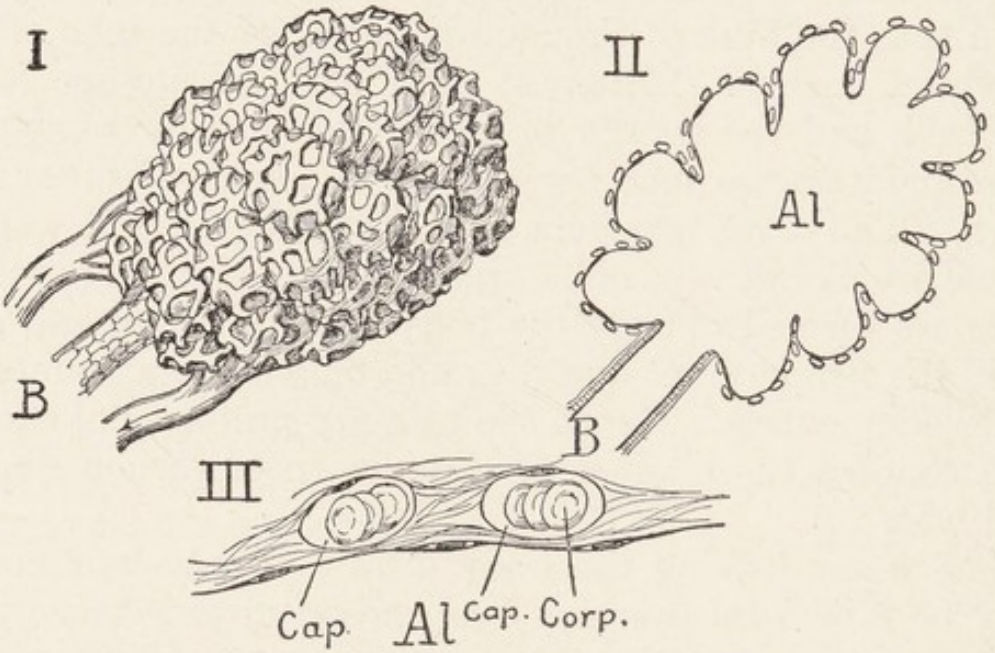


Fig. 21.—I is intended to suggest the form of an air-sac of the lung overlaid with a network of capillaries belonging to the pulmonary system. II is an imaginary section through such an air-sac. *B* in both I and II is the minute bronchial tube through which the air is renewed. III is a bit of detail from II, still more enlarged, showing two capillaries (*Cap.*) conveying corpuscles (*Corp.*). The air is close by (*Al*), yet two partitions intervene, the capillary wall and the wall of the air-sac.

So does the heart. Other tissues have a minor part in the general respiration. Some which are passive and stable, like cartilage, can have but little.

The carbon dioxid formed by the cells is first transferred to the lymph. The concentration of the gas in the lymph leads to its passage into the blood. A gas will always pass from a higher to a lower concentration when the two solutions are placed in communication. The delicate capillary

wall between the lymph and the passing blood offers practically no impediment to the movement. It will be remembered that the blood which enters upon the very short journey through the capillaries is arterial; that which enters the minute veins only a fraction of an inch away is reckoned venous. It has parted with a large share of its oxygen and has received carbon dioxid. It is swept on without significant change to the right side of the heart and thence to the lungs. The development of these organs is such as to multiply the surface of contact between the blood and the air within them. The capillaries of the pulmonary circulation are wrapped about innumerable elastic sacs, the walls of which are as thin as those of the capillaries themselves. There is, accordingly, a double partition between the blood and the air, but it is of a nature to permit free gaseous exchange.

If the air in the sacs were not renewed it would accumulate carbon dioxid in increasing amount, while its oxygen would progressively diminish. This tendency is normally counteracted through the effects of breathing. The lungs have no power to move of themselves; the changes which they undergo are due to the displacement and return of the thoracic walls. This is not the place to analyze the breathing movements. The muscles employed are of the skeletal order. Being so, they are not automatic, and it follows that every breath taken is the expression of a separate and distinct act on the part of the central nervous system. Each time the chest is made larger the air presses in along the breathing passages to fill the space created for it in the host of widened sacs. The return of the chest walls to their first position reduces the capacity of the sacs, and air is pressed out along the same channels by which it entered. The action is that of a pair of bellows not provided with the usual inlet valve.

It is not to be conceived that we empty and refill the air spaces of the lungs with each breath. We usually expel something like one-fifth or one-sixth of the air contained and replace that fraction with fresh air. When allowance

is made for the rather long and capacious passages between the air-sacs and the nostrils the impression that our breathing is rather ineffective becomes strengthened. To offset this idea we must remember that the movements occur fifteen or eighteen times a minute, providing thus for at least two fairly complete renewals of the whole volume of air within that time. Still it is a fact that when the breathing is rarely deepened beyond the constant habit, some portions of the lungs, notably their upper extremities, are but little subject to extension and contraction. By the deepest possible breathing we can increase the proportion of the air removed and replaced to perhaps three-fourths of the total at a single movement. A quiet breath, unmodified by the influence of attention, muscular activity, or any other temporary condition, is said to amount to about 500 c.c. (30 cubic inches or 1 pint). Reckoning sixteen breaths in a minute, this will mean 8 liters of air breathed in that interval, about 500 in an hour, or 12,000 in a day. Fresh air has but a small content (0.03 to 0.04 per cent.) of carbon dioxid. The air expired has 4 per cent., more or less; 4 per cent. of 12,000 liters is 480 liters, a fair average volume to represent the daily output of this gas. This quantity, changed from volume to weight with correction for temperature, is about 800 grams.

The air to which the blood is exposed in the lungs is at least as rich in carbon dioxid as that which we breathe out. Coming into relation with air of such a composition the blood by no means frees itself of its large carbon dioxid content. It carries on to the left side of the heart and so to the general arterial system perhaps nine-tenths of the carbon dioxid which it contained when it entered the lungs. The actual amount in venous blood is in the neighborhood of 50 in 100 c.c. of blood. As much as 45 c.c. in 100 will usually remain in blood which is counted arterial, and which carries a maximum of oxygen. Carbon dioxid does not seriously interfere with the capacity of the blood to carry oxygen, and the converse is equally true. It may be well to state that the color of blood varies with the extent to which

the corpuscles are charged with oxygen and is independent of the carbon dioxid present.

While there is no question of the propriety of calling carbon dioxid a waste-product, it does not follow that the system would be benefited by its complete removal. How far this is from being the case has been shown by the important experiments of Yandell Henderson. He has demonstrated that any considerable lowering of the carbon dioxid below the high standard noted above as characteristic of arterial blood results in marked prostration, often involving the suspension of breathing and perhaps resulting fatally. The inference is that a certain concentration of carbon dioxid is a desirable source of stimulation to the nervous system and especially to the respiratory center. The intimate connection between this gas and breathing is manifest when its percentage in the blood is ever so little increased. A noteworthy deepening of the respiration promptly results. Since this is true it is not strange that a reduction of the carbon dioxid should cause inhibition of the breathing movements.

Water Elimination.—Water leaves the body by all the possible excretory routes. Statements regarding the proportion taking this or that course can have but little value, so great is the variation under different circumstances. If we exclude the effects of exercise and of unusual temperatures we may expect to find somewhat more than half the whole amount to be removed by the kidneys. The daily volume of the urine is customarily set down at 1200 to 1500 c.c. The remaining excretion of water will be almost wholly accounted for by the perspiration and by evaporation from the breathing passages. Of these two, the former is commonly more considerable. Some loss of water will occur in the feces, but normally this is not to be compared with the quantities discharged in the three ways just mentioned.

When the external temperature is high the water passes in increased amounts through the skin and the perspiration may greatly exceed the urine. The urinary secretion

may shrink somewhat or may be kept near the standard as a result of the water drinking which is stimulated. The water discharged through the skin during the hot weather and also during muscular activity does not serve primarily as a vehicle of waste, but rather as a means of ridding the body of heat. This matter will be discussed at length at a another time. The evaporation from the respiratory tract probably varies less widely than the perspiration. The body seems bound to saturate all the air that is breathed, so that this loss increases with the volume of breathing and is greater when the air is dry than when it is humid.

The Kidneys and the Urine.—The chief significance of the kidneys is their function of excreting the distinctive products of protein metabolism. A secondary service is the disposal of inorganic salts. The two glands are placed to the right and left of the spinal column at the level of the lower ribs. Each kidney receives a large short artery from the aorta which passes between them. Each returns a large vein, not to the portal system, but to the chief venous trunk of the body. The kidneys, in consequence of this arrangement, constitute short cuts or "shunts" in the circulation, and are perfused by an exceptionally large quantity of blood. No portion of the blood can long escape their influence. The urine discharged by the many tubular units of the kidneys is conveyed through the ureters, contractile vessels which lead to the bladder. This is a saccular organ capable of accommodating much urine when dilated, and of contracting again to nearly complete expulsion of its contents. Its walls of muscle (the same type found in the alimentary canal) are obviously under nervous control and much subject to reflexes.

Urine of average composition is a complex solution containing some 3 or 4 per cent. of dissolved solids. The leading substance is urea, the chief nitrogenous waste of the system, and the index, according to Folin, of the exogenous metabolism. Its origin has been discussed. Evidently the duty of the kidney is less to manufacture urea than to select and remove from the blood the urea

originating in the liver and elsewhere. Second in abundance among the urinary constituents we ordinarily find the mineral salts. The quantity of these depends in a

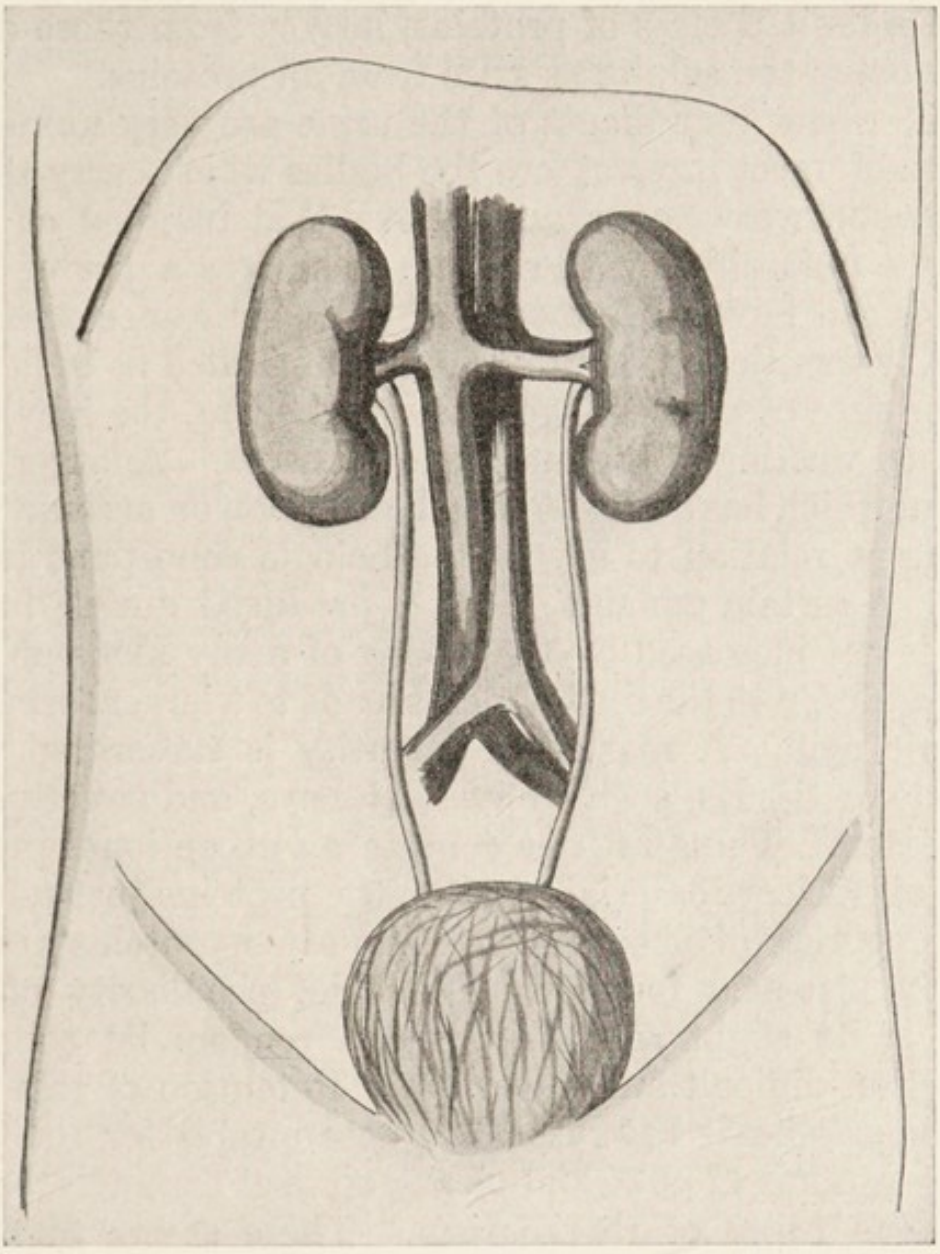


Fig. 22.—The kidneys and the urinary bladder. The two kidneys are shown within an outline which suggests the body cavity. Their advantageous connections with the chief artery and vein of the system are indicated. Below is the bladder reached by the two ureters. These vessels enter the bladder low down and behind—not at the level where they disappear from the figure.

large measure upon the amount in the diet, and as sodium chlorid is the one taken most freely, so it will generally be the principal inorganic compound in the urine. The

chlorids of the mixture are accompanied by phosphates and sulphates. These are not to any extent salts which have been eaten, but, like the urea, they represent modified fragments of protein molecules. The phosphates come from a limited class of proteins, largely from those of the cell-nuclei; the sulphates arise from all proteins.

The minor ingredients of the urine are very numerous. Those of most interest are the bodies which carry the nitrogenous waste over and above that handled as urea. To one unfamiliar with organic chemistry a list of their names can have little meaning. The substance creatinin, already mentioned, is provisionally regarded as indicative of the rate of true endogenous metabolism, the inevitable gradual wasting of the nitrogenous tissues. Another compound which has attracted much attention on account of its apparent relation to several pathologic conditions is uric acid. A certain amount of this is produced during fasting and is not increased by the taking of many kinds of food. The addition to the diet of meats leads to a larger formation of uric acid. A maximum quantity is elaborated when glandular tissues, such as liver, kidneys, and sweetbreads, are eaten. These articles contain an exceptional proportion of nuclear material rich in the proteins just referred to as sources of phosphates. The same proteins are evidently uric-acid formers. The chief peculiarity of uric acid is its slight solubility, which renders its complete excretion difficult and uncertain. Retention of this crystalline substance has been held accountable for the painful symptoms of gout and of a good deal that goes by the inclusive name of rheumatism. There seems to be an increasing disposition to absolve it from such charges.

We have by no means exhausted the list of normal urinary constituents, but the student must be referred to other sources for the details. The most commonly occurring compounds of an abnormal character are sugar and albumin. The significance of the sugar should be clear in the light of what has been said. Its transient appearance as a result of free consumption does not indicate a diseased

condition, but only dietetic indiscretion. The possibility of emotional glycosuria will also be recalled (page 146). Very frequent or continuous elimination shows that the body has not the usual power to oxidize its sugar. The kidneys are not generally at fault; the defect is in the metabolism of the pancreas or elsewhere. An abundant escape of albumin (presumably drawing upon the protein mass of the blood) is commonly due to a disordered condition of the kidneys. It takes place, for example, in Bright's disease.

Urine when freshly secreted is ordinarily acid to litmus. It may be alkaline when much vegetable food is eaten, and becomes so on standing in any case. The change is due to a bacterial fermentation whereby urea is transformed into ammonium carbonate. An ammoniacal odor develops in connection with this alteration and the liquid is likely to become turbid. The deposition of a sediment under such conditions is no cause for anxiety. It has often been represented by unscrupulous quacks to be a serious symptom. The urine of the herbivora, which is normally alkaline, becomes acid when the animals are fasting, and it may be pointed out that they are then carnivorous—living upon their own flesh and fat.

How much urine is secreted depends largely on the quantity of water taken, so far at least as this is in excess of the perspiration. Kidney activity is stimulated by almost any dissolved substance foreign to the standard composition of the blood. The nitrates, for example, are absorbed rather freely from the intestine and afterward removed by the kidneys in a large volume of water. They, therefore, belong to the class of bodies known as diuretics. The active principle of coffee and tea has the same action. In securing their own elimination such compounds may promote the excretion of others. Diuretics bring about their effect partly through modifying the circulation, and partly, it is believed, through direct influence upon the kidney cells. As regards the first mode of working, it may be said that the kidney is readily responsive to increased

blood-flow, especially if it is attended with high arterial pressure. Difficulties with the heart, if they entail retarded circulation and lowered pressure, frequently lead to deficient output.

Other Factors in Excretion.—The lungs and the kidneys perform so large a share in the disposal of metabolic waste as to leave relatively little of the work undone. The feces, however, include small quantities of miscellaneous excretions, and it is assumed that the precise part borne by the intestine and the liver (in the separation of bile) could not be taken by the kidneys. The modified bile-pigments of the feces illustrate this specific action. The share of the skin in the removal of waste is popularly overestimated. The belief that "the pores must be kept open" lest poisons gather in the system is so fruitful of wholesome practices that one is reluctant to question it. Candor requires, however, that the physiologist repudiate the moral in the story of the Italian boy, who died because the surface of his body had been sealed with gold paint for a few hours. If the case is authentic, he must have died because of the character of the application and not from toxic products of his own evolving. Volunteers have submitted to have the skin shellacked and have not suffered any other ill effects than sensitiveness to heat and cold.

Perspiration is almost purely a mineral solution and the salts it carries could doubtless be cared for by the kidneys. When made profuse by severe exercise, it contains in small amounts some organic constituents like those of the urine, but its highest possible rating as a vehicle of nitrogen excretion is not impressive. The same may be said of the assistance rendered by the skin to the respiratory tract. Carbon dioxid passes from the skin in measurable quantities when there is abundant perspiration, but the largest loss which can occur in this way seems insignificant when compared with the discharge from the lungs.

CHAPTER XVIII

THE ESTIMATION OF METABOLISM

It is more than sixty years since the first well-equipped laboratory for the quantitative study of human nutrition was opened in Munich. Before that time much had been accomplished in the analysis of foods, the measurement of rations, and the examination of urine, but no satisfactory knowledge of the general metabolism could be had until means should be devised to entrap and measure the gaseous outgo of the body. This difficult task was accomplished by the construction of the first *respiration chamber*, now one of several in various centers of scientific research.

In the long run there must be a correspondence between the food and the metabolism, the income and the outgo, but on a single day there is no necessary agreement between them. This is radically demonstrated on a day of fasting, when the income is *nil* and the outgo is considerable. It is to the excreta that we attend, therefore, when we wish to judge to what extent various materials have been broken down in the body. Studies of the food may be valuable, but in our first discussion we shall limit ourselves to the simple case of the subject without income. A great deal can be learned about the metabolism by determining two chemical elements—the carbon and the nitrogen of the waste-products. Other facts can be ascertained when the quantity of oxygen consumed is noted. Water excretion is frequently measured also.

Nitrogen Elimination.—The fact is already familiar that the nitrogen leaving the system is found almost wholly in the urine. An additional fraction is in the feces. Concerning this latter item it will be remembered that we cannot easily say how largely it is a residue signi-

fying incomplete absorption and how far it is a true waste-product. If feces are discharged during long fasting the nitrogen contained must be the body's own contribution. On the whole, the fecal nitrogen is nowadays regarded as an excretion unless it is clearly excessive. The nitrogen of the perspiration can usually be ignored.

When we assume all the nitrogen eliminated to have come from the decomposition of proteins, a certain error always exists, but it is not great enough to be considered in the present elementary treatment of the subject. Nitrogen constitutes about 16 per cent. of protein. Accordingly, the excretion of 16 grams is taken to stand for the destruction of 100 grams of protein. This is not far from an average amount when the diet is freely chosen. In the opinion of an increasing number of authorities it is higher than it should be for the best nutritional condition. To arrive at an estimate of the protein metabolized we multiply the quantity of nitrogen in the outgo by 6.25 (an operation which is equivalent to dividing by 16 to find 1 per cent. and multiplying by 100 to obtain the total). This was a familiar procedure before the erection of respiration chambers made possible a complete survey of the metabolism.

Carbon Elimination.—A subject at rest excreting 16 grams of nitrogen may be expected to excrete something like 200 or 250 grams of carbon in the same period. This will be in the respiratory carbon dioxid so largely as to make the urinary and fecal carbon appear insignificant. Figures from an actual experiment are:

In the respiration	208 grams.[1]
In the urine	6 "
In the feces	11 "
Total	225 "

This carbon may have been furnished by all three types of body substance—the proteins, fats, and carbohydrates—in numberless possible combinations. The amount of protein decomposition has already been fixed at 100 grams.

[1] 763 grams carbon dioxid.

Such an amount of protein must have yielded in its falling apart a quantity of carbon represented by the percentage of that element in the compound. The actual percentage is about 53, so that in this instance 53 grams of the 225 may be ascribed to protein as a source. The remaining carbon, 172 grams, must have been derived from non-nitrogenous material. How far it has come from fat and how far from carbohydrate we cannot exactly determine without additional data.

It is of value to know all the circumstances of such a trial. If the twenty-four hours under consideration is the first fasting day and the diet of the day before has been the ordinary one, we may assume that the subject entered upon the experimental period with a fair stock of glycogen. This will be used rather freely at the outset, but more and more slowly as the hours pass. Carbohydrate, accordingly, contributes largely to the support of the organism during the first day of abstinence, and thereafter bears but a very small part. To say that the glycogen of the body is used up in a single day of fasting would not be correct; the fact is rather that the rate of consumption diminishes sharply. In proportion to this diminution in the use of carbohydrate the fat is called upon increasingly. For any day of hunger after the first it is substantially true that the individual is living on protein and fat.[1]

Let us continue the discussion of our numerical illustration with the added statement that the day is the second rather than the first in a fast. The 172 grams of carbon from non-protein material may now be attributed to fat. The percentage of carbon in fat is about 77. A simple calculation (dividing by 77 and multiplying by 100, or, what is the same thing, multiplying our first quantity by 1.3) gives 223.6 grams of fat as the amount destroyed in the

[1] The following figures are from Publication 77 of the Carnegie Institution, 1907: Average metabolism of several subjects on the first and third days of fasting,

	I	III
Protein	60[g]	78[g]
Fat	135	155
Glycogen	110	21

body during twenty-four hours. The total metabolism is then 100 grams of protein and 223.6 grams of fat. It is not safe to conclude from this that the loss of weight will prove to be just equal to the sum of the two items. It may be found to be either more or less, the result depending chiefly on the relation of the income and outgo of water. Generally, during a fast there must be a large and continuous loss of water from the body. The destruction of tissue liberates water in the proportion of nearly 400 grams for each 100 grams of protein disintegrated. This water tends to be eliminated. If it were not, the percentage of solids in the body in starvation would steadily decline.

Could there be conditions under which all the non-protein carbon could confidently be assigned to carbohydrate sources? Not in the fasting state nor commonly on a mixed diet. The case might be approximated by giving ample rations with minimal fat and maximal carbohydrate for days together. This is nearly equivalent to the nutrition of the herbivora. If our supposed human subject yielded the amounts of carbon and nitrogen already quoted while adequately fed upon protein and carbohydrate, we should not be much in error in assuming that the carbon from non-protein had been evolved from starches and sugars metabolized. Carbon forms about 40 per cent. of carbohydrate,[1] and, if we reckon according to the same principle as before, we find that 172 grams of carbon could have come from 430 grams of carbohydrate, more or less. Under more ordinary conditions of feeding —and on the first day of a fast—both carbohydrate and fat would share with protein the sustaining of the body's activities.

The Respiratory Quotient.—The modern respiration chamber is a small room with impervious walls and carefully controlled ventilation. The carbon dioxid of the air drawn off is either determined directly or estimated from measured samples bearing a known relation to the

[1] Just 40 per cent. of dextrose, about 42 per cent. of cane-sugar, and about 44 per cent. of starch.

total volume. In chambers of the best type the oxygen consumption is also ascertained. If we know both the carbon dioxid production and the oxygen absorption we can, of course, compute the ratio between the two. The value of this ratio, based on the volumes and not the weights of the two gases, is known as the respiratory quotient. It is figured by dividing the volume of carbon dioxid by the volume of oxygen. So determined it has most of the time the character of a proper fraction, or, rendered as a decimal, it is less than one. This is a way of saying that the carbon dioxid discharged is generally less than the oxygen which has disappeared in the exchange.

Every molecule of carbon dioxid holds combined the equivalent of a molecule of oxygen. It follows that if all the oxygen were devoted to the formation of carbon dioxid the two volumes would be equal and the ratio between them would be unity. The failure of a part of the oxygen to reappear as carbon dioxid indicates that it has been combined in some other way. It has actually gone to form the second great respiratory product, the water of the metabolism. The interest which physiologists feel in the respiratory quotient springs from the fact that it varies with the prevailing employment of one kind of material or another in the general oxidation which is going on. The decimal value of the ratio is elevated in proportion to the prominence of carbohydrate in the process.[1] It is lowest when fat is bearing a principal part. Since, at the beginning of a fast, carbohydrate is called upon to meet the requirement, while its place is taken by fat a few hours later, the respiratory quotient will show a decline which marks with exactness the shifting of the current.

It would be beyond the scope of this discussion to show how the respiratory quotient can be made the basis of equations which determine how much fat and how much carbohydrate are broken down to give a certain output of carbon dioxid. Suffice it to say that the possibility exists,

[1] Lusk, "Elements of the Science of Nutrition," Fourth Edition, W. B. Saunders Co., Philadelphia, 1928, p. 65.

and is highly fruitful of results in the quantitative studies of nutrition laboratories. The meaning of the respiratory quotient is sometimes altered by temporary conditions. Perhaps the most interesting of these is the peculiar increase in carbon dioxid outgo exhibited by an animal which is rapidly fattening on a diet rich in carbohydrates. Such an animal may show for days together a respiratory quotient in excess of unity, that is, it produces carbon dioxid not accounted for by the observed oxygen intake. This extra carbon dioxid is explained satisfactorily as having come from the carbohydrate undergoing transformation to fat. (See also Chapter XV, page 147.)

Equilibrium.—Our nearly uniform weight, maintained for periods of years, suggest that income and outgo are often nicely balanced. Complete equilibrium demands strict equality between the income and outgo of water, of mineral matter, of nitrogen, and of carbon. The realization of these conditions is not likely, though it is often closely approached. Partial equilibrium, that is, equality between intake and output for one class of compounds with inequality for another, is more common. The most frequent striking of a balance is between the nitrogen of the food and that of the excreta. Nitrogenous equilibrium is the rule rather than the exception. The tendency of the body to establish this correspondence, in spite of wide variations in the diet, was noted long ago. It was said that the organism refused to store protein when supplied with large amounts of this kind of food. This is true in the narrow sense that the body does not add freely to the adult measure of its living tissues when offered extra protein. Yet, as we have seen, the return of all the nitrogen fed does not of necessity mean that the body has retained no part of the protein supplied to it. The chief reason why there is such a marked disposition to make the output of nitrogen equal the income is found in the fact that all the amino-acids beyond the small quantity used for protein synthesis are deaminized. So long as this is the case, raising the nitrogen of the food must result merely in

adding to the urea excreted. The non-nitrogenous residues may find more or less permanent lodgment in the tissues in the form of glycogen or fat.

Nitrogen retention is to be expected during growth when the protein syntheses are more extensive than the endogenous decomposition. The recovery from illness or from a fast is another instance when the body protein must definitely increase. This is really only a special case of growth. A liberal protein supply has been demonstrated to accelerate the healing of extensive wounds.[1] Changes of climate or the pursuit of athletic training may encourage some degree of protein storage. And without seriously qualifying what has just been said it may be stated that abundant nitrogenous food may have the same effect, but the nitrogen retention secured by forced feeding is always limited to a very small fraction of the protein given.

The roughly maintained equilibrium, which is, after all, a striking example of the adjustments of the organism, is to be traced to the singular reliability of the appetite. This is the agent which prompts so surely to the taking of extra food when one exchanges an inactive life for one of bodily activity. The most radical changes in the total metabolism are unlikely to lead to lasting variations in body weight beyond slight gains and losses, which, by the way, are often the reverse of what was anticipated. Exercise, which is supported by large oxidation, may even result in some increase of weight, showing that the appetite has rather more than met the precise need of the body. The average recruit in a training camp gains weight in spite of unwonted and fatiguing exertions.

Carbon Retention.—When a quantitative comparison is made between the compounds in the diet and those excreted it is not infrequently found that carbon is being stored, though the nitrogen of income and outgo may be balanced. What can be inferred as to the nature of the substance added to the tissues? Just as in the previous case where we desired to interpret the meaning of the

[1] Clark, Johns Hopkins Hospital Bulletin, xxx, 1919, No. 339.

carbon loss during fasting, we have to consider the respective share taken by carbohydrate and by fat. As before, it is important to know the condition of the subject prior to the trial. If the day is the first of feeding after a fast there will be some recruiting of the gylcogen in the body, and a part of the carbon retention may be attributed to a gain of this material. Otherwise, when carbon is stored in the midst of a period of liberal feeding, the probability is that fat rather than carbohydrate has been deposited.

Applying the same factors as in the earlier instance, we multiply the retained carbon by 1.3 if the circumstances point to its having been held as fat. An excess of 10 grams of carbon in the income over the outgo would be assumed to indicate the addition of 13 grams of fat to the supply in the body. An amount of this magnitude would not show itself decisively in the weight, being easily disguised by the temporary gain or loss of water that might occur at the same time.

Starvation.—The statement has been made that when food is withheld the system at first makes large use of glycogen to supply its needs, but presently must draw on its fat reserves. From the first it is at the same time breaking down protein. In a prolonged fast the fat of the body may be almost entirely used up. When this condition is reached an increased destruction of protein may set in, and it is a sign that the end of the siege is not far off. This is signalized by the "premortal rise" of nitrogen excretion. It has been noted in starving animals and in tragic fashion in the personal experience of Loewy, a German physiologist, reduced by the restrictions of the war.[1]

The losses suffered in starvation by the various tissues are extremely unequal. There is clear evidence that the most essential organs are protected from wasting by the consumption of those that can be better spared. In a cat deprived of food for thirteen days and losing about one-

[1] Lusk, Physiological Reviews, i, 1921, 523.

third of its original weight the fat was reduced by 97 per cent., the liver by 53, the muscles by 30, and even the bones by 14. Yet the heart and the central nervous system had scarcely diminished at all. (The losses were estimated by comparing the organs of the fasting animal with those of a normal cat.)

Dogs survive starvation for incredible periods. Kumagawa kept one fasting until its death on the ninety-eighth day. Hawk compelled a dog to go without food for one hundred and seventeen days, nursed it back to vigorous health, and then conducted a second fast of one hundred and four days without killing the unfortunate animal. The loss of weight in these long periods was about 60 per cent. The Russian Awrowrow denied a dog water as well as food; death came on the sixtieth day when the body weight had been reduced to about two-fifths of the normal.

Human subjects are said to have fasted for fifty days. Several times volunteers have been under close surveillance for periods of more than a month without food and valuable scientific data have been recorded. Perhaps the model study of this kind is the one made upon Levanzin at the Carnegie Nutrition Laboratory.[1] The fast continued for thirty-one days. The loss of weight was nearly 22 per cent. (The change was from 133 pounds to 104.) The study of the excreta indicated that this loss must have been the sum of about 8 pounds of fat and 20 pounds of average nitrogenous tissue which, it should be remembered, contains 75 per cent. or more of water. No doubt the glycogen present in the beginning was quite completely removed. Levanzin was in fair condition at the end of the period, though in an unhappy frame of mind.

[1] Benedict, Carnegie Institution of Washington, 1915, Publication 203.

General reference: Sherman, "Chemistry of Food and Nutrition," Macmillan, New York, 1923. Also Bayliss, "The Physiology of Food and Economy in Diet," Longmans, New York, 1917.

CHAPTER XIX

THE ENERGY OF THE METABOLISM

THE initial statement in this book—that living things are transformers of matter and energy—is a text to which we have closely adhered. In recent chapters the emphasis has been placed upon transformations of matter. We shall now pass on to speak of the energy evolved by animals and particularly by the human body. The fundamental facts are presumably clear. The energy of the income is potential in the complex molecules of the food. It is released in the oxidative decomposition processes of life and made kinetic. It appears chiefly—often solely—in the form of heat. Measurements of the heat production of living organisms are generally to be accepted as indicative of the total energy production. Certain exceptions to the rule will soon be noted.

Fuel Values.—Since energy can be transmuted from one form to another it is possible to make the units which stand primarily for one kind do duty for all. It is our constant practice to use the units of heat to measure all the energy of metabolism. The unit which we shall employ is the large *Calorie*, approximately defined as the amount of energy required to raise the temperature of 1 kilogram of water one centigrade degree. The large Calorie is preferably distinguished from the small by the capital C. The small calorie is $\frac{1}{1000}$ of the large; no further reference to it will be made. When a combustible organic substance of a standard composition is completely oxidized a definite quantity of heat is evolved. The heat produced by oxidizing 1 gram of any compound is its *fuel value*.

The highest fuel value recorded is that of hydrogen, about 34 Cal. This is the amount of heat produced when

a gram of hydrogen gas (11 liters) is oxidized to water. One gram of carbon oxidized to carbon dioxid gives nearly 8 Cal. These two illustrations do not bear directly on our physiologic inquiry, for the body does not use the free elements for oxidation, but their compounds. It is, therefore, of more interest to turn to the fuel values of carbohydrates, fats, alcohol, and proteins, since these are the actual sources of heat and kindred energy. The calorific value of a compound is not precisely that of the carbon and the hydrogen contained in it and not yet bonded to oxygen, although some early work of a useful kind was based upon that assumption. It is to be noted that the oxygen in the physiologic compounds reduces their potency; the less they contain the more largely they will consist of elements subject to oxidation. This is the main reason why fats have fuel values greatly in excess of those of carbohydrates. A gram of fat contains nearly twice as much carbon as a gram of sugar. It also contains much hydrogen with unsatisfied affinities for oxygen.

The actual heat production observed when a gram of starch is burned is a trifle more than 4 Cal. Sugars, which are slightly richer in oxygen than starch is, have a little lower fuel value. The figure (4 Cal.) is fairly representative of carbohydrates as a class. The oxidation of 1 gram of fat liberates about 9.3 Cal., or $2\frac{1}{4}$ times as much as starch. A gram of grain alcohol fully oxidized gives an intermediate quantity, about 7 Cal. All these non-nitrogenous compounds are made to yield the same simple products, namely, carbon dioxid and water, whether they are destroyed by literal burning outside the body or by the metabolic processes. We shall see shortly that the energy which is found to be set free in their oxidation can be proved to be equal in the two cases.

Protein stands somewhat apart in its behavior. A gram of dried protein burned in oxygen gives nearly 6 Cal. But some of the products generated in such a laboratory test are not those which the body forms from protein and excretes. Urea, for example, is not found after the actual

burning of protein. Urea itself has a certain capacity for oxidation and a low but distinct fuel value, something like 2.5 Cal. per gram. The residual fuel value in urea is a sign that some portion of the energy latent in protein is constantly lost to the animal economy. Bacteria may profit by it, but it seems not to be available for the higher living forms. There are certain products other than urea which remain after the decomposition of protein molecules and which likewise represent unused energy. Some of these minor products accompany the urea in the urine, while others are mingled with the feces. To make accurate allowance for the energy lost with these incompletely oxidized compounds is a difficult matter. The estimate arrived at credits to a gram of protein 4 Cal. or a little more. It is a coincidence with very convenient results that this is almost exactly the same as the figure for carbohydrate.

The Total Daily Metabolism.—The widest limits between which the metabolism of an adult may vary may be set down as 1000 and 10,000 Cal. per day. The lowest level will be approached when there is complete rest and protection from cold during the twenty-four hours. The maximum will be reached, if ever, when a large, powerful man performs the heaviest muscular work. The food taken on a single day influences the result less than would be anticipated. (As already pointed out, the appetite follows the metabolism rather than precedes it.) High protein feeding has an effect which will be discussed later.

Of course, the average for an individual will generally fluctuate much less than is suggested above. It will rarely fall below 1500 or rise much above 3000 under the conditions of city life. For a sedentary subject it is probably reasonable to fix upon 2400 as a mean. If for sixteen hours of waking we allow 100 Cal. per hour, and for eight hours of sleep 60 per hour, the estimate adds up to 2080. For the performance of any great amount of

muscular work a good deal larger total must be assumed.[1] Farmers in widely separated countries have been found to employ rations representing about 3500 Cal. per day. Army rations usually furnish as much as 4000. Maine lumbermen have reached twice this figure.[2] Active boys in a superior preparatory school (St. Paul's, Concord, N. H.) are served with meals that sum up to 4350 Cal. daily, and buy enough outside to bring the total to 5000.[3] It will be suggestive if we consider how much of a single food-stuff would be required to furnish a total of the lower order.

Two thousand Calories could be obtained by the oxidation of about 500 grams of starch or sugar. The meeting of the energy requirement is not the only qualification to be demanded of a day's dietary. A ration of pure sugar is obviously not to be recommended, though the consumption of candy to such an extent may be entirely possible for some subjects. The quantity of fat needed to afford the same heat value will be in the vicinity of 216 grams. One can hardly conceive of eating clear fat to this amount. Making a similar calculation for alcohol, we find that a little less than 300 grams of this compound will theoretically meet the need. A palpable absurdity is apparent. While the attempt to use alcohol exclusively as a fuel for the body would evidently be disastrous, it is interesting to consider that a lamp burning 300 grams of absolute alcohol in a day would equal a human being as a source of energy. The flame would be a very small one and the comparison gives one a feeling of dissatisfaction and disappointment.

Since protein is nearly equivalent to carbohydrate as a source of energy, the theoretic ration of protein would be the same as that of sugar, namely, 500 grams. The prac-

[1] Benedict has suggested the following standard:

8 hours' sleep at 65 Cal.	520 Cal.
12 sedentary hours at 100 Cal.	1200 "
4 hours' light exercise at 170 Cal.	680 "
	2400 Cal.

[2] U. S. Department of Agriculture, Bulletin No. 149, 1904.

[3] Lusk, loc. cit., p. 759.

tical impossibility of eating so much protein is evident when it is remembered that protein is acceptable only when softened and expanded with liberal quantities of water. Lean meat, which is not strictly a straight protein food, but which approaches that composition, is three-fourths water. White of egg, in which the solid portion is almost all protein, is seven-eighths water. The attempt to dry such material and so to reduce it to the smallest bulk produces a mass resembling hardened glue or shellac. To subsist on the proteins of meat alone, the fat having been removed, one would be compelled to eat some five pounds daily. Travelers have described certain peoples as living almost wholly on meat or fish, but this does not mean a pure protein diet, the fat undoubtedly figuring largely. The Eskimos necessarily eat but little carbohydrate, for they can obtain no vegetable food of importance; it seems plain, however, that they have increased both fat and protein consumption and not protein alone.[1]

The foregoing suggestions make clear the inconveniences and the unhygienic aspect of any attempt to live on a single type of food. It is a fact, furthermore, that one could not under any conditions continue indefinitely to eat only non-nitrogenous food. Protein metabolism never ceases and a certain nitrogenous income must be provided. We cannot, therefore, judge the fitness of a diet solely by its heat value. It must measure up to a reasonable standard in this respect, but it must also include a suitable proportion of protein. Another criterion, not so commonly insisted upon, is that a sufficient quantity and variety of

[1] Heinbecker (Journal of Biological Chemistry, lxxx, 1928, 461) gives an interesting account of the dietetic habits of the Eskimos of Baffin Land. Their food is almost wholly derived from the bodies of marine animals, largely from seals. The weight of meat consumed by adults varies from 4 to 8 pounds daily. Much of it is eaten raw. A summer ration may contain about 280 grams of protein, 135 grams of fat, and 54 grams of carbohydrate (glycogen) per diem. This does not represent a high energy value—about 2600 Calories—but the stature of the race is small and in winter the consumption of fat is said to be largely incresaed. Babies are nursed for as long as two years.

mineral compounds shall be supplied. Of course, these scientific characterizations of the diet are inadequate unless attention is paid also to attractiveness and digestibility.

When a subject freely chooses his food, unprejudiced by chemical knowledge, he is apt to make use of all three classes of food-stuffs to a considerable extent. Carbohydrate will usually amount to more than half the total solids of the ration, while protein and fat show a curious tendency to be taken in nearly equal weights. An example of such a selection, perhaps the one most frequently quoted, is the following:

Protein	100 grams	410 Calories.
Fat	100 "	930 "
Carbohydrate	250 "	1025 "
		2365 "

Of late years, observation having been extended to large numbers of people, it has become evident that Americans of student and professional classes rarely choose to eat as much as 100 grams of protein.

Calorimetry.—We have been speaking of the amounts of heat set free in the oxidation of various food materials, and of the energy liberated by animals and men as an accompaniment of their metabolism. The determination of such data requires the use of calorimeters. These are of various forms, but have the same underlying principle. In case a food sample is to be burned it is enclosed in a small chamber, preferably in an atmosphere of oxygen, and its combustion is initiated by means of an electric spark. The heat is imparted to a large mass of water surrounding the chamber and can then be estimated by the elevation of temperature observed in this water. This is an elementary and somewhat sweeping statement; numerous corrections would be necessary in practice.

One of the earliest attempts to gage the heat production of an animal consisted in confining it within a chamber having double walls and ice between. The amount of ice melted could thus be made the basis for the estimate desired. The employment of a water calorimeter evidently

does away with the unnatural chilling which must have been entailed in this primitive trial. The large and costly calorimeters in modern laboratories for the study of human nutrition are of the water type. No adequate idea of the difficulty involved in such work is likely to be grasped by reading this condensed presentation. Ventilation must be maintained and the circulating air returned to the chamber with its temperature unchanged. The evaporation of water must be accurately measured, for if this were ignored a great deal of heat produced in the metabolism would escape measurement. (In the evaporation of 1 kilogram of water heat to the amount of 536.5 Cal.[1] will be made latent.) Changes in the body temperature cannot be overlooked. If, for example, a human subject equivalent in heat capacity to 50 kilograms of water should experience a rise of temperature amounting to 0.5° C. during an experiment, 25 Cal. would have been retained in his body. If, instead, there were a fall of 0.5° there would have been a discharge of 25 Cal., and the observed heat output would have been greater than that due to the current metabolism.

Now the question may be asked whether we can be sure that the observed heat production (corrected for body temperature changes and supplemented by the heat loss through evaporation) is a just representation of the total energy set free. May there not be other forms of energy than heat? What are the facts concerning muscular work? We cannot say positively that no energy eludes the calorimeter, but the impression is constantly being confirmed that any such escape must be insignificant. As to the energy of movement it can be shown that under most conditions this will eventuate in heat. This is an important matter and deserves to be carefully illustrated.

Let us take for an example the case of the heart. This organ does a great deal of work in forcing the blood through the vessels. Does this work appear as heat so as to be

[1] This is the figure at the freezing-point. It increases slowly with rising temperature.

arrested and recorded by the calorimeter? There is no doubt that it does. The conversion is effected as the resistance to the blood-flow is encountered and overcome. The heart produces some heat within itself, and some additional heat due to its metabolism is made to appear in all parts of the body. Wherever the blood is driven there is friction, which is a means of transforming the energy of motion into heat. The same statement applies to the breathing movements. Work is done, in the physical sense of the term, each time the ribs are lifted, but with their return to the expiratory position this work is reconverted into heat. So, too, all ordinary forms of exercise may be shown to result in heat production.

Nevertheless it is possible to devise conditions under which a part of the metabolic energy will not be given to the calorimeter. Suppose, for example, that the subject within the apparatus is employed in taking books from the floor and placing them upon shelves. As long as he pursues this form of activity a share of his evolved energy will become potential and be lost to direct observation. It may be said to exist as "energy of position" in the mass which he has elevated. In other words, it has been stored. If, after a day of this labor, he should occupy himself in removing the books from the shelves and laying them upon the floor, he would be giving to the calorimeter more heat than that actually produced as a result of his metabolism. When the books had all been returned to the original level the sum of the calories for the two periods would justly represent the energy production of his body. One could conceive of two calorimeters placed side by side, in one of which a man might turn a crank operating a shaft which should pass into the second chamber and there revolve a wheel against the resistance of a brake. Most of his energy would be registered by the first calorimeter, but a fair proportion of it, standing for most of his muscular work, would be apparent in the second.

Direct and Indirect Calorimetry.—We have said elsewhere that the proof of the validity of the principle of the

conservation of energy for living things was a great achievement of the nineteenth century physiologists. The method of this proof may now be outlined. We have just seen that the total energy production of animals, including man, may be satisfactorily measured in calorimeters, provided that the amount of evaporation is known and any changes of body temperature considered. This procedure is *direct calorimetry*. Now, of course, it is possible during the same period to collect the excreta and to determine the character and the amount of the metabolism according to the principles explained in the last chapter. Knowing the metabolism—so many grams of protein, of fat, and of glycogen destroyed—we may credit to each of these its respective fuel value and calculate the number of calories which could theoretically result from just such oxidation. We may then compare the energy as determined from the living organism and the energy which should have been liberated in the formation of the measured wastes.

To make the matter plain, we may refer once more to the case on which the numerical estimation of metabolism was previously based. The subject was credited with a metabolism of 100 grams of protein and 223.6 grams of fat. (This, it may be recalled, is the usual assumption when the day is one of fasting and does not closely follow carbohydrate feeding.) The apparent heat value of the calculated metabolism will be as follows:

100 grams of protein at 4.1 calories	=	410 Calories.
223.6 grams of fat at 9.3 "	=	2079 "
Total.....		2489 "

This bit of reckoning is an instance of *indirect calorimetry*. It is found in practice that direct and indirect calorimetry lead to results so nearly identical as to make it certain that the discrepancy between them is accidental. The two figures differ in modern work by less than 1 per cent.

The correspondence between the observed and the calculated calories means this: that the animal displays no

powers of movement or heat production which cannot be referred to the oxidation of organic compounds in its body, and so eventually to the stores of chemical energy in its food. It is an engine, a transformer, and not a creator of energy. A glimpse of this conception came within the vision of the brilliant Count Rumford more than one hundred years ago. He had become convinced that heat must be a form of energy rather than a substance.[1] His conclusions had been drawn in part from the observation that there seemed to be no limit to the quantity of heat obtainable from small masses of metal in the process of drilling. With a flash of insight he looked at the horse which was walking in a circle to move the drill, and queried whether the heat in the iron turnings might not be a derivative of the muscular work of the animal, and whether the same energy had not in some sense pre-existed in the food given to it. The verification of his induction was long deferred, but has at length been made entirely conclusive. The credit for this demonstration is shared by many workers, but most conspicuously by Rubner, in Germany, and Atwater, in this country.

Let us return once more to our quantitative illustration. If the day of the experiment had been one of ample feeding instead of fasting, and the diet had consisted of protein and carbohydrate, the metabolism might have been held to have involved these materials rather than protein and fat. The supposition has already been entertained and may now be made a basis for indirect calorimetry. From p. 188 we copy the amounts of protein and carbohydrate, multiplying by 4.1, the value common to both:

100 grams protein	410	Calories.
430 " carbohydrate	1763	"
Total	2173	"

Comparing this sum with the 2489 Cal. previously determined, we see that for a given production of carbon dioxid the evolution of heat will be greatest when fat is the

[1] Jordan, "Leading American Men of Science," Holt, New York, 1910.

exclusive non-protein source, and least when the metabolism is as nearly as possible on a carbohydrate footing. The difference is some 15 per cent.

If both carbohydrate and fat had participated in the decomposition underlying the observed excretion, the heat of the metabolism might have had any value intermediate between 2173 and 2489 Cal. The figure obtained by direct calorimetry might in such a case of mixed metabolism be used to determine the part borne by carbohydrate and fat respectively. But, as indicated before, the respiratory quotient can be used to solve the problem. Direct calorimetry is rarely resorted to in these days.

There is a fair proportionality between the consumption of oxygen and the energy set free, whatever the assortment of the materials undergoing oxidation. While fat has a much higher fuel value than carbohydrate, it also requires much more oxygen for the catabolism of an equal quantity. Lavoisier's plan of measuring metabolism on the basis of oxygen absorbed did not entail any gross errors. Regardless of the combination of food-stuffs being burned it is approximately true that the consumption of one liter of oxygen is associated with the production of 5 Calories. The simpler forms of apparatus for determining metabolism depend on this principle. They are much used in hospitals.[1]

[1] Benedict, Boston Medical and Surgical Journal, clxxxviii, 1923, 567.

CHAPTER XX

THE FACTORS WHICH MODIFY METABOLISM

The circumstances which radically affect the quantity and kind of decomposition going on in the body must already be evident. There can be no hesitation in placing first among these conditions muscular activity. Minimal metabolism attends the most nearly complete state of rest which can be secured. It is somewhat lower during sleep than during a like period of lying awake, doubtless because the waking subject cannot so successfully abolish muscular contraction. When one is sleeping metabolism obviously continues in certain of the breathing muscles and the beating heart. We cannot doubt that it proceeds also in the glands, the muscular coats of the alimentary canal, the nerve-centers, and many other localities.

Basal Metabolism.—This expression has come to be a very familiar one in medical circles of late. What is meant is the rate of heat production in a state of rest and in what is called the "post-absorptive" condition, that is to say at a time when the digestion and absorption of the last meal can be assumed to be complete. This must be realized twelve to fifteen hours after eating. The subject must be relaxed, comfortably warm, but awake.[1] The metabolism is determined by indirect calorimetry as explained in the preceding chapter or, quite satisfactorily, by a calculation based on the measured consumption of oxygen.

[1] For most people there is a difference of some 10 per cent. between resting and sleeping metabolism. The obvious suggestion is that we relax more completely when we sleep than we can voluntarily. It is reported that among the Chinese the sleeping rate is scarcely lower than the waking; they relax more successfully than we do. Necheles, American Journal of Physiology, xci, 1930, 661.

The result of such trials is usually expressed in Calories per square meter of body surface per hour. The normal for an adult male is well established; it is close to 40. A variation of 10 per cent. upward or downward is not regarded as significant. The extent of the body surface has been estimated by ingenious and laborious procedures and formulæ have been deduced which make it possible to obtain it approximately for any individual whose weight and height are known. An average value is 1.75 square meters. Evidently the basal metabolism for a man of this stature must be 40 × 1.75 or 70 Calories per hour.

Age and Basal Metabolism.—In the newborn the basal figure is below the adult quantity, but within a few months it rises to exceed it. At five years of age it is near 60, at twelve it is still as much as 50. These determinations have showed us that children have a high food requirement for bare maintenance over and above which we must provide liberally for their growth and great muscular activity. With advancing age the basal rate very gradually declines and in the octogenarian it may have fallen to 35. The standard of 40 Calories per square meter per hour, quoted as applying to the vigorous adult male, is not reached by the undernourished. Prolonged fasting has been known to bring it down to 28 or thereabouts.[1]

Sex.—The basal rate for a woman is about 7 per cent. below that for a man, about 37 against his 40. This probably does not mean that the protoplasm of the female body is less active than that of the male; it means rather that the amount of living tissue is less in the body of a woman than in that of a man having the same surface. If we compare average types it is plain that adipose tissue is more abundant in the female. The muscles are disguised by its presence so that they are inconspicuous even in very strong women. Adipose tissue has little metabolism of its own: it follows that a subject having much

[1] Kleitman, American Journal of Physiology, lxxvii, 1926, 233. Such a reduction attended Hoelzel's forty-two-day fast.

of it is not so large in terms of active protoplasm as the lean individual of equal height and weight. When this principle does not apply, as in young women who have practised severe self-denial for the sake of slender figures, the low basal metabolism may be referred to subnutrition.

The Ductless Glands and Basal Metabolism.—A large body of data secured in recent years has proved that the basal metabolism rises and falls with changes in the delivery of the internal secretions by the tissues which prepare them. This is most firmly established in the case of the thyroid, an organ of which more will be said in Chapter XXVI. Its activity is known to be under the influence of the nervous system. An excessive production of the thyroid hormone increases the rate of metabolism. In some instances of this kind the basal figure has been nearly doubled. Subjects who are oxidizing their bodily stores so rapidly can hardly be kept from progressive loss of weight. They have to eliminate so much heat that their skins are constantly warm and moist. They cannot tolerate heavy clothing. Less commonly cases of the opposite type are seen in which the thyroid has a subnormal activity. The skin is cool and dry, there is inertia and a tendency to gain weight, while the basal metabolism may be 20 per cent. or more below the standard. The adrenal is another organ which affects the rate of decomposition.

Feeding and Metabolism.—When food is being absorbed the metabolism according to our definition is no longer basal. It is definitely elevated. But the effect of food is, in general, so much less than the effect of muscular activity as to be readily concealed by changes in the exercise taken. Thus, while it is broadly correct to say that a fasting man metabolizes less material than a man who has abundant food, the relation will be immediately reversed if the starving subject is compelled to work more actively than his fellow. An animal which is denied food is economical in its metabolism, but the economy is secured chiefly through its decided tendency to remain quiet. When the influence of muscular activity is ex-

cluded so far as possible we discover some suggestive facts with reference to the different food-stuffs.

Suppose that a man's metabolism is determined for two successive days, the first of fasting, the second of feeding, without increased exercise. Let us assume that the metabolism of the first day turns out to be 2000 Calories. The food allowance for the second day may be designed to supply 2000 Calories. (This must be the *net* value of the ration, the amount actually assimilated.) It can be predicted that the metabolism of the second day will not remain at 2000, but will rise somewhat in consequence of the taking of food. The increase will not be striking; the new total may be something like 2200 Calories. A far greater increment would have resulted from the performance of moderate muscular work. The precise extent of the advance in metabolism following feeding will be conditioned by the make-up of the diet. If protein is a prominent feature the acceleration will be more evident than if the food furnished is mainly non-nitrogenous.

The increase of metabolism above the fasting level when the mixed diet supplied has the value of the apparent fasting requirement—2000 Calories in the hypothetical case above—may be, as indicated, in the vicinity of 10 per cent. If the food fed is practically all carbohydrate the ensuing rise of metabolism will probably be less than this, perhaps 6 per cent. A similar limited effect follows the consumption of fat. When an animal is given protein to cover its theoretical need the heat production for the next twenty-four hours may be augmented by 30 per cent. or more. The facts are expressed by saying that protein has a high *specific dynamic effect* compared with the non-nitrogenous foods. Protein is abundant in those articles of diet which have the name of being heating foods. The description is seen to be accurate. The eating of much meat in warm weather must add to the discomfort of the eater. The consequence is something like that of opening a furnace draft when the house is already too hot

for the pleasure of its tenant. On the contrary, high protein rations are appropriate for those who have to face cold weather.

It is not clear just how the specific dynamic effect of feeding is brought about. The obvious suggestion is that it is an expression of the work required of the alimentary tract for the digestion of the ration. It might be supposed that the motor activities of the organs and the secretory processes taking place at the same time would call for increased oxygen supply and result in greater production of carbon dioxid. But this does not seem to be the case. The canal may be made to work upon innutritious material to the full extent usual with normal food; it can be stimulated by cathartics and yet no increase of metabolism is discovered. The whole mechanism operates with remarkable economy. It is not digestion itself, but the absorbed products which must be assumed to speed up the oxidations in the body.

Metabolism and Work.—Very moderate activity suffices to double the basal rate of heat production. More vigorous exercise raises the figure in many cases to 200 or 300 Cal. per hour, while we have records of as much as 600 Cal. per hour. Waller has made many measurements of the metabolism of men variously employed. The calculation was based upon the quantity of carbon dioxid exhaled through a mouth-piece into a "Douglas bag," a container expanding like a pair of bellows. Thus tested, a longshoreman doing time work produced 284 Cal. and on a piece work basis 430 Cal. per hour.[1] The highest records have been made by a professional bicycle rider exerting himself to the utmost upon a stationary bicycle inside a calorimeter. The total for a day observed upon an athlete working to the limit of endurance may reach 9000 Cal. Changes so extreme as these could hardly fail to attract early attention. Lavoisier in the eighteenth century noticed that exercise led to increased consumption of oxygen. Everyday experience of the heating and the

[1] Journal of Physiology, lii, 1919, lix.

"winding" effect of activity would lead to the clear impression of heightened metabolism.

When it had become plain that muscular contractions must involve increased destruction of material, the question arose as to the nature of the substance sacrificed. Chemical teaching in the middle of the nineteenth century was dominated by the influence of Liebig. It was his view that the performance of muscular work could be supported only by the consumption of protein. The impression was a natural one, since muscle is so largely composed of protein. He recognized that carbohydrates and fats were oxidized in the respiratory process, but held that heat alone and not movement resulted from their metabolism. The distinction which Liebig attempted to draw between the service of protein and non-protein material was destined to be wiped out in consequence of a certain memorable trial. The reference is to the so-called "Faulhorn experiment" of Fick and Wislicenus.

By the year 1860 the conception of the convertibility of energy from one form to another had become familiar. A valuable datum, the mechanical equivalent of heat, had become available. (One Calorie is equal to the energy consumed in raising 426.5 kilograms 1 meter.) The fuel values of a number of substances were known. Two young scientists, Fick and Wislicenus, conceived a project for testing the prevailing belief in the unique service of protein as the support of muscular activity. They knew that the nitrogen of the urine would afford the approximate measure of the protein undergoing destruction in a given interval. If a known amount of work were done it would be possible to find out whether the protein consumed in the same time would account for all of it.

They ascended the Faulhorn, a mountain rising 1956 meters above the lake at its foot. In reaching the top each experimenter must have done an amount of work represented by the product of his weight by the vertical height attained. (Much additional work must have been done also—by the heart, the breathing muscles, and in the

execution of other movements—for which no credit is given in the calculation.) The figured work, therefore, was a minimum quantity. For Fick it was 129,096 kilogrammeters; for Wislicenus, a heavier man, it was 148,656. The investigators collected their urine while on the path and for some hours after completing the ascent. They ate only non-nitrogenous food, that the excretion might not be increased merely as a result of diet. The nitrogen found in the urine indicated in each case the destruction of between 30 and 40 grams of protein. The highest theoretic contribution which such a quantity of protein could have made to the work done would have been only half the known total, and, of course, a smaller part of the actual performance. The inference could not be escaped; something other than protein had been used as a source of muscular energy.

The figures obtained by Fick and Wislicenus have been revised and corrected by critics in view of later discoveries, but their chief significance has never been modified. At the time of this celebrated experiment the respiration apparatus at Munich had not been built. As soon as this plant was in operation under the direction of Voit and Pettenkofer it became possible to learn much more about the effects of exercise upon metabolism. It was soon established that instead of being the sole fuel employed to furnish muscular energy, protein is not even the principal one. The nitrogen excretion of a man on a mixed diet does not increase notably in a period of work as compared with what it is during rest. On the other hand, his output of carbon dioxid, like the calories, is a reliable index of the degree of his activity. The contracting muscles evidently employ non-nitrogenous material for oxidation when the usual conditions of supply are maintained.

The question which naturally follows is as to whether carbohydrate or fat is the preferred fuel. This cannot be discussed at length, but it seems fair to say that both may be used to good purpose and with nearly equal economy. There is some ground for thinking, as already noted

(p. 38), that fat must undergo transformation to sugar or a nearly related substance before it can perform this function. The herbivorous animals may be assumed to work most of the time at the expense of carbohydrate oxidized. The carnivora use much more fat, though it is to be borne in mind that the large quantities of protein which they consume are a source of sugar within the body. Gram for gram, it must be remembered, sugar and fat are not equivalent. One gram of fat has the energy of approximately $2\frac{1}{4}$ grams of carbohydrate. Quantities of the two food-stuffs which are in this proportion (and hence equal in fuel value) are said to be isodynamic. The principle may be illustrated as follows: 50 grams of fat is withdrawn from a day's ration and 113 grams of starch substituted. A simple computation will show that the heat value of the diet has neither been increased nor diminished. The calories lost through the removal of the fat are 465, while those introduced with the starch are practically the same. Of course, the possibility of such substitutions is much limited by considerations of palatability and individual variations of digestive power.

The fact that carbohydrate and fat are freely used to yield energy for muscular movement does not exclude protein from such service. A carnivorous animal can be kept for a long time strong and active upon a diet composed almost wholly of protein. Yet it remains possible that carbohydrate is the chosen fuel during feeding of this kind. When enough protein is given to secure nitrogen equilibrium and to furnish energy to the full extent needed for the work done, the uncombined amino-acids must give rise to abundant sugar, and it may well be that this is the chief factor in the muscular metabolism. An engine is made of iron and steel, but its regular fuel is coal; a muscle is made essentially of protein, but protein is not its usual fuel. Protein food must be needed in definite amounts for the original development of muscles and also for the increase in their substance under conditions of training. It is not clear that any considerable supply is needed for their

best working when the desired level of development has been reached. This distinction between *growth* and *operation* has important bearings upon theories of hygiene.

The Influence of Cold.—Exposure to cold greatly increases the non-nitrogenous metabolism of men and all warm-blooded animals. But when we observe their reactions closely we find that, for the most part, they constitute a special case of muscular activity. The organism is stimulated to reflex responses, among which we recognize shivering, general tenseness, and briskness of movement. There is some evidence of a moderate rise of heat production not associated with muscle contraction in response to external cold. This matter will be explained more fully in Chapter XXI.

Mental States and Metabolism.—After hearing of the striking correspondence between the degree of muscular work and the extent of metabolism, one is disposed to ask what are the facts regarding mental work. When it is said that mental states have no distinct influence, apart from that which is secondary to the changes in tissue activity which may attend them, a feeling akin to disappointment is often manifested. Yet a little reflection will convince one that positive effects are scarcely to be expected. The central nervous system, important as it is, constitutes, after all, only 3 or 4 per cent. of the body. Most of its substance is stable and relatively passive in its nature. If its really active cells were to double their average metabolism the addition to the heat production and carbon dioxid elimination of the subject would not be significant in the totals observed. A slight change in the state of the muscles would suffice to offset and disguise it.

An emotional experience is much more than a cerebral phenomenon. In times of excitement the skeletal muscles are played upon by the nervous system and metabolism in consequence may be largely increased. But this is not the direct result of the brain process; it is merely a special case of muscular activity. An emotion, pleasurable or the

reverse, is a kind of exercise and often one of marked intensity. This is recognizable in the increased heart action, in the quickened breathing, and in the contractions which bring about characteristic attitudes and expressions.

Mental application of a kind which can be more or less successfully separated from these muscular accompaniments cannot be shown positively to affect the metabolism. A short time ago a trial was made at Middletown, Connecticut, in which a group of students in Wesleyan University took *bona-fide* examinations in a respiration chamber which was at the same time a calorimeter. Each man took his turn, spending three hours over his paper and experiencing the usual anxiety and strain attendant on such a proceeding. On other days each subject spent a like period in the chamber engaged in copying printed matter. Thus it was possible to compare in about twenty cases the metabolism of a period of brain work with the metabolism during a time in which similar muscular movements were made, but in the absence of conscious effort. There was no distinct difference.

More recently a similar result was obtained in the case of proof-readers.[1] These people certainly concentrate to good purpose, and it will be agreed that their work is exacting. But it is pursued by the adept with a minimum of postural strain; in fact, it is consistent with very complete relaxation. Waller and de Decker found no change in the metabolism when their subjects entered upon or discontinued work.

Brain cells undoubtedly have peculiar metabolic products and make demands upon the blood for supplies of a somewhat different order from those required by any other tissues. But their distinguishing wastes can hardly be recognized when mingled with the outgo from so many other organs, and it is equally difficult to discover just what they appropriate for their nutrition. The notion that certain articles of diet are brain "foods" rests on very unsafe assumptions. The popular association of phospho-

[1] Journal of Physiology, liii, 1920, cv.

rus with the brain and its activity has no more justification than could be claimed for sulphur or any element present in the proteins.

From what has been said it will be evident that the diet must be increased for the support of muscular work, but that no more food is needed for the student occupied with his books than for the same man at leisure. The chances are that his leisure days will be spent in less sedentery fashion than his days of application, and that his appetite will lead to a larger consumption in his so-called resting time.

Maximum and Minimum Excretion of Carbon and Nitrogen.—By way of summarizing certain facts of importance the following statements may be made:

The maximum excretion of carbon results from the performance of the heaviest muscular work. Carbon excretion is little affected by feeding.

The minimum excretion of carbon occurs when rest is as complete as possible. Protection from cold favors a low carbon secretion chiefly because it permits muscular relaxation.

The maximum excretion of nitrogen results from high protein feeding. Nitrogen excretion is little influenced by muscular activity.

The minimum excretion of nitrogen occurs not in fasting, as might be hastily concluded, but when non-nitrogenous food is liberally supplied.[1]

[1] An interesting study is that reported by Deuel (et al.), Journal of Biological Chemistry, lxxvi, 1928, 391. The subject consumed about 400 grams of carbohydrates—corn-starch and cane-sugar—daily for thirty days; the diet contained a little fat, salts, vitamins, but practically no protein. The loss of nitrogen sank to about 2 grams per diem.

CHAPTER XXI

THE MAINTENANCE OF THE BODY TEMPERATURE

ALL animals are producers of heat, and must, therefore, maintain temperatures above those of their surroundings unless the evaporation of water more than compensates for the heat of metabolism. We speak, however, of warm-blooded and cold-blooded animals as though some were far more liberal than others in their calorific output. This is actually the case. But a better distinction between the two classes may be found in the fact that some animals allow themselves to be warmed and cooled readily, while others keep near to a constant standard of internal temperature. We call a frog a cold-blooded animal, but what we really mean is that it accepts for its own the temperature of its environment. On a very hot day the frog may be as warm as a man; in winter the frog is chilled through and through, while the tissues of a human being everywhere save at the surface are kept at the same temperature as in summer.

Animals which have a fixed standard to which they adhere under all ordinary conditions are spoken of as *homothermous*. This trait is shared by birds and mammals. Our interest, of course, centers in man's remarkable capacity to keep his deeper tissues at the same level in spite of radical external changes and equally sweeping changes in his own metabolism. The means by which this result is attained differ somewhat with different animals of the homothermous order. We shall confine our attention almost entirely to the human problem.

The common clinical thermometer bears the mark "Normal" opposite the point on its scale corresponding to

98.6° F. (In all the following discussion the familiar Fahrenheit system will be used.) The standard just quoted is for the mouth. The body temperature is often estimated by placing the thermometer elsewhere, as in the armpit or the rectum. The rectal temperature is the most reliable, and is usually higher by half a degree, or a little more, than that of the mouth. It is clear that the temperature of the skin cannot be a constant one; it is affected both by the external conditions and by the variations of blood-flow in the superficial vessels.

There are small but distinct changes of body temperature during each day. The lowest figures are noted early in the morning before one has become active and when the sense of prostration is apt to be overpowering. A gentle upgrade is maintained until the maximum is reached in the late afternoon or early evening. The average extent of the rise is rather more than 1° F. It coincides suggestively with the temperamental change, which is to be observed from a prosaic and literal frame of mind to a condition of emotional instability. Compared with the morning, the evening is a feverish period. When there is actual fever the diurnal ascent of the temperature often adds considerably to the restlessness and discomfort of the patient as night approaches.

After we have made allowance for such irregularities it remains true that the approximate constancy of the temperature is one of the most wonderful facts which the physiologist has to explain. Uniformity of temperature implies equality of heat production and heat loss. Our task, then, is to show how this equality is continued in the face of variable factors tending to disturb it. Artificial contrivances for keeping constant temperatures in certain chambers may be considered with advantage before we attempt to analyze a mechanism so much more intricate than they. There are two principles on which incubators or thermostats may be operated: (1) The heat given to the system may be increased or diminished to keep pace with the heat lost; (2) a constant supply of heat may be

provided and adjustments made to favor its escape or to conserve it, according as the tendency is toward a rise or fall in temperature.

The first principle is illustrated by those thermostats in which gas flames are automatically caused to rise when the apparatus begins to cool off and are cut down when it begins to be warmed above the intended level. The second way of securing the same result is exemplified by the common incubator used for hatching eggs, in which the heat is furnished by a lamp kept burning at the same height at all times, while a ventilator, opening and closing, dissipates or retains the heat as required. In the living body we can recognize the working of both these principles, but it is rather surprising to find how much is accomplished by the second without the aid of the first. In other words, the constant internal temperature is maintained much of the time by the promotion or the retarding of heat loss without any appeal to the tissues for metabolic support.

Our practice of adapting our clothing to the season and to in-door and out-door life is an extension of the means which the organism itself employs for the same purpose. Extra clothing hinders the escape of heat from the body and makes possible the maintenance of the normal state with no increase of oxidation in spite of some degree of external cold. A race of naked savages must certainly vary the amount of their metabolism much more positively from summer to winter than we do with the habits of our civilization. Animals may enjoy the protection of heavier coats in cold weather, and they show, moreover, an instinct to assume those positions that reduce to a minimum their surface exposure.

To explain in detail how changing circumstances are met, let us imagine a man placed successively in atmospheres of different temperatures. We will begin with a room at 68° F., a condition which we regard as agreeable and which we aim to produce when artificial heating is in use. If our subject has spent an hour in this room he has very likely had a metabolism of 100 Calories, and he has in

the same time discharged by radiation, conduction, and evaporation a similar amount of heat. His blood is some 30 degrees warmer than the air around him. Let him now take his place in a room where the thermometer stands at 84° F. Suppose him to remain for an hour in this disagreeably warm apartment. His temperature will be found to rise but little, perhaps not at all. Yet the change has reduced the difference between his own temperature and that of his surroundings from about 30 degrees to about 15. The tendency of his environment to withdraw heat from his body must have been halved. What, then, has happened? Has his metabolism fallen to 50 Calories or has there been a readjustment to facilitate the removal of the full 100 Calories? The latter is found to be the case.

The withdrawal of heat from the body is favored by two reflex changes. One of these consists in an increase in the amount of blood flowing through the skin and thus exposed to the cooling influence of the outside air. The other is seen in the breaking out of perspiration. The evaporation of the water thus brought to the surface cools the skin and the blood beneath it. The blood then mingles with that which has been passing through the deeper tissues and the rising temperature is checked. It is well to insist just here that the appearance of the skin gives little indication of the rate at which the sweat is being secreted. So long as evaporation keeps up with the arrival of the water at the pores there will be no visible moisture. We notice the perspiration most when it is failing to accomplish its object, that is, when it accumulates instead of being vaporized. The evaporation of water from the respiratory passages is, of course, one means of removing heat, but with human beings this is not a quantity which increases with external warming. It does enter into the adaptive reaction in the case of animals which pant.

Let us now transfer our subject to the unusual temperature of 105° F. The radiation and conduction effects will now be reversed; the blood will tend to be warmed rather than cooled as it approaches the surface. The metabolism will continue unabated. The body is thus exposed to

warming from without, while it does not cease to heat itself from within. How can it escape a steady rise of its internal temperature leading to prostration and death? Benjamin Franklin answered this question when he pointed out that the sole resource of the organism in such a situation must be its power to evaporate water. To dispose of 100 Calories in an hour by evaporation alone demands the secretion of about 200 grams of water in the same time, an amount which can readily be produced.

When the air is warm the humidity has much to do with human power to endure the condition. If there is full saturation and a temperature as high as that of the blood the heat of metabolism will be pent in the body and heat-stroke is inevitable if there is not a prompt relief; 100 Calories added to the average human body in an hour will raise its temperature by nearly 4° F. A second hour of such an upgrade could hardly be survived. Men may live and work for several hours on a stretch in dry air with the temperature around them as high as 130° F., but they cannot be active in saturated air at 90° F. The first of these conditions is realized in the stoke-holds of ocean steamers; the second, in certain deep mines. Everyone knows that the most trying weather we have to put up with is not that which makes the record for the mercury, but those days which are less warm, but which we describe as muggy or sticky. We are acceding to a correct instinct when we are relaxed and indolent under such circumstances.

We may now return to the starting-point and submit our imaginary victim to temperatures lower than 68° F. If he is taken to a room where the thermometer is at 60° F. he will probably feel chilly. We are affected more by a slight change in the vicinity of 65° F. than in any other part of the scale. The fact is, apparently, that when the external temperature is cut down from 68° to 60° F. the skin temperature, on which our sensation depends, is reduced by a good deal more than 8 degrees. This is due to the reduction in the volume of blood in the cutaneous vessels. It is the expression of the endeavor of the organism to economize to the utmost its outgo of heat. Dis-

comfort is permitted to develop as an incident of the adaptation. The metabolism still remains about as it has been throughout the series of trials.

If the room temperature is now lowered decidedly and no wraps are provided the body can no longer maintain itself by mere economy of heat loss. It must shift from the method of the incubator with a constant flame and an adjustable ventilator to the other form of regulation—that of the thermostat with variable flame. That is to say, the metabolism must be stimulated. A sign of this rallying on the part of the heat-producing tissues is seen in the onset of shivering. This is obviously a form of muscular exercise, and as such is attended with increase of metabolism. When we resist the impulse to shiver, as we sometimes do, we merely adopt another kind of contractile activity with its accompanying contribution of heat to the body. If we analyze the experience of being cold we find that we can recognize a disposition to muscular tenseness, while it is familiar enough that when the cold is severe we cannot keep from moving briskly and so supplying the necessary heat. It is desirable to reiterate that the muscles are not merely organs of movement, but our main reliance for heat production. Cold weather generally means large metabolism, but the connection is indirect; the increase is largely a special case of the rise always associated with exercise. So, too, the increase of appetite which is usual in winter is secondary to the greater use of the muscles. It is held by many that the needed increase in heat production is in part separate from muscle contraction. To some extent its seat may be in organs other than muscles, as the liver.

Humidity makes for discomfort in cold as well as in warm weather. It seems at first unreasonable to say that moisture can make us more sensitive to heat in summer and also to cold in winter, yet this is true. The climate of our Atlantic coast is notorious for the "penetrating" character of its cold, and this in spite of the fact that the thermometer does not fall so low as it does a short distance

inland. The paradox is easily explained. We have said that high humidity in hot weather interferes with our comfort and efficiency by hindering free evaporation. In winter it has no such influence, because even though the cold air is fully saturated it ceases to be so when it has been warmed by contact with the skin. Evaporation can, therefore, never be retarded seriously by moisture in cool air. What we notice in cold weather is the increased conducting power of air containing water vapor. Damp air may fairly be said to partake of the nature of the water that is in it; water feels colder to the hand than does air of the same temperature because it abstracts the heat more rapidly. Similarly, moist cold air takes heat more rapidly than does dry cold air. This property is present just as surely in warm humid air, but it can affect us only when there is a wide difference in temperature between the skin and the surroundings.

Temperature Maintenance During Exercise.—We have been discussing the ways in which the human body guards itself against changes of temperature which tend to impress themselves upon it from the outside. Another question is in regard to how it escapes the tendency to overheat itself when, during exercise, its metabolism is doubled, trebled, or even more strikingly augmented. Reflection shows that it employs the two reflexes on which it relies for defense against the heat of the warm room, namely, increased surface blood-flow and increased perspiration. These are rendered more efficient by the hastened circulation, a condition not produced in any great degree by external heat without the activity.

A supplementary factor exists in the deepened breathing which takes heat from the system, both in the act of warming the respired air and in the process of saturating it. Still another factor can be recognized in the fanning effect of the movements of parts of the body or of the body as a whole. A man running brings the exposed portions of his skin constantly into contact with fresh volumes of air and slips away from the air which he has just warmed and saturated. The cooling of his blood is in this way con-

siderably facilitated. If he is not progressing through space, but carrying on his activities in one place—for example, in sawing wood—his arms and trunk still make short excursions and exchange old air for new. No doubt an important factor is the displacement of the heated air from within the clothing. A breeze makes a considerable difference with the heat output of a man's body.

Fever.—When the body temperature is found to rise above its normal level and to persist at an elevation which brings many ill consequences upon the subject, what shall we name as the cause of the disorder? Shall we say that the metabolism is excessive? Studies made upon fever patients show that their nitrogenous metabolism is often surprisingly high, an indication of rapid destruction of the tissues, but the total heat production is not impressively large. We shall more nearly express the facts if we say that there is interference with heat loss. Frequently we can see evidence of a withholding of the perspiration. Perhaps it is best to say that the central fact in fever is the setting up of a false standard by the nervous system to which for a time there is an adherence as strict as that obtaining in health for the normal one. This perverted action of the nervous system is brought about by the poisons in the circulation at such times. Transient fever may be brought on by very severe exercise; it is experienced by men who run Marathon races. In these cases the controlling centers are probably acting in the normal way, but cannot secure the complete removal of the extraordinary quantities of heat which are produced.

Summary.—The maintenance of a nearly uniform body temperature is the result of a balance between heat evolved and heat dissipated. So long as the external conditions are not such as to cause shivering, muscular tension, or instinctive activity of some other form the organism regulates its temperature almost wholly by making adjustments to promote or to restrict the loss of heat. The wearing of clothing adapted to the season makes it possible to minimize the demands made upon the muscles for extra

heat. Decidedly low temperatures and exceptional exposure can be withstood only by calling upon the contractile tissues for an increased heat production.

The statement is often made that warm-blooded animals produce more heat under the influence of external cold while the reverse is true of the cold-blooded. This is supported by figures, but it is found to be a superficial fact. If the tissues in either case are actually warmed their metabolism is accelerated, if they are cooled it is retarded. The increased metabolism of the homothermous animal resisting cold is a reaction on the part of cells which have not suffered a lowering of their temperature. The influence governing their behavior is nervous rather than thermal.

Reference: Barbour, Physiological Reviews, i, 1921, 295.

CHAPTER XXII

THE HYGIENE OF NUTRITION

It is convenient to make a division under this general heading between those factors not directly connected with the diet, which none the less deserve consideration, and those which do concern the choice of food. Probably too little attention is paid to the fact that disorders of digestion and nutrition frequently arise when the food eaten is above criticism, both as to quantity and kind.

Nervous Conditions Affecting Digestion.—Enough has already been said to make it plain that the processes occurring in the alimentary canal are greatly subject to influences radiating from the brain. It is especially striking that both the movements of the stomach and the secretion of the gastric juice may be inhibited as a result of disturbing circumstances. Intestinal movements may be modified in similar fashion. Emphasis has been placed on the dependence of the whole digestive process upon a good start. This can hardly be too strongly enforced. The good start can scarcely be secured if the mental state of the subject is not favorable to the enjoyment of his meal.

Cannon has collected various instances of the suspension of digestion in consequence of disagreeable experiences, and it would be easy for almost anyone to add to his list. He tells us, for example, of the case of a woman whose stomach was emptied under the direction of a specialist in order to ascertain the degree of digestion undergone by a prescribed breakfast. The dinner of the night before was recovered and was found almost unaltered. Inquiry led to the discovery that the woman had passed a night of intense agitation as the result of misconduct on the part of

her husband. People who are seasick some hours after a meal often vomit undigested food. Apprehension of being sick has probably inhibited the gastric activities.[1]

Just as a single occasion of painful emotion may lead to a passing digestive disturbance, so continued mental depression, worry, or grief may permanently impair the working of the tract and undermine the vigor and capacity of the sufferer. Homesickness is not to be regarded lightly as a cause of malnutrition. Companionship is a powerful promoter of assimilation. The attractive serving of food, a pleasant room, and good ventilation are of high importance. The lack of all these, so commonly faced by the lonely student or the young man making a start in a strange city, may be to some extent counteracted by the cultivation of optimism and the mental discipline which makes it possible to detach one's self from sordid surroundings. Alcohol works to the same end, but is a perilous resource under these circumstances.

Children are very often the victims of sharp attacks of indigestion. Their sicknesses, which are accepted with little surprise in many families, are almost always held to be due to injudicious eating. While this is a reasonable belief in many cases, it may be asked whether emotional causes of indigestion in children are considered as much as they should be. How common it is to see children made to cry while at the table by ill-timed rebukes. The quick temper and thoughtlessness of parents destroys the happiness of many a meal. Granting that instruction in table-manners ought to be given at suitable times, one may still protest against the downright rudeness of elders toward children

[1] Miller, Bergeim, and Hawk (Science, lii, 1920, 253) have demonstrated the retarding of digestion which attended worry over an examination. On the other hand, Holder, Smith, and Hawk (Science, li, 1920, 299) found that a subject under their observation successfully assimilated a diet which had been rendered as repulsive as possible. Various foods were minced, stirred up together, and blackened, then eaten in the presence of a vile odor. The quality of the material was good, but the trial brought the volunteer to the verge of nausea. This shows the power of a strong constitution, but need not modify our general teaching.

when it is shown in the infliction of ridicule and humiliation. Consideration of others' feelings is the finest element in deportment.

Moreover, it is probably fair to claim that children may be injured by being forced to eat food which they dislike. The aversions of early life are singularly strong. What passes for a foolish whim may be an instinctive loathing. There is an element of hypocrisy in the attitude of parents who are selecting precisely what they please to eat, while compelling little children to swallow food which repels. To oblige a child to finish a plateful of food against its inclination may be crass brutality. Of course, children cannot be humored in the selection of eccentric diets, but they need not be made to eat when they would rather go hungry. There is little likelihood that they will refuse the staple articles. Occasionally a child may be encountered so wanting in appetite as to prefer other pastimes to eating. Such an anomalous case is most difficult to deal with and some compulsion in the matter of feeding may be justified.

Unhappiness may give rise to digestive difficulties which do not disappear with the removal of the first cause. It is not hard to show how this may be. Suppose that the power to digest and absorb food is lessened by central inhibitions. A consequence is likely to be the accumulation of unabsorbed organic material in the colon and perhaps higher up as well. Bacterial decomposition will be fostered. Some of the products of such a process may be sufficiently like the normal products of enzyme action to play a part in nutrition, but others will probably prove distinctly detrimental. With the entrance into the circulation of such bodies there is originated what is known as *auto-intoxication*. (It has been urged by the authors of one of our best manuals of hygiene, "How to Live,"[1] that the term ought to be reserved for disorders due to abnormal products of the body's own metabolism. There is obvious ground for the claim that a poisoning induced by the

[1] Fisher and Fisk, Funk & Wagnalls, New York, 1918.

activities of micro-organisms is not a "self" intoxication. But it will be hard to alter the common designation.)

Long ago it was recognized that the reception into the system of bacterial products might be a cause of general ill health, of headache, and of somnolence. Within a few years the impression has gained ground that poisons from the colon have a much larger and more definite share in the development of disease. Much that goes by the name of rheumatism appears traceable to this source. Some of the toxic compounds seem to have the property of dissolving the red corpuscles of the blood, leading thus to anemia and the serious crippling of the energies which accompanies it. Nervous symptoms are among the most frequent nowadays referred to this condition, seemingly so remote from the brain.

Physicians apply the term "vicious cycle" to a set of conditions in which the establishment of one tends to accentuate the others, and these, in their turn, add to the intensity of the first. We can see how a vicious cycle may become operative in the case of a person whose digestive abilities have been once reduced by mental depression. Auto-intoxication may be induced and one of the clearest results is a further depression of spirits. In this way a lasting injury may be done and the indigestion which began as the effect of temporary unhappiness may be perpetuated in spite of the return of favorable circumstances. Auto-intoxication may come from errors of diet as well as from emotional causes, and a further discussion of it will be postponed. It is fair to say as a comment upon these paragraphs, now standing through successive editions, that less emphasis is placed upon auto-intoxication than was formerly the case (1931).

Physical fatigue as well as mental may interfere with the progress of digestion. It is well that the appetite usually flags in times of exhaustion, so that one is in a measure insured against the tendency to overtax weakened organs. But when the fatigue is habitual there is an unfortunate dilemma; the body must have abundant food to support

the heavy labor and it is not well able to care for the food eaten. Loss of weight is common when a man is so situated. Deprivation of sleep emphasizes this state of affairs, and by dulling both the appetite and the digestive capacity it proves for many people the surest means of reducing adipose tissue.

Other possible causes of indigestion may be mentioned briefly. Taking cold is one of these. While the congestion and inflammation which so often follow exposure to drafts and dampness are most frequently centered in the mucous membranes of the nose and throat, a corresponding involvement of the alimentary canal is not rare. Diarrheal attacks are common in the spring and fall when the weather changes are erratic. They are probably to be classed as intestinal "colds." Another source of alimentary trouble is to be found in uncorrected defects of vision. While headaches are the most persistent symptoms of astigmatism and other ocular imperfections, indigestion is not uncommon, and its disappearance when glasses are worn seems sometimes almost magical.[1]

Quantity of Food.—The familiar teaching of the periodicals and popular books is that people generally eat too much and would be better in every respect if they should cut down their intake. Often the statement is recklessly made that we eat twice as much as we ought. When reduction in diet is recommended it is apparently assumed that the weight can be preserved and the same program of life followed in spite of the proposed retrenchment. This turns out to be a fallacy, as will be shown. Another assumption freely made is that there are small and large eaters in the community quite apart from stature and occupation; some are believed to be economical in constitution, while others are spendthrift.

We hear it said that one individual "gets more of the goodness of his food" than another does of his. But this

[1] With a balloon in the stomach to register its contractions Lebensohn has found that these are interrupted when lenses producing errors of refraction are held before the eyes. (American Journal of Ophthalmology, xii, 1929, 562.)

does not seem to be the case unless the comparison is extended to include victims of chronic diarrhea. People who are not obviously abnormal absorb a high and nearly uniform proportion of their food. As to the spendthrift organizations mentioned above they are indeed to be found. The most striking examples are found among subjects with overactive thyroid glands. But something of a like extravagance in metabolism is to be suspected in numerous individuals who are judged to be hearty eaters and who yet remain thin. Gulick[1] has made a most instructive study of his own nutritional problem.

He was reputed to be a man who could not gain weight. He had, however, a normal basal metabolism and could not, therefore, be rated as a hyperthyroid. By conscientiously taking increased portions of food he succeeded in adding about 25 pounds in a little more than a year. The original ration represented about 2700 Cal. while at the height of his drive he reached 4100. In round numbers he increased his mass 20 per cent. by raising his food intake 50 per cent. His basal metabolism did not rise. The extravagance inherent in this man's system appears when his rations are compared with his theoretical needs. At the time when he was consuming 2700 Cal. it appeared that 2250 should have sufficed. When his supply was 4100 it seemed as though 3200 ought to have provided for his maintenance and estimated activities. It would be of extreme interest to have corresponding figures for other cases.

The simple fact is, as Lusk[2] has pointed out, that any man whose weight is constant is eating just enough *for that weight*. Therefore, he cannot be said to overeat unless he is overweight. If he weighs more than he should he cannot escape the reproach of eating too much. All the advocacy of reduction in rations should evidently be concentrated upon those who are definitely above the standard in avoirdupois. Whether the weights accepted

[1] American Journal of Physiology, lx, 1922, 371.
[2] Science, xlv, 1917, 345.

as normal are really the best possible for health and efficiency may be open to discussion, but otherwise there are no uncertainties in the problem.

The metabolism or consumption of food in active life may be said to be separable into three fractions: First, we have the Basal quantity representing the bare necessities of the resting and fasting organism. Second, there is a rather small quantity, sometimes referred to as the Cost of Digestion,[1] it stands for the expenditure, over and above the Basal, stimulated by the daily food. Third, there is the Work fraction which may vary within the widest limits. If the weight is to be maintained the net income of food must equal the sum of the three.

If the income is reduced the Cost of Digestion is automatically lowered. But this is a small item; there must be a reduction of the Work fraction or a loss of weight, stored fuels being called upon to supplement the diet. The way in which the system reacts to an enforced cut in the ration is a matter of the greatest interest. We can conceive of two possibilities: there may be loss of weight with a full performance of routine work or there may be maintenance of weight with a discontinuance of a part of the daily activity. Instinct will probably impel toward the latter result. A compromise between the two courses is likely.

During the war restriction of food supply was acute in many regions and did not seem remote in the most favored lands. An experimental study of the effects produced by definite and severe restriction was carried out at the Carnegie Nutrition Laboratory[2] and its main features must be recounted. The volunteers who underwent the hardships of this trial were students from the International Y. M. C. A. College at Springfield, Massachusetts. It will suffice to indicate the procedure followed with the principal squad, composed of twelve young men.

[1] The term is ill chosen, for it has already been pointed out that the extra metabolism following the taking of food is not due to digestive activities.

[2] Carnegie Institution of Washington, Publication 280, 1918.

First of all a general inquiry into their dietetic habits when free from compulsion was made. It appeared that they secured average allowances of from 3200 to 3600 Calories per day. They were at once limited to about half this ration and the decline of weight was noted. This amounted eventually to something like 12 per cent. of the initial; that is, subjects who had weighed 150 pounds fell away to 132. The time necessary to effect this loss varied from three to ten weeks. The desired reduction of weight having been accomplished, the feeding was cautiously increased until the progressive fall was checked. About 2000 Calories answered for maintenance at the new level which was held for two months, more or less.

During this period of equilibrium all manner of observations and tests of condition were made. Gymnasium determinations of muscular power and endurance showed no important change. The blood-pressure was low. This is of interest as confirming the common assumption that we can cut down blood-pressure when desirable by restricting the diet. The heart-rate during rest in bed dropped below any previous experience of the subjects; often it was in the thirties. There was marked constipation, which was counteracted so far as possible by adding bran to the food. The resting metabolism fell not merely in proportion to the 12 per cent. loss of body weight, but much more. It was reduced by about 18 per cent. when referred to the unit of weight or surface. (This means that a man whose original basal metabolism was 1500 Calories was found to have, after cutting down his weight by 12 per cent., not 1320 Calories, but about 1100 as his new standard.) Many of the bodily processes must have been slowed very decisively.

The students were able to carry out their daily physical exercises and to keep their examination marks up to the level of their former grades. The most serious effects of this subnutrition were sensory and temperamental. The discomfort was intense. It was at all times hard to exclude thoughts of food, while to see others eating without

restraint was torture. There was marked sensitiveness to cold. Muscular activity was successfully maintained, as has been said, but it was with a feeling of reluctance and unwonted effort. It may be pointed out that the instinct to avoid work when short of food is biologically sound; it makes for conservation of resources and so for longer survival. Sexual impulses died away.[1] The life of the individual had taken precedence over racial interests. Reproduction is appropriate to times of surplus supply, not to periods of dearth.

These young men were of the highest character and of exceptional self-control. They were able to keep on with their allotted tasks while they doubtless economized effort in non-essentials. Given subjects having less of principle and discipline we find it easy to see that the situation might have led to dishonesty or, with a populace, to disorder. This has been exemplified in Europe.[2] But it is the testimony of witnesses that prolonged and extreme undernutrition disposes at last to apathy rather than to turbulence. All activity is shunned, even though the hope of bettering intolerable conditions may be held out as an incentive. Observers abroad have noted the pathetic fact that the children have lost the impulse to play.

Reduction of income is not always due to poverty or to actual shortage in the food supply of a community. It may be brought about by want of appetite. There are great numbers of people, particularly middle-aged and elderly women, who present a picture much like that of the Springfield squad save for the fact that they are not hungry. They eat lightly, are under weight, constipated, sensitive to cold, perform their routine tasks faithfully, but seem to have little enthusiasm for anything outside the habitual round. Their outlook is not particularly cheerful; at best they may be described as "resigned and

[1] Miles, Journal of Nervous and Mental Diseases, xlix, 1919, 208.
[2] Lusk, Physiological Reviews, i, 1921, 523. For the skilful meeting of the emergency in Denmark, see Hindhede, Journal of the American Medical Association, lxxiv, 1920, 381.

patient"—often they are morose, bigoted, suspicious. They stand contrasted with another type characterized as "hearty and comfortable" which is certainly easier to live with. Few will now claim that the lowest metabolic level at which equilibrium is possible is in any sense the best standard to be sought.

In many instances the underweight individual cannot arbitrarily increase his intake of food; his limited appetite forbids. This was not true of the members of the Springfield groups, for their inclinations led them to resume full diet and rapidly to regain their lost weight when they were free to do so. *The want of a proper appetite is the great impediment to successful nutrition; the possession of an appetite out of proportion to existing needs is the essential cause of obesity.* Many people who definitely need to eat more and so to attain to a higher nutritional level find it hard to alter their habits. They are like those who have long lived in poverty and become committed to the severest frugality in all things; it is not easy for such to adopt a more liberal scale of living when increased means are provided. A difficulty like this stands in the way of restitution among the half-starved populations of Austria and Poland. There is an uneasy consciousness of the want of food, but the appetite itself has been enfeebled and the capacity to eat full rations with pleasure is regained only by slow degrees.

What shall we say when we are assured that a fat man is a small eater?—or that a lean man consumes enough for two? We may concede that there are moderate variations in constitution. It is an important consideration that the heavy man probably takes little exercise. The work fraction of his metabolism may be quite small. The lean man is often active, either in useful employment or in nervous unrest. Another point is this: that the reputed large eater is, in many cases, one who enjoys a large meal now and then. He may have a capacious stomach and give impressive demonstrations of his gastronomic prowess, but his average intake may not be especially large. He

may be an irregular rather than a great eater. We often assume that our ancestors ate more than we do. Very frequently, no doubt, this was the case, for most of them led more active lives. Aside from this, it may well be that we emphasize their feasts and forget their fasts. They had somewhat gross conceptions of what should constitute a banquet, but their festive affairs may not have been so numerous as we have supposed.

It may be of interest to insert here a description of an eighteenth century dinner. The occasion was the ordination of a minister at the Old South Church in Boston in February, 1761. A current newspaper gave the following account:[1] "There were six tables that held one with another eighteen persons each, upon each table a good rich plumb pudding, a dish of boil'd pork and fowls, and a corned leg of pork with sauce proper for it, a leg of bacon, a piece of alamode beef, a leg of mutton with caper sauce, a roast line of veal, a roast turkey, a venison pastee, besides chess cakes and tarts, cheese and butter. They had the best of old cyder, one barrel of Lisbon wine, punch in plenty before and after dinner, made of old Barbados spirit." The impression is of an overhwelming and most unhygienic repast with an excessive amount of protein from animal sources. We must bear in mind that the season was winter and that many kinds of vegetable food were therefore not to be had.

The Peculiarities of Protein.—While the advice to limit all forms of food is constantly heard, it is the use of much protein which is most vigorously condemned. The most active movement in favor of careful limitation has probably been that led by Chittenden some years ago.[2] He demonstrated that his own needs over a long period could be met by a protein allowance of about 35 grams a day. Under his supervision a number of athletes trained

[1] Alice Morse Earle, "The Sabbath in Puritan New England," Scribners, New York, 1892.

[2] "Physiological Economy in Nutrition," Stokes, New York, 1904.

and performed with credit on a daily supply of 55 grams. These figures are striking indeed when it is noted that the protein consumed by college oarsmen just before this time had been from 133 to 174 grams per day.[1] The Maine lumbermen referred to on page 195 included more than 150 grams in their hearty rations. We do not hear so much about the virtues of a minimal protein intake as we did formerly, but it is still maintained that excess has its dangers.

The decisive effect of a large protein allowance upon the metabolism—an effect in the direction of a seemingly useless increase—has been mentioned. Other peculiar properties call for discussion. We may conveniently distinguish the influences proceeding from an excess of protein in the intestine from those which are associated with an excess of nitrogenous metabolism. In regard to the first it may be said that protein far more than the non-nitrogenous foods is capable of generating toxic substances and so of becoming a cause of true auto-intoxication. An unabsorbed surplus of protein is, therefore, to be avoided.

If, however, the absorption is as complete as can be desired, reasons can still be given for keeping the protein income of the body relatively low and depending largely upon carbohydrates and fats in preference to nitrogenous food. Emphasis has been placed elsewhere on the simplicity of the normal oxidation products formed from sugar and fats in contrast to the numerous and rather complex bodies which arise from the working over of the protein derivatives. Carbon dioxid and water are disposed of by the healthy system with apparent ease. The nitrogenous wastes require preliminary treatment by the liver and perhaps by other organs, and must then be removed from the blood by the kidneys. The principal one, urea, is not commonly a source of trouble, but the minor attendants, such as uric acid, are viewed with disfavor.

[1] Atwater and Bryant, U. S. Department of Agriculture, Bulletin 75, 1900.

One is naturally led to the opinion that high protein feeding must lay a burden upon the liver and the kidneys, but it is probably just to assume that what is a severe tax for one person may not be so for another. The native efficiency of these organs is doubtless as variable as many other inherited qualities. It has been assumed that Oriental races with low protein consumption must be comparatively free from kidney disease. Contrary to this impression, the limited statistics available seem to show a high prevalence of Bright's disease in vegetarian India. Nitrogenous by- or end-products, whether having their origin in the decompositions within the colon or in the metabolism, are presumably responsible for the premature fatigue of which we have spoken. An additional injury which may be laid to their charge must now be considered. This is the production in later life of arteriosclerosis.

The saying is current among physicians that "a man is as old as his arteries." It is certainly a fact that the stiffening of these vessels is a chief cause of malnutrition and waning power in the tissues of the aged. If arteriosclerosis sets in prematurely, other features of a senile decline may be expected. Metchnikoff has sought to establish a connection between the overconsumption of proteins and early loss of elasticity and adaptability in the human circulatory apparatus. Such a connection has long been believed to hold for alcohol. We seem brought to admit that this serious impairment of efficiency may spring from intemperance in eating as well as in drinking.

The postponement of old age by frugality in feeding seems in a measure possible. Yet we must remember that self-denial in this respect may defeat its own end, since it may too greatly weaken the digestive capacity. An alternative to low diet, it has been suggested, may be found in the deliberate regulation of the bacterial conditions in the intestine. The claim is made, and seemingly with good reason, that a harmless type of fermentation may be encouraged with the result that the undesirable decomposition may be prevented. This is the theory underlying

the various modes of sour-milk treatment so much in vogue during the last five years. Lactic acid in moderate amounts appears to be quite devoid of danger to one's health. Its presence in the canal is hostile to the development of the organisms which cause radical putrefaction of the proteins and definite auto-intoxication. A dominant acid fermentation may be secured either by the taking of sour milk (kephir, koumiss, matzoon, etc.) or by swallowing from time to time cultures of the lactic organisms, together with sugar for them to work on.

"Fletcherism."—This term was widely familiar about the year 1905. It was derived from the name of the very magnetic and influential man who in books and lectures proclaimed the favorable results of prolonged mastication. By this practice, carried to incredible lengths, he seems to have restored himself from a state of unsatisfactory health to extraordinary efficiency and zest in living. It was his experience that under his system he came to eat less than before and in particular inclined to a low protein allowance. For a short time he had many followers, but they commonly fell away from the exactions of the regime.

Attention should be called to a study by Holck[1] recently concluded. It was designed to discover whether the experiences of Fletcher could be verified. Five years of most conscientious routine were devoted to the trial. There was a period of seventy-five weeks during which all food was chewed as long as tolerable. Many months of uncontrolled feeding preceded and followed this interval, affording a basis for comparison. The reduction of intake noted by Fletcher was again observed; in round numbers it amounted to 500 Calories per day (from about 3500 to about 3000). There was a fairly steady loss of body weight amounting to something like 25 pounds in seventeen months. The subject had been overweight and this was not unwelcome. Food consumption and weight in-

[1] "Diet and Efficiency," University of Chicago Press, 1929. Valuable for review and bibliography.

creased when the pursuit of the Fletcher technic was discontinued.

Holck failed to find that he inclined to cut down his protein more than the other fractions of the diet. Muscular endurance and typewriting accuracy were impaired. There was no shortening of sleep, a gain stressed by Fletcher. The solitary favorable item was reported to be a sharpened insight into chess problems.

Constipation.—The comparative harmlessness of even extreme constipation when associated with sparing feeding and active absorption has been granted. Such inaction of the intestine when it accompanies more liberal indulgence in food must be unfortunate and must favor some phases of auto-intoxication. Many people resort periodically to the use of cathartics when they feel slightly "under the weather," and enjoy a buoyant recovery of energy and ambition when the disturbance is over. It is natural to interpret such an experience as showing, first, the existence of a source of poisoning, and, second, its successful removal. But the relief experienced may be due in great part to the easing of mechanical tension which has been producing reflex and sensory disturbances (Alvarez).[1] The wise man, however, will not be satisfied with knowing a way out of such disorders; he will aim to prevent their recurrence. The habit of depending upon laxatives instead of general hygiene is to be deplored. Irrigation of the colon to relieve from auto-intoxication is often resorted to as a part of medical treatment with good effects, but is not to be advised so long as attention to diet and exercise can be made to serve the need.

[1] How important this is has been made clear by Donaldson's experiments. Five volunteers refrained from defecating for four days. They were very uncomfortable and experienced the symptoms usually attributed to auto-intoxication. But the same ill feelings could be reproduced in the absence of constipation by packing the rectum with cotton. Journal of the American Medical Association, lxxviii, 1922, 884. For a remarkable example of intestinal arrest without toxic symptoms, see Geib and Jones, Journal of the American Medical Association, xxxviii, 1902, 1304. The stasis continued for a year and three days.

Cases of constipation are of various types and the expert judgment of the physician is required to differentiate and treat them.[1] It is often pointed out that regular evacuations do not guarantee freedom from constipation. The advance of the intestinal contents may be slow. Sadler has said that "the movement may be like the Missouri Pacific train which appeared to be on schedule, but was, in fact, twenty-four hours late." Quite often progress as far as the region of the spleen is all that can be desired, while there is most unfortunate sluggishness in the reactions of the terminal part of the canal. Laxatives give little assistance to such subjects. Suggestion is often surprisingly helpful. Hertz tells us of a boy who had proved refractory toward many kinds of treatment whose difficulty was promptly relieved by a financial arrangement. He was to receive six pence for the fulfilment of his daily obligation and forfeit a shilling for each omission. After he had incurred one penalty we are told that he became a pattern of regularity—as the author pleasantly says, "he went on and made his fortune."[2]

Obesity.—The accumulation of adipose tissue in burdensome and disfiguring deposits is regarded as mirth provoking, but should be viewed with due appreciation of its seriousness.[3] In the light of what has gone before, there is no escape from the conclusion that during the period of increasing weight the diet must have been in excess of the requirement. Yet when a person has once become notably stout he is often reputed to be a light eater. It is likely to be found that he cannot reduce his allowance of food without feeling quite uncomfortable. Various means may be resorted to in the attempt to abate the unwelcome condition, but frequently without success. Thus outdoor exercise, which, of course, increases the metabolism and should destroy the body fat, may stimulate the ap-

[1] Hertz, "Constipation and Allied Intestinal Disorders," Oxford University Press, 1909.
[2] *Ibid.*, p. 259.
[3] Fisher and Fisk, "How to Live," p. 212.

petite to an extent which fully corresponds with the oxidation, and so defeats it own purpose.

Reduction of adipose tissue by fasting is possible, but not popular. Several other methods have been tried. The Banting system, formerly much in vogue, consisted essentially in a diet containing a maximum of protein. It was held that such a diet would keep the muscles and glands from losing substance, while not promoting the formation of fat. We have seen, however, that fat formation from protein is at least theoretically possible. The success of the Banting treatment probably depended upon two factors: first, foods rich in protein are satiating, and an unconscious cutting down of income is therefore likely; second, the specific dynamic effect of so much protein would be expected to increase the metabolism.[1] Restriction of water drinking is often recommended. Laxatives are sometimes used, presumably to hinder absorption, or to create an uneasy state in which loss of appetite may be expected. A procedure which seems rational is the selection of a rather bulky but not highly nutritious diet, including fruit and the coarser vegetables. By this means hunger can be fairly appeased, while the actual quantity of food entering the circulation is not sufficient to maintain carbon equilibrium. The suggestion may be made that a man seeking to reduce should select the food which is his second choice rather than the dishes he likes best. He will probably be satisfied with less.

It has never been easy to explain the difficulty experienced by overweight subjects in reducing. Perhaps the key to the situation is indicated in an article by Nissler and Gordon.[2] They have observed the variations of blood-sugar in obese individuals. Regardless of one's

[1] Steady and extensive weight reduction without undue hardship has been reported for the patients of Strang, McClugage, and Evans (American Journal of the Medical Sciences, clxxix, 1930, 687). The diet prescribed has averaged 58 grams of protein, 14 grams of carbohydrate, and 8 grams of fat: only 360 Calories. The protein is relatively high as in typical Banting treatment, but, absolutely, all the items are low.

[2] Pennsylvania Medical Journal, xxxii, 1929, 123.

build marked hunger attends the fall of blood-sugar to an abnormally low level. This is a frequent result of the administration of insulin. The studies of Nissler and Gordon show that in the corpulent a craving for food sets in when the sugar of the blood is still at a concentration which would not establish hunger in one more fortunately constituted. Bodily comfort is secured only by forcing the glucose in the circulation to a rather high percentage. This encourages the deposit of fat as was instanced in Wilder's case (p. 153).

A question inviting discussion is whether one should aim to cut out fats or carbohydrates when attempting to lower the calorie content of the diet. Of course both may be restricted. Since starches and sugars form so large a proportion of most rations it might seem more practical to keep watch of them than to attend scrupulously to the allowance of fats. Nevertheless Nissler and Gordon urge—and their reasoning is impressive—that the blood-sugar must be kept up as a concession to the peculiarity of the obese and that the chief sacrifice must be in the fatty foods. These, it will be remembered, have little direct influence on the circulating sugar.

Carbohydrates and Fats Compared.—In the discussion contained in the foregoing chapters the impression has probably been conveyed that carbohydrates and fats are freely interchangeable. One statement has been made which qualifies this conception, namely, that fat cannot completely replace carbohydrate in a diet containing the ordinary allowance of protein (p. 151). The substitution leads to acidosis. There is ordinarily no tendency to let the fat crowd out the cheaper starches and sugars. The opposite condition is of more practical interest; in Central Europe during the war fats were hard to obtain and average diets were correspondingly ill-balanced.

It had been assumed that carbohydrates could quite successfully take the place of fats in human food. But the attempt to push this substitution as far as possible brought out the serious drawbacks of a fat-free ration.

Starling[1] has summarized them somewhat as follows: The bulk of the diet becomes burdensome. This bulk is due in part to water and in part to cellulose. In systems weakened by hardship irritation of the canal and edema of the tissues may result. The food is excessively subject to fermentation. The stomach unloads its contents too rapidly and premature hunger and faintness are experienced. There may be definite failure to secure the vitamins associated with fats, although the use of greens tends to prevent this.

[1] "The Feeding of Nations," Longmans, London, 1919, Chap. IV.

CHAPTER XXIII

THE HYGIENE OF NUTRITION (Continued)

WATER; MEAT; SUGAR

Water.—There are particular foods which call for individual notice; one of these is water. The fact is already familiar that this compound so abundant in nature is also the largest item in the income of the human body. It is an essential part of all the tissues, and its percentage in their make-up cannot be materially reduced while life continues. It has been described before as an important vehicle of excretion, and we have seen that when it evaporates it often provides for the removal of heat, which would otherwise accumulate in the body to its hurt. When the discharge of water is unusually great the feeling of thirst is roused and dictates a renewal of the stored supply.

We can vary considerably our practice of water drinking. Hence this is a matter often dealt with by writers on hygiene. The common teaching is to the effect that one can hardly drink too much water unless it be at mealtimes. The beneficial results supposed to accrue from free drinking are assumed to include the avoidance of constipation[1] and the promotion of the elimination of dissolved waste by the kidneys and possibly by the liver. There seem to be no reasons for doubting the soundness of these popular ideas. The drinking of a great deal of water is an excellent habit, and consumption of tea, coffee, and other beverages in which water is the principal constituent has this in its favor—it leads people to take much more water than they would otherwise.

[1] McCollum and Simmonds (loc. cit., p. 87) strongly recommend copious drinking of salt water (1 per cent.) in the morning. The salt retards the absorption of the water, which rapidly traverses and flushes the canal. These writers assert that the tract before breakfast contains nothing but what we can reject with advantage. The reader will note the clash of this teaching with that of Burnett (p. 104, note).

It is probably correct to say that the duties of the kidneys are made lighter when we give them more water to excrete. This may be contrary to the general impression, for the temptation is to judge the work of a gland by the volume of its output. But in the light of facts which cannot be discussed here we are led to believe that concentration rather than sheer amount of secretion is what puts the tubules of the kidneys to the severest test. They act at the greatest disadvantage when required to excrete a maximum of solids in a minimum of water. The urine almost always has a concentration much higher than that of the blood from which it is derived, and it is fair to assume that the separation of the two fluids would be made easier if the difference of concentration could be lessened. Water drinking is the natural way to secure this result. "Water," says Osler, "is, after all, the great diuretic."

While teachers of hygiene are well agreed upon the value of water in liberal quantities as conducing to health, there has been much said against its free use with meals. We can hardly question the impression that many cases of indigestion have been benefited by the prohibition of water at the table. An approach to Fletcherism is favored when the saliva is not aided by swallows of water. Slower eating is likely, and slower eating may be expected to satisfy the appetite with a smaller actual intake. The idea that the digestive juices are seriously diluted by water taken with the food does not seem to be well founded. Laboratory experiments show that dilution of the fresh secretions is at least as likely to increase as to diminish their activity. It must be borne in mind that the dilution of a liquid containing a fixed amount of enzyme does not reduce the quantity of the enzyme, but only makes it act in a larger volume of the mixture.

Very cold water swallowed rapidly may chill the mucous membrane of the stomach and possibly retard the proggress of gastric secretion. Digestion itself may also be slowed if the contents of the stomach are cooled. But bacterial fermentation should apparently be delayed just

as definitely as the normal hydrolysis, and we ought not to make too much of these possibilities. Hawk, at the University of Illinois, once made a number of trials which are entirely favorable to the practice of drinking all the water that one chooses with meals. He has shown that the fecal nitrogen is lower when water is taken in large volume than when it is forbidden. This fact he holds to indicate more complete digestion and more thorough absorption. His subjects were in the best of health, and his results do not contradict those of physicians who have found the restriction of water beneficial in particular cases.

The opinion is commonly held that drinking much water favors increase of weight. To a limited extent such increase of weight may result from actual retention of water. We can see that a definite addition to the adipose tissue may proceed from the tendency to eat more food when water is taken freely. Perhaps the converse of this form of statement is more accurate; namely, that weight is lost when water is restricted and the quantity of solid food unconsciously diminished. Sometimes an erroneous inference may have been drawn from the fact that stout people drink a great deal of water. This is in part a consequence rather than a cause of their condition. Subcutaneous fat is a hindrance to the escape of heat from the body, and its presence during warm weather necessitates an unusual amount of perspiration. This, in turn, produces thirst.

Meat.—Much that is written tends to create the impression that meat is entirely unlike any other food. Its peculiarities are constantly exaggerated.[1] When Erasmus Darwin excused himself from Lenten abstinence on the ground that "all flesh is grass" he perverted Scripture, but uttered a physiologic truth. Meat has two distinctive characters: it is very rich in proteins and in extractives. It is not any richer in protein than are dried peas and beans, but while these vegetables contain a large proportion of carbohydrates, lean meat contains these bodies

[1] Lusk, American Journal of Public Health, xiv, 1924, 297.

very scantily. A diet of lean meat, therefore, comes near to being a straight protein diet. A plate of beans is equivalent in composition to a plate of meat and potato.

Vegetarianism has sometimes been advocated upon humanitarian grounds and sometimes because of its supposed favorable effect upon health. The idea that the destruction of animal life for human nutrition is morally wrong cannot be discussed here. It is true that not many people would kill animals for their own use if there were no other way to obtain meat. It is equally true that so many of the noblest and gentlest people that ever lived have enjoyed meat and fish that we cannot well credit the claim that flesh foods cause deterioration of character. Attention has often been called to the exceptional kindliness of the Esquimaux, a carnivorous race.

A diet containing much meat is naturally a high protein diet, and is, accordingly, subject to the drawbacks already mentioned in this connection. These have been seen to include an unprofitable spurring of the metabolism—more particularly objectionable in warm weather—and the menace of auto-intoxication. The typical proteins of meat are probably not better nor worse than other proteins in these relations. There is, however, greater, likelihood of overconsumption of proteins when meat is the source because of its very attractiveness. Men, especially those who spend money freely, are certainly prone to such indiscretions; while women set an example of temperance in this as in so many other practices. So far as the proteins eaten are destined to be reconstructed into those of the blood and tissues, it may be asserted that meat proteins are peculiarly well suited to the purpose. Their molecular correspondence with the pattern to be imitated is close. But the demand for amino-acids for this use seems to be small.

The real individuality of meat is owing to the presence in it of the secondary substances which we call extractives. These give it its odor and, in conjunction with mineral salts, its flavor. Their absolute amount is not large, but

they are of much interest. They have been described by writers, holding meat in disfavor, as waste-products of animal life. The characterization seems broadly to be a justifiable one, though our disgust at the notion is not necessarily well founded. The extractives of meat certainly originated during the lifetime of the animal through the breaking down of its proteins, and were destined for ultimate excretion, either unchanged or after some alteration. It is hard to escape the conclusion that our pleasure in the taste of meat is due to compounds nearly akin to those of the urine.

Furthermore, it is plain that the opponents of meat are correct in making the point that when we receive these extractives we are simply adding to the duties of our own kidneys. When we eat 50 grams of protein in beans we have later to excrete about 8 grams of nitrogen in urea and other forms. When we eat 50 grams of protein in beefsteak we must subsequently excrete the same quantity of nitrogen plus that of the extractive bodies. The addition is not a large one, but it is partly in the form of uric acid and perhaps other bodies less tractable than urea. The advisability of limiting meat in rheumatism and related conditions has long been a tradition. Considering that our ancestors ate a great deal of meat one wonders whether this habit affected their health in any specific way. Eighteenth century literature certainly suggests an occurrence of gout and calculus beyond what is now familiar. Yet we are told that the Esquimaux, the champion meat-eaters of the world, escape these troubles.

Two experienced Arctic explorers familiar with Esquimaux living have completed a year of subsistence on animal food under the climatic conditions of New York. They ate a variety of meats and meat broths, their only vegetable supply being tea. The daily ration furnished 100 to 135 grams of protein, 175 to 200 grams of fat, and only 5 to 10 grams of carbohydrate. The maximum Calorie value is less than 2500. (Cf. Heinbecker on Esquimaux Diet, p. 198, note.) There was some loss of weight

during the first month, afterward a constant condition. There were progressive losses from the bodies of the subjects of calcium and phosphorus, but no derangement of health was apparent. There was a detectable acidosis evidenced by the presence in the urine of incompletely oxidized products of fat metabolism, but there were no subjective symptoms. It is probable that habituation to such feeding had much to do with the success of this unusual trial.[1]

While the extractives may be held to account for some of the possible ill effects of meat, they are also the source of its especial virtue. Palatability itself is of great hygienic worth, and these substances confer qualities which for most people cannot be equaled apart from meat. The promotion of gastric secretion in the normal subject and its establishment in the invalid are most surely secured by means of these same extractives. Aside from their favorable influence upon the stomach, they are probably mild stimulants in the same sense in which coffee and tea can be called so.

Some kinds of meat are well known to occasion indigestion. Pork and veal are particularly feared. While we may not know the reason why these foods so often disagree with people, it seems probable that texture is an important consideration. In both these meats the fiber is fine, and fat is intimately mingled with the lean. A close blending of fat with nitrogenous matter appears to give a fabric which it is hard to digest. The same principle is illustrated by fat-soaked fried foods. Under the cover of the fat thorough-going bacterial decomposition of the proteins may be accomplished with the final release of highly poisonous products. Attacks of acute indigestion resulting from this cause are much like the so-called ptomain-poisoning. But it is best to reserve the term for those cases in which the harmful bacterial change had taken place in the food before it was eaten.

[1] Du Bois et al., Abstracts of Communications to the XIIIth International Physiological Congress, Boston, 1929, 70.

Texture is an exceedingly weighty factor in determining the ease or difficulty of digestion for any food. It is this which makes the recognized difference between new and old bread and between the upper and the under crust of a pie. Dry bread or pastry takes up the saliva as blotting-paper would, and starch digestion is immediately begun even at the center of the morsel. Saturated food material does not imbibe the digestive juice in this way. Osler has said, with his usual picturesqueness, that "pie north of Mason and Dixon's line and hot bread south of it have done more harm than alcohol." Fats are best cared for when emulsified if liquid, and when of a flaky or crystalline character if solid. This last quality is realized in good bacon.

Sugar.—The reader will have noted that the starch, which is usually the most abundant compound in the daily income of man, is converted to a sugar before it is admitted to the circulation. The question arises why it is not equally well to eat sugar altogether in place of starch. This is the actual habit during the period of milk feeding in infancy. The enzymes that act upon starch are not freely furnished until some months after birth. In later life, however, starch comes to be the main reliance of the race. Experience has shown that cane-sugar is often productive of indigestion. Can we find definite reasons for the superiority of starch to sugar?

The fact has previously been mentioned that much sugar causes alimentary glycosuria, while this is never produced in strictly normal subjects by the freest eating of starch. Here we have a clue to the difference between the two classes of carbohydrates. The glycosuria is not in itself a serious matter, but it shows that the solubility of sugar and the slight changes requisite for its digestion lead to its very rapid absorption. The digestion of starch is a more gradual and protracted process, and the resulting glucose is not formed so swiftly as to raise the concentration of the intestinal contents appreciably, nor delivered to the blood so abruptly as to increase markedly the percentage of sugar

in circulation. It seems safe to assume that the storage of glycogen is effected more smoothly and easily after the ingestion of starch than after the taking at one time of a large quantity of sugar.

Highly soluble bodies of low or moderate molecular weight are said to confer on their concentrated solutions the property of high osmotic pressure. This is not the place to discuss what is meant by the expression. For practical purposes it can be said that concentrated solutions take water from tissues with which they may be brought in contact. Hence an irritant effect is to be expected. This is exemplified by the action of strong salt solutions in producing vomiting. Everyone who is fond of candy knows that it can be eaten until a point is reached at which an uneasy sensation of satiety verging on nausea is developed. This is relieved by drinking water, which, of course, lowers the concentration of the syrupy gastric contents and so lessens the irritation. Hard candy, dissolving gradually in a large quantity of saliva, must produce a less concentrated and irritating solution than that resulting from the rapid "melting" of soft bonbons.

Cane-sugar is much sweeter than sugar of milk or the other sugars which arise in the course of digestion. It is, therefore, cloying and its free use may blunt the appetite for other foods. It is said also to be more disturbing to the stomach than the others. These two properties perhaps account sufficiently for the ill effects which are attributed to the increasing consumption of candy in this country. Still it is probable that the evils resulting have been much exaggerated. There is, however, no question that the constant eating of candy threatens to damage the teeth, and the indirect impairment of the digestive powers may be serious.

The relation between sugar and the decay of the teeth is apparently quite simple. Sugar is prone to ferment, a change brought about by bacteria which are inevitably present in the mouth. The chief product of such bacterial decomposition is lactic acid. This acid attacks the lime-

salts of the teeth at points where the enamel has been chipped or worn away, or where it fails to meet the gum. The dissolving of the lime-salts leaves a soft and perishable organic structure which readily undergoes true decay. Every tiny deposit of sugar in the crevices of the teeth may soon become a focus of acid production and a center of disintegration. The popular impression that plain sugar is not so hurtful as sugar mingled with other substances in candy has this basis: pure sugar is so readily dissolved by the saliva that it is not likely to remain long clinging to the teeth. On the other hand, sugar which is mixed with fatty materials like chocolate may be sealed into crannies or retained under the edge of the gum with unfortunate effect. One who is bound to eat much candy should be willing to exercise unusual care to free the teeth from the remains, and may, in spite of his pains, have periodical days of reckoning at the dentist's.

There is much testimony to the effect that free indulgence in sugar is bad for the complexion. When we consider this tradition we must remember that pimples and other gross blemishes are directly due to infections from without. If their development is conditioned by feeding, the relation must be indirect and referable to changes in the resistance of the tissues. It is a suggestive fact that in diabetes we have a great increase in susceptibility to surface infections. Perhaps an increased concentration of sugar in the blood has this influence in all cases.

Cane-sugar is not to be thought of as a relish or accessory, valuable chiefly to make possible the preparation of numerous tasty dishes. It is true that the lack of sugar in war-time galled us most as it limited the variety of our fare. But, beyond this, sugar has a very substantial position in the American diet. The average per capita consumption in this country is about 100 pounds a year. It furnishes, when obtainable, at least one-eighth of our supply of Calories. Its replacement by other food is a problem of great magnitude. Many people think of candy and other sweet food as "unsubstantial." This is

far from the truth. Confections, ice-cream sodas, and other extra foods contribute largely to the ration in many cases. (A four-ounce cake of sweet chocolate may have a value of 600 Calories.[1])

Glucose.—The glucose of commerce is made from corn-starch by treatment with weak hydrochloric acid, which is afterward neutralized by sodium carbonate, leaving a small percentage of sodium chlorid in the product. The resulting substance contains a considerable quantity of the dextrins—bodies intermediate between starch and sugar—some maltose, and dextrose to the extent of about 50 per cent. of the whole. Such a mixture is hardly to be distinguished from that which exists at a certain stage in the salivary or pancreatic digestion of starch. It is hard to account for the intense popular prejudice constantly manifested against this food product. The only possible objection to its free use is connected with its tendency to induce glycosuria, an effect secured somewhat more readily with glucose than with cane-sugar. During the shortage of cane-sugar which prevailed in France in wartime glucose was sweetened by adding a little saccharin and made a fair substitute.

Food Accessories.—It is perhaps unnecessary to enlarge upon the service of those compounds which are classed under this head. The double value of the extractives of meat which favor digestion both because of the flavors which they develop and because of their direct action upon the stomach wall has been sufficiently emphasized. The various condiments are believed to have a similar significance. So far as they season the food so as to make it more acceptable they must evidently promote secretion. Their power to call forth the gastric juice by a purely local effect is not so well established, but they are known to increase the blood-flow in the mucous membrane, which must help to sustain the local activities.

Tea and Coffee.—These beverages owe what limited

[1] C. G. and F. G. Benedict, Boston Medical and Surgical Journal, 1918, clxxix, 153; 1919, clxxxi, 415; 1921, clxxxiv, 436.

food value they have to the cream and sugar usually mixed with them. They give pleasure by their aroma, but they are given a peculiar position among articles of diet by the presence in them of the compound caffein, which is distinctly a drug. It is a stimulant to the heart, the kidneys, and the central nervous system. It is chemically related to uric acid, but is not known to yield this inconvenient waste-product in the human body. Individual susceptibility to the action of caffein varies greatly. Where one person notices little or no reaction after a cup of coffee, another is exhilarated to a marked degree and hours later may find himself lying sleepless with tense or trembling muscles, a dry, burning skin, and a mind feverishly active. Often it is found that a more protracted disturbance follows the taking of coffee with cream than is caused by black coffee.

It is too much to claim that the use of tea and coffee is altogether to be condemned. Many people, nevertheless, are better without them. For all who find themselves strongly stimulated it is the part of wisdom to limit the employment of these decoctions to real emergencies when uncommon demands are made upon the endurance and when for a time hygienic considerations have to be ignored. If young people will postpone the formation of the habit they will have one more resource when the pressure of mature life becomes severe.[1]

Chocolate and its derivative, **cocoa,** may be regarded as having somewhat similar properties. There is a measure of drug action, though it is less pronounced than in the case of coffee. Here the active principle is theobromin, nearly related to caffein. Chocolate is more than a food accessory, being exceedingly nutritious. A chocolate habit is easily formed, but, aside from threatening damage to the teeth and contributing to overweight, it is comparatively innocent.

Mineral Salts.—These compounds have been referred

[1] See Hollingworth, "Caffein and Mental and Motor Efficiency," Archives of Psychology, The Science Press, New York, 1912.

to in an earlier chapter as forming an essential part of the tissues. Hence they must be supplied in sufficient quantity and variety during the period of growth. The danger of failing to do this is only occasional, though there are certain cases of malnutrition in which the central difficulty seems to be the lack of such constituents in the body of the child. The actual trouble is probably with the assimilation rather than with the diet. Thus, in rickets there is an evident deficiency in the quantity of lime-salts incorporated into the developing skeleton, but it is not necessarily true that there is any shortage in the amount offered in the food.[1] Still it is the judgment of Sherman that a deficiency of calcium is the most common of all dietetic faults.[2]

When the full stature is reached the need of a continued salt income is less marked, though there is reason to believe that the demand always exists. A certain loss in the urine and through the skin seems bound to occur, though the usual excretion of salts is far greater than the bare minimum, and appears to indicate a needless excess in the income. The salts of the diet have much to do with its palatability, and so deserve a place with the organic condiments.[3] An unusual quantity of saline matter may be supposed to impose a hard task upon the kidneys, and is known to aggravate any dropsical tendency that may be present.

Sodium chlorid is the one salt which we take pains to secure. We are inclined to think of it as a mere relish, but it has been shown that it has a deeper significance. The Austrian physiologist Bunge has found that it is sought both by animals and men whose food is largely or entirely vegetable. It is repugnant to those that are approximately carnivorous. Bunge points out that vegetable foods are generally rich in compounds of potassium and relatively deficient in those of sodium. He has demonstrated that when an excess of potassium salts is eaten

[1] Lusk, "Elements of the Science of Nutrition," The W. B. Saunders Company, Philadelphia, 1928, 481–486.

[2] McCollum and Simmonds, loc. cit., pp. 32, 33.

[3] Job vi, 6.

the kidneys discharge the foreign material promptly, and in doing so let slip a good deal of the sodium chlorid from the blood. Accordingly, it is inevitable that the steady consumption of foods rich in potassium[1] should create a demand for sodium. The seeking of common salt to meet the need is a singular illustration of the almost unerring working of instinct.

Stefansson has furnished an amusing instance of the dislike for salt which is to be relied on in those who live entirely upon a diet of flesh. When he first went among the Esquimaux he found himself in danger of losing his provisions at a ruinous rate. Policy required that he offer refreshments to all comers and their appetites were appalling. The embarrassment was happily relieved by the simple measure of salting the food merely to the degree which he himself found agreeable. The visitors thenceforth were content with very modest portions.

Iodin is now recognized to be an element which must be furnished by the diet, though the amount needed is minute. It abounds in sea-water and sea-food. It may be too scantily present in the food and drinking-water of some inland regions. In such sections of the country thyroid disorders are prevalent. Experience has shown that they can be largely banished by adding salts of iodin to the income of the population. But this is a measure which calls for most judicious control; excess as well as deficiency may be disturbing to health.

The Acid-base Balance.—If the constituents of a ration are mixed and completely burned the residual ash may be either acid or alkaline. The proteins leave behind them definite quantities of sulphuric and phosphoric acids. These may be dominant in the mixture, or they may be more than offset by the alkalies furnished by the combustion of certain foods. Most fruits and vegetables leave alkaline remains. So does milk. It is to be noted that a food may have an initial acidity, as in the case of the apple or the orange, and yet contribute at last to the al-

[1] Potatoes have this character.

kaline side. This is equally the case with milk which sours so intensely under bacterial influence. Lactic acid and most of the fruit acids burn and literally "vanish into thin air"—be it outside the body or in the metabolism. An exception, within the body, is afforded by benzoic acid which the tissues fail to oxidize. It remains like the sulphuric acid from the proteins to be dealt with by the kidney. Hence cranberries, plums, and prunes which contain benzoic acid add to the task of acid excretion which the body has usually to perform.

If the ash of the diet is acid the urine must be so. It is ordinarily on this side of neutrality. There is evidence that an excessively acid urine is undesirable; it does not so surely bear away the minor waste-products like uric acid. Hence it is commonly taught that a neutral or alkaline residue is a characteristic to be sought in making up a ration.[1]

Food Values.—American householders are now reading and hearing a great deal about economy in selection and the conservation of food. The subject is too large to be dealt with here. Just a word may be ventured regarding the errors of judgment into which it is easy to fall. The fact which needs always to be borne in mind is that the water and the innutritious part of any article of diet must be deducted to obtain a true estimate of its potentiality. How greatly these components may reduce nutritive worth, and how delusive mere bulk can be will be appreciated after considering the following equivalents (in fuel value):

1 lb. butter = 1.1 lb. bacon = 1.8 lb. oatmeal or cheese = 2.1 lbs. flour or sugar = 4.2 lbs. lean meat = 8.4 lbs. potatoes = 11.2 lbs. milk = 15.4 lbs. onions or oysters = 16.8 lbs. squash = 19.6 lbs. skimmed milk = 42 lbs. lettuce or celery.

[1] Lusk, loc. cit., 485.

General reference: Friedenwald and Ruhräh, "Dietetics," W. B. Saunders Co., Sixth edition. Also, Sherman, "Chemistry of Food and Nutrition," Macmillan, Third edition.

CHAPTER XXIV

FOOD POISONING

It is probably safe to say that within the lifetime of the average individual critical illnesses occur which one is tempted to regard as cases of food poisoning. Yet there is a good deal of doubt concerning the accuracy of the term in many of these instances. In any attack of indigestion the element of poisoning may be present; but the poison has usually been generated within the alimentary tract by an unfortunate type of decomposition and the food may have been perfectly wholesome when it was eaten. We should, so far as possible, limit the designation to cases where the food has been clearly at fault, and not the temporary conditions prevailing in the canal.

As regards the food itself, we should distinguish between that which is truly poisonous and that which is the bearer of infection. Infected food may cause typhoid or scarlet fever, but it is clear that these diseases are in a different class from the genuine poisonings. Nevertheless, it is hard to draw the line with certainty. Simple diarrheal attacks which ensue after a particular food has been eaten may be due either to organisms introduced with it or to the toxic character of the food itself. The impression seems to prevail that the first possibility is much more common than the second. Food that really deserves to be termed poisonous should remain so even though sterile. On the other hand, the sterilization of poisonous food by heating to the boiling-point or higher may decompose and render harmless certain of the toxic substances as well as destroy the micro-organisms.

Our pure food laws are framed to guard consumers

against "decomposed" food products. Most people need to be reminded that a great deal of decomposition is perfectly consistent with wholesome quality. In fact, there are cases in which decomposition is deliberately encouraged. Many cheeses testify by appearance, consistency, and odor to the advanced stage which the process has attained. They rarely cause trouble. A considerable degree of similar change is often tolerated in meat. Our feeling in regard to the matter seems largely determined by tradition and prejudice; we object intensely to the earliest signs of such deterioration in eggs.

Idiosyncrasy.—In any discussion of this kind allowance must be made for individual peculiarities. Many people have found by bitter experience that they must avoid certain foods. Some cannot eat lobster, others are seriously affected by strawberries. Still others must do without butter, a curious fact, inasmuch as this is a milk product and everyone must have begun life upon a milk diet. A severe reaction toward potato has been recorded. In a case where this had been observed, the victim, a highly intelligent woman, expressed the belief that her repeated sicknesses were due to mental suggestion, her ingrained fear of potato. She told a friend that she wished to be tested by being given some potato in an unrecognizable form. The experiment was soon tried, a sponge cake being made with potato flour and eaten by the unsuspecting subject. A sharp and exhausting illness promptly followed.

There are rather frequent instances of idiosyncrasy toward eggs. A most striking one may be described. A baby of nine months was given for the first time a little poached egg. It swallowed one spoonful, spat out a second, and smeared some upon its face and fingers. Almost immediately vomiting set in, diarrhea followed very shortly, and wherever the egg had touched the skin there was a swelling and eruption. Some weeks later the child was again made sick when it ate a crumb of frosting which it had found on the floor. It is an interesting fact that a normal tolerance for egg was secured by giving minute

quantities from day to day and gradually increasing the amount. Severe reactions to particular foods are classed under the term "allergy." Such sensitiveness has much in common with the susceptibility to certain pollens which is the basis of hay-fever. It also reminds us of the asthmatic symptoms exhibited by some individuals in the presence of horses or cats.

True food poisoning has until recently been due in most cases to animal products. Meat and fish have been most often implicated, while milk and ice-cream have occasionally figured in the accounts. Generally the foods responsible have been rich in protein. It would be natural to expect similar poisonous decompositions among the legumes, and, in fact, a rapidly increasing number of instances are being recorded in which beans appear to be concerned. Certain foods not at all rich in protein—for example, tomatoes—have recently been inculpated. Before we take up the subject of animal food poisoning attention should be called to the possibility of dangerous properties which may develop in cereals.

Ergotism.—This is a form of disorder which has been rather common in Europe. While it cannot be said to threaten our own people upon any extensive scale it may fairly stand as an example of its class. The grain which is involved is rye. When this has been damaged by a certain microscopic fungus it becomes definitely poisonous and continues to be so even after cooking. Persons who consume this cereal may develop the most various symptoms. Sometimes a chronic condition is induced, in which there is a slow decline due to degeneration within the central nervous system. Sometimes acute attacks occur with convulsions, or the chief effect may be a strange interference with the circulation leading to gangrene of the extremities.

Poisoning by Meat and Fish.—We may evidently distinguish between poisonous meats which were rendered so during the life of the animal and those which have become dangerous owing to postmortem changes. Instances

of the first class are not now common. There is a remote possibility that an animal may eat something which can make its flesh unwholesome. Certain cases of sickness attributed to the meat of partridges have been referred to the supposed inclusion of laurel in the diet of the birds when hard pressed for food. Animals suffering from various diseases may prove to have poisonous properties if their flesh is marketed and eaten. The practice of "emergency slaughter"—killing and dressing for consumption animals which are near to natural death—is happily rare. Not many years ago ghastly examples of this criminal procedure were recorded and the victims were numerous. One is reminded of the thrifty counsel given to the Hebrews in Deuteronomy xiv, 21.

When meat which was originally wholesome becomes poisonous because of changes wrought in it by micro-organisms we have the conditions for *ptomain-poisoning*. There is no doubt that the term has been misused and made to cover many cases of acute indigestion in which the trouble had been less with the food than with the alimentary tract of the sufferer. We are not usually warranted in designating as ptomain-poisoning solitary reactions on the part of individuals when many other persons have eaten a certain food without ill effects. The multiple cases are much more likely to deserve the designation. although even here, as already noted, it is hard to draw the line between true poisoning and the transmission of germs capable of mischief. Many authorities now urge that the term be discarded.[1]

The standard picture of ptomain-poisoning is, apparently, that given long ago by Ballard (Wellbeck epidemic, cited by Osler. Ham was the food responsible). The average time between eating the food and experiencing the first symptoms was about twenty-four hours. It has often been shorter. The onset was generally sudden, often absolutely without warning, though in other cases there

[1] Warren, "Medical Science for Everyday Use," Lea & Febiger, 1927, Chap. XX.

were premonitory signs, such as languor and fleeting pangs in the abdomen. Sometimes the initial experience was of faintness and vertigo, sometimes of chilliness. Within a short time the abdominal pain became most severe, producing prostration and cold sweating. Diarrhea and vomiting shortly set in. Muscular weakness rapidly became extreme; headache and thirst were common. The temperature rose, in some subjects, to 104° F. The pulse was fast and feeble. Death from exhaustion sometimes occurs in such cases, but in the great majority speedy recovery takes place. It is favored, no doubt, by the thoroughness with which the system has eliminated the poison.

There have been particular outbreaks in which the symptoms were quite unlike those just described. There are even types of poisoning attended with few signs of alimentary disturbance, the chief effects being upon the central nervous system. This has been characteristic of the occurrences of mussel-poisoning, which have been reported from Germany. In these the symptoms are those of profound collapse with numbness, dilated pupils, and rapid, failing heart. The effects resemble quite closely those produced by atropin.

Botulism.—By this name is known a type of food poisoning which is not particularly common, but which is remarkably clear cut in its manifestations. The clinical picture has been familiar ever since 1820, when it was first recognized in the cases of persons made ill by sausage. Since then there have been occasional records of similar prostrations until a total of several hundred has been reached. Sausage meat has by no means been the sole offender. Canned string beans have been frequently implicated; so have ripe olives. A specific organism, Bacillus botulinus, which does its work in the absence of oxygen, is believed to develop the intensely poisonous property.

The victims of botulism have no fever and no acute pain. The central fact is the abolition of function of certain nerve-centers, especially those of the cranial

division of the system. As a result there are disorders of vision, disturbances of equilibrium, and, subjectively, distressing vertigo. Impaired control of the muscles about the throat may result in difficulty with speech and with swallowing. All the secretions are diminished, and there is stubborn constipation. Death supervenes in as much as 60 per cent. of the cases, usually between the fourth and the eighth day. Botulism is, therefore, far more mortal than ordinary food poisoning. Recovery is halting and protracted. Permanent effects, such as local paralysis of either sensory or motor order, may remain.

The liability of sausage meat to undergo poisonous decomposition reminds us that any food substance is far more subject to the action of micro-organisms when it is finely divided. A large piece of meat may be quite sterile internally and the agents of disintegration will make but slow progress working from the surface. When it is minced they are immediately introduced into every part, and at the same time the natural barriers to their spread, the partitions of connective tissue, are broken down. Hamburg steak illustrates the same condition.

Attention should be called to a common source of error in fixing upon the food to be held accountable for an apparent case of poisoning. Laymen, and often practitioners also, unhesitatingly place the blame upon some article eaten at the previous meal. Particularly is this the tendency when some food is conspicuous in material vomited. We must consider that the real cause of the trouble may have been received into the system many hours before the onset of the acute symptoms, so that one or two entirely wholesome meals may have been enjoyed in the period of incubation. With botulism the delay may extend over two days.

When we deal with any statistics of food poisoning we must keep our sense of proportion by noting how small —one might almost say infinitesimal—is the fraction of a product which even falls under suspicion. Thus Geiger[1]

[1] Journal of the American Medical Association, 1923, lxxxi, 1275.

points out that canned salmon has been implicated more often than any other single food in a list of recent outbreaks, but that nevertheless for every can which seemed to cause trouble *two and a half million cans* were innocent.

Metals, Preservatives, and Adulterants.—Much indigestion and general ill health is popularly attributed to these causes. There is little doubt that they have been overemphasized. The technic of the canning industry has been greatly improved. Articles which tend to dissolve much tin are placed in enameled containers. Tin in such quantities as may conceivably enter other canned goods has not proved demonstrably harmful. Lead from solder is now excluded by the use of a new type of seam sealed only on the outside.

Copper has been considerably feared as a possible poison, but there is no certainty that it has often figured in this way. It was formerly used quite generally to intensify the color of canned peas and other green vegetables, but it has fallen into disfavor and been largely replaced by organic materials, such as chlorophyll. Metal from cooking utensils may enter the food in small quantities; it is not at all likely to be a source of trouble. Many cases of severe sickness following the eating of ice-cream have been ascribed to the dissolved metal of the freezer. An extended study of poisonous ice-cream, conducted by Vaughan and Novy, has made it probable that the toxic substances are organic rather than metallic.

There is no doubt that ice-cream may be intensely poisonous. The investigators just mentioned have tested samples of it which would act as almost instantaneous emetics, producing no other effect because not retained long enough. Inasmuch as a spoonful of such ice-cream is more active than an equal quantity of pure zinc sulphate it has been inferred that the metal cannot possibly be the agent concerned. Still, it is conceivable that obscure compounds formed by the union of metals with organic bodies may be much more toxic than the simple and familiar salts.

There is a widespread prejudice against the use of antiseptic substances for the preservation of foods. Our laws carefully restrict the practice. While our preference for fresh and natural food is undoubtedly wholesome, it is hard to prove that material harm has been done by such preservatives. If the choice must be made between foods which have undergone a prolonged and gradual decomposition and foods of the same age kept by the aid of antiseptics in minute quantities, the latter must in many cases be the safer. The mention of benzoate of soda may be productive of disgust, but the same ingredient is native in certain foods, such as cranberries. The common adulterants are not likely to endanger health; a distinction has to be drawn between alterations in food which make it injurious and those which are merely fraudulent.

We shall do well to refer once more to the possible inadequacy of certain diets (Chapter XVI). Such disorders as beriberi and scurvy might be regarded as chronic food poisonings, but it is better to place them in a separate class. True poisoning is due to the presence of some agent and not to a lack of a specific body. Polished rice is not poisonous, it is simply insufficient by itself. One reason why foods that have been kept for an unusually long time are not to be recommended is that some of the valuable compounds originally present may have disintegrated; it may not be just to call such foods poisonous, but their nutritive properties may have suffered some impairment.[1]

[1] See Jordan, "Food Poisoning," University of Chicago Press, 1917.

CHAPTER XXV

ALCOHOL

Alcohol occupies a peculiar position among the constituents of the diet of mankind.[1] A perfectly dispassionate estimate of its values and its drawbacks is arrived at with difficulty. Most discussions of the subject are frankly partisan and, therefore, partial. Alcohol affects the human system in many ways, and it is possible to select for emphasis either those aspects of its action which are detrimental or those which are favorable. In this way a writer may be entirely accurate in all his affirmations and yet fail to be just to a complex question because of what he leaves unsaid. One cannot properly approach such an analysis of the effects of alcohol without first learning the extent of its use the world over. In our own environment there is a feeling of hostility toward the intoxicant which would excite wonder in many countries enjoying an advanced civilization. Intemperance is deplored by thoughtful people everywhere, but the demand for total abstinence is sectional, though probably extending steadily.

The older literature abounds in the praise of wine. The Bible itself has many appreciative references to its potency as a comforter. It has also eloquent passages which condemn its abuse and records of abstinence on the part of certain sects or guilds among the Hebrews. No better physiologic distinction has ever been drawn than in the verse which places "wine which *maketh glad* the heart of

[1] This chapter should, perhaps, be recast to read in the past tense. The discussion which it contains may be regarded as closed. But it has seemed unnecessary to modify it. If the influence of alcohol is now a matter of history it may still be of interest to recall the time when it was a living issue.

man" in comparison with "bread which *strengtheneth* man's heart." To "make glad" is to minister to feeling, to "strengthen" is to confer power which can be demonstrated to an observer—an objective instead of a subjective result. We cannot point to many great men in the history of nations who have entirely avoided the use of alcohol.

Here in America there was little concerted protest against the use of alcoholic drinks until the nineteenth century. The Puritans, with all their restriction of recreation and self-indulgence, were singularly tolerant of hard cider and Jamaica rum. This laxity extended to all classes of society. About one hundred years ago Lyman Beecher described the immoderate drinking which was a feature of an ordination to the ministry in a Connecticut parsonage, host and guests being clergymen. Beecher himself became a vigorous leader of the movement for temperance, which was not until some years later an agitation for total abstinence. A New Hampshire town-meeting (Francestown) voted in 1819 that the unseemly consumption of liquor at funerals be discouraged.

Edward Everett Hale has told us in his "A New England Boyhood" of the common practice of serving wine at children's parties about the year 1830. He also tells us that when the "Franklin Medals" were annually awarded to Boston schoolboys, an entertainment and banquet was provided from which the youths departed in a tipsy condition. The utter impropriety of these proceedings shows us in an impressive manner how far we have moved from the standpoint of that age. The offenses of the time appear the more aggravated when we reflect that the liquors used were largely of the strongest type.

The world has long had one conspicuous example of consistent abstinence on the part of a great population. This is afforded by the Mahometan peoples. It is said that the Lascar sailors who visit our ports can be allowed shore leave with implicit confidence that they will return to the ship as sober as when they left it. A seaman who erred

in this respect and was remonstrated with by his captain is reported to have excused himself on the ground that he had embraced Christianity.

Something will be said of alcohol under each of five heads. We shall proceed to consider it as a relish, a food, a drug, a cerebral alterative, and as a poison. While such a treatment is most convenient, it must be recognized that alcohol can scarcely exert a single influence unmixed with the others. One of the five aspects named may be particularly prominent for the moment, but traces at least of the others are to be looked for. It is this intricacy of action which makes it so hard to weigh the facts with equity. Another disturbing consideration is found in the very unequal susceptibility of different persons to the temporary effect of alcohol as well as to its habit-forming property.

Alcohol as a Relish.—It must be sufficiently clear from what has gone before that anything that adds to the zest and pleasure of a meal may be expected to promote digestion. The only exception to this rule may be looked for when the relish in some way interferes with the digestive process. Alcohol or, more correctly, alcoholic beverages may certainly be held to enhance the enjoyment of dining, and must, therefore, favor the digestion and absorption of food. It is often claimed in rebuttal that alcohol retards the action of enzymes. This is doubtless true of high concentrations, but no such mixtures can possibly be made to exist in the stomach. Rapid dilution by the juices and rapid absorption of the alcohol through the lining membrane combine to bring down its percentage to a level which cannot hinder the normal hydrolysis.

The appeal of wines and cocktails may be said to be due quite as much to the minor substances which they contain as to the alcohol. Pure dilute alcohol would not be attractive to many people. At the same time the extractives conferring flavor and fragrance do not seem to make a complete beverage when the alcohol is removed.

With the frank admission that the finer alcoholic drinks may be promoters of digestion, we may fairly couple certain qualifying statements. First, such stimulation is unnecessary for those whose health is what it should be. Second, the employment of such means to spur the appetite leads readily to overeating. It is also to be observed that the use of alcoholic relishes gives no sanction to drinking apart from meals.

Alcohol in the stomach has the effect of increasing the local blood-flow, and it is well established that absorption is thereby promoted. Whether it takes its place with the extractives or meat as a chemical agent to excite gastric secretion is not so certain. It is hard to discriminate between the influence which it exercises through the central nervous system and that which it may exert upon the stomach wall in a more direct manner. The maximum favorable effect upon the digestion is produced by a small quantity of alcohol. Larger quantities are notoriously apt to nauseate and to precipitate disgraceful scenes, all too common in connection with elaborate banquets.

Alcohol as a Food.—There has been a great deal of opposition to the claim that alcohol can be reckoned a food. It has seemed to many of its antagonists that the admission weakens their position, but this is not necessarily the case. To say that alcohol may be a food is not to deny that it is a dangerous one. Professor Atwater was roundly censured by leaders of the total abstinence movement for a publication which is really a powerful tract in favor of their position. He had said that alcohol might serve as a food, and all his earnest warnings against it were regarded as discounted. His experimental work on the subject is entirely conclusive.

The fact has been reiterated that the chief use of food is to undergo oxidation with release of energy. Alcohol in considerable amounts may be oxidized to carbon dioxid and water in the human system. When it is thus oxidized the heat value of each gram is about 7 Calories. There

seems to be no provision for the retention of alcohol against a future time of need nor for its conversion into glycogen or fat. Its oxidation is bound to take place with little delay, and it is in this respect not so adaptable to the changing demands of the organism as is carbohydrate. Nevertheless we must grant that it may take its place in the diet as a substitute for other non-nitrogenous foods. Atwater's experiments, as well as many parallel studies, have made this evident.

A subject was brought into equilibrium on a ration without alcohol. It was then found possible to withdraw carbohydrates and fats to a certain extent and to replace with alcohol in isodynamic amounts without disturbing the equilibrium. The well-known fattening effect of moderate drinking may be explained as due in part to the whetting of appetite and in part to the sparing of carbohydrate and fat by the alcohol which is utilized in their stead. Fifty years ago the same fact was recognized by George Henry Lewes, in his interesting "Physiology of Common Life." He tells us how a convention of total abstainers once gathered in the city of Frankfort, in Germany, and how the cooks in the hotel in which the delegates lodged were put to it as never before to supply the pastry and pudding ordered by these unfamiliar patrons. The guests for whom the table had heretofore been set were accustomed to supply with alcohol a want which the teetotalers met with carbohydrate.

How far the substitution of alcohol for other non-nitrogenous foods may be carried has been much debated. If it is given too freely its oxidation is incomplete and, what is of more practical importance, the cerebral effect becomes prominent. To make the utmost use of alcohol as a nutrient it must be taken in small quantities and frequently. There seems to be a general agreement that from 50 to 75 grams of alcohol in twenty-four hours is about as much as can be allowed to an adult without untoward reactions. If we assume the larger amount to be permissible, it follows that alcohol may furnish as much as

500 calories, or about one-fifth of the day's total. The requirement may be translated into terms of various beverages: whisky, something less than ½ pint; sherry or port, 1 pint; champagne, 1 quart; beer, 3 quarts.

Meltzer has said that "alcohol in health is mostly a curse and in sickness mostly a blessing." Its peculiar merits in illness are connected with the fact of its appetizing character and with the circumstance that it requires no digestion. In this it resembles glucose. When alcohol is given to a patient no call is made upon the digestive glands. Hence it may be tolerated and absorbed when most foods would remain undigested. So far as it can be introduced into the circulation at such a time it becomes a source of heat and spares the dwindling stores of the system, but there is an obvious tendency on the part of physicians to restrict the use of alcohol in sickness. Statistics from representative hospitals show a marked shrinkage in the consumption of liquors during the last few years.

Alcohol as a Drug.—Certain properties of alcohol may be conveniently brought under this head, although no sharp line of demarcation can be drawn between these qualities and others to be dealt with later. The drug effect is obtainable from rather large single doses in contrast to the nutritive effect which was said above to be best secured by small amounts given at intervals. The most striking reaction of the system to alcohol in doses which may be regarded as having the drug effect is manifested by the circulatory apparatus. The taking of a glass or two of wine, especially on an empty stomach, will usually cause increased heart action and a flushing of the skin, accompanied by the subjective impression of warmth. This bringing of more blood to the surface of the body may be expected to lessen the volume of blood passing through the internal organs.

The chief value of alcohol as a drug is connected with this tendency to abate internal congestions. The central fact in the process which we call "taking cold" is an excess of blood in the mucous membranes. This may be continued for a time without ill consequences, but is always a

menacing condition, lowering the local resistance to infection and so inviting disease. Alcohol has been much used to "break up" incipient colds and with very good success. Its influence upon the distribution of the blood is not unlike that of quinin and some other drugs; it is also similar to the action of hot applications to the skin.

The supposed warming power of alcohol needs critical examination. It is a fact not generally recognized that we have no reliable sensations indicative of the true body temperature. We realize only the surface conditions. If a thermos flask and an ordinary bottle are both filled with hot water we know that the second will be much warmer to the touch. But this is precisely because *it is losing heat.* A man who is out in the cold may produce a sense of comfort by taking alcohol, which will send more blood into the cutaneous vessels, but this pleasant glow is the sign that heat is passing from the body to its surroundings. It may be purchased at the cost of an expenditure which is imprudent. Arctic explorers seem well agreed that dependence on alcohol during exposure to intense cold is unwise, and that it is better to suffer a greater degree of discomfort than to rely upon its delusive support. This must be most distinctly the case when the hardships are to be borne for an indefinite period. It is more rational to give alcohol after exposure to wet and cold than during the trial. Afterward it may help to readjust the circulation and to ward off possible evil results.

Alcohol as a Cerebral Alterative.—After all, the main reason why humanity clings to alcohol and is with so much difficulty won over to abstinence, is found in its singular influence upon temperament. This is at the root of its social employment. The rather awkward term, "cerebral alterative," has been chosen to avoid the more familiar but questionable name of stimulant. Much discussion has been carried on concerning the right of alcohol to this designation. Stimulant and narcotic are opposing terms. Alcohol in large quantities is clearly a narcotic; whether it is invariably so is a subject of lively

debate. It might be supposed that there would be no difficulty in deciding. Observation of men slightly affected by wine shows them to be animated and talkative; the natural verdict would be that they exemplify stimulation. Yet all the results of taking alcohol can be explained upon the theory that it is a narcotic. To show how this may be it is only necessary to point out that many operations of the nervous system are normally inhibitory in nature. When a reticent man becomes garrulous, it need not be inferred that he is stimulated in the best sense of the word; it may be more accurate to say that an agent which is essentially depressing in its influence has attacked first of all the inhibitory centers. Loss of self-consciousness is an obvious feature of the reaction, and loss of self-respect is reached by an easy transition.

A genuine stimulant should be an aid to application. Alcohol, on the contrary, is hostile to perseverance. Our word dissipation, which we use for intemperance, is a very suggestive one. Scattering rather than concentration is the essence of the mental state produced. A keen thinker has said that we tacitly contrast alcohol with coffee, a recognized stimulant, when we acknowledge the difference between the feelings with which we should view the use of one and the other by the engineer of a limited train. We instinctively feel that coffee will favor his unswerving attention to duty and that alcohol will make him less reliable. Alcohol in small quantities leads to inconsequence in thinking and is a handicap to any steady pursuit. On the other hand, the facile changes in the currents of mental life, the lightness and the unexpectedness of one's remarks, may promote social ease and the power to be entertaining. If alcohol is the foe of application it is also the foe of prosiness.

Too much emphasis can scarcely be brought to bear on the wide disparity between what a man thinks that alcohol does for him and what an impartial study shows that it really does. That "wine is a mocker" is a shrewd observation. The subjective impression is often of an ex-

altation of capacity which objective testing fails utterly to confirm. A subject does certain problems before taking a drink of whisky and comparable ones afterward. He says that the second task was done with greater speed and with a nonchalant confidence in his results. The watch says that he was slower, and checking up the work shows that the errors were more numerous. It is evident that his judgment of his own performances is unreliable. This is true also of manual operations. The recent tests made upon German type-setters have shown that speed and accuracy are both made to suffer when alcohol has been taken even in very limited amounts. Here, again, the subjects have an impression of their own superior accomplishment under alcohol, which turns out to be erroneous. More disastrous in its consequences is the fatuous assurance of the intoxicated chauffeur.

It has been freely admitted above that a little alcohol may promote sociability, but there can be no question that the reputation which alcohol possesses of bringing out the best wit and humor of which men are capable is largely unfounded. The reason is not far to seek. This reputation rests on the reports of men who were themselves influenced by the same agent which was working upon the nervous systems of the speakers to whom they were listening. Their reminiscences are to be taken with more than a grain of salt. The auditor who is "vinously exalted"—to use a phrase of Holmes—is an exceedingly lenient critic. He applauds with delight sallies which a neighbor, who has turned down his glass, perceives to be inane, if not in bad taste.

The justification of the social use of alcohol must be based on its power to produce this singular state of mind. It removes the consciousness of fatigue and the feeling of care. The attention is limited to the present moment and immediate interests. The faculty of discrimination is dulled, and with the consequent lowering of esthetic and intellectual ideals there comes a bland self-satisfaction and a naïve admiration of one's fellows. A vigorous

writer has called this process "drugging for delectation." Can such an artifice be defended? It is most difficult to answer this question with entire justice to both sides. Perhaps it may be impossible to answer it in sweeping fashion for all men. One who is cynical and pessimistic by nature may really view his affairs more justly and judge his neighbors more equitably while under the influence of wine. This may be true of other temperaments, the neurasthenic, for instance. But the optimist—and may we not say the normal individual?—is not likely to be bettered by such an agent. Increased buoyancy and good humor in such subjects means silliness. If it is true, as is claimed, that gatherings of total abstainers are comparatively doleful, the lesson may be, not that alcohol is necessary to good fellowship, but rather that the average nervous system is below par. We doubt whether a man ought to rest content with any lower measure of health than that which will insure the social virtues without chemical aid.

With advancing age it may be unreasonable to demand so high a standard. As infirmities increase there must usually come a time when comfort rather than efficiency is to be sought. When it is clear that this time has arrived there is much to be said in favor of the more or less regular, moderate use of alcohol. It is a great anodyne. Granting this, we may also point out that the beneficent effect in age will be more surely obtained by those who have not exhausted the consolations of alcohol in earlier years.

Alcohol as a Poison.—It seems hardly necessary to enlarge upon the poisonous properties of alcohol. That these have been ridiculously exaggerated is obvious; that they are very real is equally clear. The spectacle of drunkenness and the shame and misery that attend it are too familiar. No one who begins to use alcohol can be quite sure that he will continue within bounds. The temperate lives of his relatives cannot be held to prove him secure. Susceptibility to the tendency to increase the indulgence is found again and again in young men of clean heredity and fine

gifts. Alcohol constantly opens the way to sexual license. It is the justification of such books as "The Plastic Age" that they enforce this brutal fact. Many a collegian will testify that it is only when moral and esthetic standards have been perverted by drink that a prostitute appears otherwise than repulsive to him. The only absolute safety is in total abstinence. Yet the chances do not favor the ruin of the average man who adds alcohol to his diet.

Aside from the habit-forming property, it is becoming more and more widely recognized that alcohol often impairs the health of men who cannot be charged with intemperance. It predisposes to diseases of the heart, liver, and kidneys. It notoriously lessens the chance of survival when the user contracts pneumonia. It makes him an unfavorable subject for surgical operations. By hastening the development of arteriosclerosis it shortens the period of active and effective life. Insurance examiners are glad when they can record of an applicant that he is a total abstainer.[1]

We often hear people say that it is "bad" liquor that is harmful. This is often said where the reference is to the non-descript, illicit beverages sold where prohibition is supposed to obtain. There may be some ground for the claim that cheap and crude liquors are worse than those that are more choice. But the impression probably rests chiefly upon the sort of men who use the two kinds. Expensive and delicate liquors are taken by men of discrimination, who usually exercise self-control. The prime object is not intoxication. Open a wine-cellar to the reprobate who drinks anything he can buy or beg, and he will soon be as abject as though he were limited to his usual sources of supply.

The arguments advanced for prohibition on economic grounds have considerable weight and especially in time of war. The amount of grain diverted to the manufacture of liquor is absolutely large. But the brewers and distillers show that it is small compared with the total of the cereal crops and they make much of the value of their by-products

[1] Series of articles by Fisk in The Atlantic Monthly, 1916, 1917.

for feeding stock. There are better reasons than the economic for encouraging abstinence in a national emergency. At such a time we should forego entertainment if the sacrifice makes us more efficient. If hardship is involved it is such as rightminded people should rejoice to accept. What more stimulating assurance could be given to our soldiers than the knowledge that the civil population had cheerfully submitted to a restriction required of the men in khaki?

Enough has been said to show how various are the aspects of alcohol. It has been easy to treat them separately in the preceding paragraphs, but no such separation is possible in practice. The undoubted value of the alcoholic relish, its occasional merit as a significant part of the ration, and even its virtue as a drug cannot be utilized without some experience of its cerebral effect and the risk, not always remote, of forming a habit. The hygienic ideal to be striven for is a robustness of life which shall make alcohol superfluous as relish, food, or drug, and a cheerful, active mind which needs no artificial aid to keep it hopeful and sympathetic. The attainment may not be an easy task. Grief and worry and overwork may be added to an original depression of temperament, but the use of alcohol is never more unsafe than when sorrows are the excuse, and never so selfish and cowardly as when the motive is to shun responsibilities that ought to be faced. Men do not often see the sinister suggestion in the high spirits of one who has forgotten his cares for an evening by the most moderate indulgence. They fail to see that the banishment of the sense of pressing duties is the very characteristic of the drunkard when, developed to a logical extreme, it makes him indifferent to every obligation of conscience and of love.

The man who has never come to set a high value upon alcohol must stand amazed at the resistance now exerted against the enforcement of prohibition. Every voter has sworn to support the Constitution of the United States.

Every federal officer has assumed additional and solemn obligations to do so. Yet responsible citizens, with an air of pride rather than shame, involve themselves in perjury and come near to treason. We learn of officials corrupted, we read tales of hardships endured by the purveyors of liquor, men whose physical fortitude and resourcefulness would be admirable in a legitimate pursuit. There is one obvious conclusion: the desire to drink is so strong that for multitudes it overrides all moral restraint. Expressed in terms of money it is productive of the vast funds constantly available to suborn the guardians of the frontier and to compensate the hierarchy of the bootleggers for all risks and losses.

This is not primarily an ethical treatment of the subject. But the existing conditions seem to the writer to place alcohol in a worse light than ever before. The urgency of the demand is startling to imagine. Consider that the taste is an acquired one. The youth given liquor for the first time does not sincerely say, "This is something I have always needed," but rather, "This is not nearly so good as I was led to expect." If the generation of drinkers could pass without making disciples of the young it is hard to believe that there would be any further desire for alcoholic beverages.

Reference: "Alcohol: Its Action on the Human Organism," by a committee of British men of science, Longmans, New York, 1918.

CHAPTER XXVI

INTERNAL SECRETION

In an early chapter of this book it was stated that there are two ways in which one organ of the body may exert an influence upon another. The more familiar and more studied method has been through the nervous connections which are maintained between all organs and the brain and cord. The existence of such ties provides for the possibility of reflex action. By this means any part of the organism may modify the behavior of any other part, not by affecting it directly, but by stimulating or inhibiting the centers which preside over the second organ. Some account of the work of the central nervous system is to be given hereafter. Before this is undertaken it is well to pay some attention to the other way in which co-ordination is promoted; namely, by the transfer of chemical products from place to place through the agency of the circulation.

This is the subject usually covered by the term internal secretion. The word hormone[1] has been used elsewhere to denote an active substance generated in one place, but destined to take effect in another. The secretin produced in the walls of the upper part of the small intestine and carried thence to the pancreas and the other digestive glands to excite them to pour out their juices is an example. So also is the contribution made by the pancreas to the blood, which proves to be so important to the utilization of sugar. In this case it seems to be chiefly in the muscles that the hormone is valuable. Other instances of similar

[1] The root-meaning of hormone is "an excitant." It has been urged by Shaefer, "The Endocrine Organs," Longmans, New York, 1916, that internal secretions may be depressants as well as stimulating agents. He proposes to call those which are inhibitory "chalones." The term is not yet in general use.

interaction can now be given, and there is reason to anticipate that the list of internal secretions will soon be made longer than it is at present.

There are several organs once regarded as insignificant which are now recognized as vital to the welfare of the whole system. Among these the *thyroid gland* has attracted particular interest. This is a small bilobed mass of tissue situated in front of the trachea below the larynx. It is one of several organs sometimes called ductless glands. The term is more appropriate in this case than in some others, since the microscope shows that the arrangement of the cells is distinctly glandular. They surround small recesses such as in typical glands would be in communication with an outlet or duct. Here, however, these cavities are blind. They are seen to contain a viscid material, the so-called colloid substance, which is evidently the product of the secreting cells. Since there is no channel leading to the exterior, the only possibility is that the distinctive secretion shall enter the circulation either directly or by way of the lymph.

The thyroid gland is frequently enlarged and then gives rise to the disfiguring swelling known as a goiter. Such enlargements are not necessarily attended with general disturbances of health, yet in many cases there are symptoms which can be referred to an excess of the active product. Palpitation, breathlessness, extreme nervousness, and marked loss of weight are likely to be observed. As noted earlier (p. 207) the metabolism is accelerated in a characteristic way perhaps by 50 or even 100 per cent. The same manifestations follow the giving of overdoses of thyroid extract. This has been employed for the correction of obesity, but it seems unwise to resort to a drug so powerful and far reaching in its action for the treatment of this condition.

Just as there may be too much of the thyroid material for the good of the subject, so there may be a serious deficiency. The relative failure of the gland to function as it should is the cause of a definite disease in human sub-

jects, and its removal from dogs is followed by a decline if not by death. Young and growing animals are most seriously affected. All the facts which have been gathered support the belief that development and general well-being depend to a considerable extent on the normal functioning of the thyroid. Very recently it has been shown that what has been called the thyroid is, in reality, a compound structure. In addition to the type of tissue which forms the main mass of the organ in man, there are four nodules of a different sort, the parathyroids. These undoubtedly have a chemistry of their own and a distinctive relation to the economy of the body. There is evidence that they influence the concentration of calcium in the blood. Extracts prepared from them increase the amount of this element in circulation. After their removal it is decidedly lowered and severe convulsions may be induced.

The full measure of the influence which radiates from the thyroid can be appreciated by considering the condition known as cretinism. This is the term used to describe the state of individuals in whom the thyroid has never performed its proper work. These subjects remain for years in a condition of arrested progress, both physical and mental. They are uncouth dwarfs with large heads, slack-walled abdomens, and feeble limbs. If they survive to the age of twenty or thirty, they will scarcely have advanced beyond the stage reached at four or five. That the lack of the thyroid is actually responsible for these shocking cases is now abundantly proved. The demonstration is found in the happy circumstance that great improvement follows the judicious feeding of thyroid preparations to cretins. The material is obtained from calves or sheep. Its administration for a few months often results in transforming a repulsive cretin into a presentable child, with a prospect of at least a moderate mental development. The actual internal secretion of the thyroid is probably represented by a definite chemical compound

lately prepared in high purity and called *thyroxin*. It contains iodin.[1]

In the dog it is possible to graft an extra thyroid into the abdominal cavity and then to remove the original gland, when the second organ will assume the functions necessary to the preservation of health. This was an important discovery, since it removed the ground for a prevalent opinion that the service of the thyroid was limited to the reflexes which it was supposed to originate. It had been thought that the gland affected the nutrition and general health by sending impulses along the nerves leading from it to the centers. A gland substituted for the native one and placed in a remote part of the body could not be in connection with the old afferent pathways, and whatever favorable effect it might have must be chemical in its origin.

There has been the same discussion as to whether the *reproductive organs* exercise their well-recognized influence on growth by nervous or by chemical means. The strange modifications of the type which are produced as a result of castration are familiar. The differences in build and temperament between the unruly bull and the tranquil ox illustrate the consequences. Such peculiarities might be referred to reflex changes due to the removal of sources of stimuli, but the present tendency is to regard them as due chiefly to the loss of active internal secretions. The case of the pancreas reminds us that an organ may well give rise simultaneously to products which are permanently separated from the blood and to others which return to it. In 1889 Brown-Séquard created a furore among people given to premature acceptance of extravagant claims when he announced that great rejuvenating virtues could be demonstrated to exist in the extracts of animal reproductive glands. His so-called "Elixir of Life" was a pulp formed from crushed testes of sheep. At some peril of infection he injected this unsterilized mixture under his skin and into the bodies of other aged volunteers. A cer-

[1] See p. 256.

tain degree of stimulation was noted, but it has usually been referred to suggestion.

Since animals and men are at their best physically and intellectually when the reproductive organs are active, the expectation entertained was not wholly unreasonable. Yet it was not to be supposed that their decline was responsible for all the losses incident to age. No extensive use of such extracts has followed the pioneer work of Brown-Séquard. But the principle has become familiar of late in connection with the grafting of testicles—the "interstitial glands" of the daily press. Preparations from the female—ovarian extracts—have a good standing in modern medicine. Given after surgical removal of the ovaries they greatly relieve many of the symptoms which commonly annoy the patient. During the progress of pregnancy we witness the most marvellous adjustment of various parts of the body to meet new requirements. The changes in the uterus, the mammary glands, etc., seem to be due to the influence of hormones disseminated by the ovaries and the embryo itself.

The *adrenal bodies* are also numbered among the organs which help to maintain the system in normal working order. These are two inconspicuous structures placed one above each kidney. Two types of tissue are present, a superficial *cortex* and an internal *medulla*. From the latter can be obtained a powerful drug-like compound, adrenin, which the living cells of these organs may be supposed to deliver under a regulating influence from the central nervous system. Destruction of the adrenals—which sometimes results from local tuberculosis—produces the singular fatal disturbance known as "Addison's bronze disease." An odd feature of this condition is the dark pigmentation of the skin, occurring sometimes uniformly and sometimes in patches. More important, however, is the steady loss of vigor affecting all the contractile tissues and leading to death. The lack of the cortex appears to be responsible for the fatal issue. Cortical extracts may greatly prolong the survival of animals from which the adrenals have been removed.

Adrenin injected into the blood-stream of an animal shows its most marked effect in the intense contraction of the small blood-vessels which is produced. This property has made the substance valuable to surgeons, since it can be used to check bleeding from cut surfaces. In like manner it can reduce congestion in inflamed tissues, for example, in a blood-shot eye. These artificial uses of adrenin can all be connected with its natural service, which is largely in the direction of a reinforcement of contractility. Cannon has recently called attention to this fact in an unexpected and interesting relation.

He has proved by delicate tests that the blood of an animal receives additional adrenin during a terrifying experience. For example, he has found the active compound increased in the blood of a cat which has been kept under restraint in the presence of a barking dog. Therefore it must be concluded that one of the many bodily accompaniments of an emotional outbreak is a stimulation of the adrenal bodies to unusual activity. The value of this reaction has just been made clear through the further researches of the same investigator. It appears that extra resistance to fatigue is conferred upon the skeletal muscles when adrenin is sent to them. The heart is stimulated, the blood is directed to the muscles rather than the viscera, and extra sugar appears in the circulation. Thus, in an emergency that might call either for flight or conflict the animal is prepared for a maximum output of energy. We have here a scientific conception of the "strength of desperation."[1]

The influence of other organs than those mentioned upon the welfare of the organism as a whole is constantly being studied. A great deal of attention is being given to the very small but distinctly compound structure, called the *hypophysis*, which is lodged beneath the brain in a hollow of one of the cranial bones. Its relation to the course of the metabolism is far from simple, but it seems to be clear that

[1] Cannon, "Bodily Changes in Pain, Hunger, Fear, and Rage," Appleton, New York, 1929.

it is an indispensable contributor to the circulating medium. Certain abnormalities of the hypophysis may be responsible for overgrowth even to gigantic stature. Opposite conditions may restrain growth and be responsible for the state of some dwarfs. Perverted action of this organ in the adult may strangely alter the features through changing the shape of the bones of the face. It is the anterior part or lobe of the hypophysis which maintains these relations with processes of development. The secretions of the posterior lobe appear to regulate the activities of smooth muscle and to modify the water-losses of the body.

Much larger and more conspicuous is the *thymus* of young animals, a mass of cells lying back of the breast-bone. It is the "neck-sweetbread" of the market. Since it is prominent during growth the inference is natural that it ministers in some way to the process of development. It almost vanishes at maturity. It is not yet possible to make very definite statements about the thymus. Removal does not seriously hinder the progress of the growing animal.

Here and there in the body are firm kernels of tissue, spoken of as lymphatic glands or, better, as *lymph-nodes*. These may be discussed among the producers of internal secretion, though it is probable that this description does not cover all their activities. They are found especially in the neck, the armpits, the groins, and in the mesentery. Wherever placed, each is set upon the route of the lymph as it comes from some region toward the chest. Thus the lymph-nodes of the neck must be passed by the lymph that has had its origin in the head, while those of the mesentery intercept that which has come from the intestine. Microscopic study shows that the lymph has to take a tortuous course among the cells of the nodes. Looked at from a mechanical standpoint these bodies are obstructions in the path. They are also suggestive of filters. Their own cells are continually becoming detached and drifting away in the lymph, a phenomenon which is a

type of internal secretion made visible. They are believed to add substances in solution as well as cells to the passing fluid.

There is good ground for the view that the lymph-nodes are a defense against the spread of infection. When a boil exists upon the arm the nodes above the place where the bacteria are working so destructively are usually observed to be enlarged and tender. The lymph which is returning from the seat of the trouble is bearing the products of the suppuration, if not the infecting organisms themselves. Apparently this polluted lymph is more or less successfully disinfected before it is allowed to pass on into the thorax to merge with the blood in the veins. The lymph-nodes of the mesentery stand as outworks of the bodily fortifications against entrance of microbic invaders from the intestine. When overpowered in their struggle, the lymphatic glands themselves become foci of infection, as in the familiar form of tuberculosis known as scrofula.

One large organ, which from its anatomic relations has been called a ductless gland and which might be expected to have an internal secretion, has failed to give satisfactory evidence of such a function. This is the spleen, which is placed below the diaphragm to the left of the stomach. It was long an enigma to physiologists. Its blood-supply is large, and its frequent changes of volume, contractions and dilations alternating in a slow rhythm, give a strong suggestion of some well-marked action in progress. It seems now to be established that the spleen is a storehouse for red blood-corpuscles, holding a considerable mass of these oxygen carriers in reserve for emergencies. Certain enzymes have been extracted from the tissue of the spleen which may have to do with the metabolism of those peculiar proteins which yield uric acid.

In a few cases of anemia improvement has followed removal of the spleen. The suggestion is that the organ normally destroys red corpuscles and that the extent of this destruction may become excessive. The benefit following such operations has usually been transient.

CHAPTER XXVII

THE NERVOUS SYSTEM

In the introductory chapter it was said in substance that the one word which most nearly covers the work of the nervous system is the word co-ordination. This statement arouses in one the impulse to protest that it leaves out of account the relations subsisting between the nervous system and the states of consciousness which are of the most immediate interest to us all. The physiologist, being human, sympathizes with such a protest, but he must continue to treat his material for the most part from an external point of observation. This is not for want of respect for the psychologic method; it is rather with frank recognition of the vastness of the realm in which that method is applicable. It is because he must defer to experts in that field that he will not enter upon it as an amateur.

Most readers need to be told with the utmost emphasis and with frequent reiteration that consciousness is the accompaniment of an excessively small share of the manifold reactions of the nervous system. In the words of President Hall, it is "a little candle burning in one room of the mind's museum." All that occurs from first to last in the life history of a fish or a frog can be explained as reflex adjustment, without the assumption of self-knowledge or conscious purpose on the part of the animal. That was a weird and fascinating picture which duBois Reymond once drew of a world precisely like our own, save that its inhabitants were unconscious. In such a world an artist without will or pleasure in his work might create a faultless statue because his inherited nervous mechanism and the

existence of materials, tools, and a model, made the result inevitable.

In the previous discussion of reflex action (Chapter V) the conception was developed that the nervous system consists of pathways capable of transmitting energy in the form of "nerve-impulses" to and from its central portion. That central part is represented in the higher forms by the brain and the spinal cord. The afferent or incoming paths begin in localities where external influences or stimuli can be brought to bear. The nerve-endings which lie thus exposed are called "receptors." They may be simple terminal twigs or bulbs subject to stimulation by pressure or temperature. They may be connected with elaborate organs like the eye and the ear. The eye is a device for converting the energy of certain ether-waves into the impulses that traverse the optic nerve. The ear is, at least in part, a device for transforming the energy of certain air-waves into impulses that run along the auditory nerve.

The impulses which arrive within the brain or the cord may cause the immediate or delayed return flow of impulses along the efferent or centrifugal paths of the system. These lead in most cases to the contractile tissues which give objective expression to animal life. It must not be forgotten that the efferent branches of the nervous system extend also to various glands and may modify secretion as well as contraction. It will be recalled that efferent impulses may initiate the flow of tears, of the saliva, the gastric juice, and the adrenal principle. Other instances are almost equally clear.

In animals of all grades responses of the reflex type are the constant duty of the nervous equipment. Those forms which we regard as highest in the scale are distinguished by a second property, that of the modification of the responses as a result of individual experience. By this is meant the capacity for training, forming habits, or learning to profit by the past. It is what makes different members of the same species vary in their behavior. It is what

makes an older member superior to a younger one in his powers of adjustment and maintenance. This is, of course, exemplified in the fullest degree by human beings. The prolonged period of growth and progress must indicate a plasticity in the arrangements of the nervous elements that is hardly ever entirely outlived.

Descartes in the seventeenth century grasped the two properties with his usual keenness. He pictured the reflex process with quaint symbolism, but with essential correctness. He likened a path of afferent transmission to a cord that is pulled. A valve is opened in the central organ and a fluid released to flow back along the nerve. Reaching a group of muscles this fluid wakes them to action. Descartes had used different analogies for the afferent and the efferent impulses, making one a mechanical twitch and the other a spurt of liquid; we now believe them to be nearly or quite identical in character. The same writer recognized the ability of the higher nervous systems to retain impressions, and likened the registration of a memory to the imprint of a seal upon wax.

Physiologically, the particular mark of the highly developed nervous axis is this capacity for recording individual and not merely racial experience. Anatomically, the advance in organization is signalized by an increasing predominance of the brain over the cord and of the "fore-brain" over the parts behind. A frog will carry out many complex reactions when the entire brain has been destroyed. That is to say that in the frog the cord is adequate for a great deal of reflex action. In a human paralytic whose injury has removed the lower half of the spinal cord from functional union with the brain, the reflexes which can be obtained from the lower extremities are few. In other words, the cord in man has become less important as an organ for correlating afferent with efferent impulses and more important as the largest of all nerves, the highway to and from the brain. We shall now set forth in some detail certain of the adaptive changes which are constantly occurring through the mediation of

the brain quite apart from attention or desire on the part of the subject.

This kind of subconscious control of organs is well illustrated in the case of the respiratory center. About a hundred years ago it was found by French workers that cutting across the nervous axis at the point where it leaves the skull—that is, where the brain passes into the cord—instantly stops the breathing. A similar cut a little higher up does not have this immediately fatal effect. It was inferred that the part of the brain next adjoining the cord must contain the special cells which stand in charge of the respiratory muscles. This section of the brain, just within the skull, is called the medulla. Later experiments have confirmed the early belief that the breathing is governed from this region. The muscles employed are not in themselves automatic. Every contraction which they make is referable to a metabolic change in the cells of the medulla. So there is a fundamental difference between the breathing movements and the beating of the heart. The former are due to central causes; the latter, to an innate quality of the contractile substance.

The respiratory center is frequently involved in reflex action. In fact, it is easy to convince one's self that hardly any considerable reflex occurs without some disturbance of the breathing as an incident. Any sort of shock will infallibly change the depth, regularity, or some other feature of the movements. Outcries following such shocks are merely respiratory reflexes, but the center is not prompted to each successive discharge by afferent impulses; it shows us the possibility of another means of regulation. This is through the influence upon the nerve-cells of the chemical composition of the blood and lymph in the vicinity. When exercise is taken the breathing is involuntarily deepened. The cause of this adjustment is found in the increase of carbon dioxid in the circulation. The center is remarkably sensitive to any rise in the percentage of this gas. Conversely, it is temporarily paralyzed by a reduction of the circulating carbon dioxid to an unusually

low level. Variations of the oxygen of the blood, unless extreme, affect its action surprisingly little.

An important work of the nervous system and one which is quite overlooked by the layman consists in the regulation of blood-flow. In our previous description of the plan of the circulation only its mechanical principles were discussed: the heart was spoken of as a force-pump and the vessels as elastic tubes. This is a proper presentation so far as it goes, but we must now proceed to show that the whole circulatory apparatus is living, and being so has the biologic characteristic of adaptation. The changes by which the ever-varying requirements of the body are met are of two kinds, changes in the force and frequency of the heart-beat and changes in the caliber of the small arteries and veins. The former are brought about by the *cardiac nerves;* the latter, by a department of the nervous mechanism which we call the *vasomotor system.*

It is a matter of familiar experience that the heart-rate is subject to striking variations. From an average of perhaps 65 per minute, when one is lying in comfortable relaxation, it can be driven to 150 or more, when one is hurrying up a grade. Such a change under the influence of muscular activity is evidently purposeful. The working tissues need a swifter current of blood to supply them with oxygen and to bear away their waste. The lungs must be visited at shorter intervals to keep normal the gaseous composition of the blood. Muscular activity is not to be supported by increased breathing alone; it is equally necessary that there shall be acceleration of the circulation. As the quick, deep breathing of one who is taking exercise bespeaks a governing center for the muscles employed, so the rapid beating of his heart suggests a central control of that organ.

Experimental proof of the central regulation of the heart is ample and detailed. Branches of the nervous system reach it from two distinct sources and are contrasted in their effect upon it. One set of fibers is said to be inhibitory, the other to have an accelerator action. The terms

would seem to explain themselves. The inhibitory fibers restrain the heart much of the time from beating at the rate which it would exhibit if nervous regulation were entirely withdrawn. An exaggerated inhibitory influence may weaken its working to the point where the circulation becomes quite inadequate and faintness is produced. In laboratory trials actual arrest of the heart of a dog may be caused, though the beat is always resumed within a minute, so that death cannot be made to result. We ought not to lay much stress upon these extreme possibilities. It would be absurd to say that the function of the inhibitory cardiac nerves is to stop the heart; that could never be for the best good of the animal. We can say with more reason that their service is to economize the strength of the heart and to provide a reserve for emergencies. This has been described as a "brake action."

The accelerator nerves of the heart have a stimulating effect which extends to the vigor as well as to the rate of its beating. When we observe a specific increase of heart action we can hardly say whether it has been produced by positive accelerator influence or by the abatement of the habitual inhibitory control. It may, of course, represent the combined result of both. The government of organs by means of the balanced action of two opposing sets of nerves is repeatedly met with in the body. It can be demonstrated for the stomach and for other sections of the alimentary canal. A singular example is afforded by the nervous relations of the iris, the colored ring surrounding the black pupil of the eye. Stimulation of one nerve causes contraction of the pupil, while widening or dilatation follows the application of stimuli to an entirely different strand of fibers.

The heart may quicken the circulation by beating at a more rapid rate and with increased power, but it cannot send the blood to a particular part of the body at the expense of another part. The total blood-flow thus depends upon the heart acting under the balanced sway of inhibitory and accelerator nerves, but the distribution of blood,

the favoring of organs which need it, is the work of the vasomotor system. The walls of the microscopic vessels, those which adjoin the capillaries in particular, are provided with muscular elements of the same general order as those which produce the movements of the digestive tract. These contractile elements are connected with the terminal branches of certain nerves. Hence the anatomic study of the tissues involved, even when unsupported by physiologic experiments, makes clear the possibility that the centers when acting reflexly or otherwise may influence the diameter of the blood-vessels and the volume of the circulation in any or all regions of the body.

Physiology reinforces anatomy at this point. For sixty years it has been certainly known that nervous regulation of the blood-flow is a fact. Much earlier than this the power was assumed to exist, "Ubi stimulus, ibi affluxus," they said, meaning that where there is activity there is an increase of blood. The paling and the flushing of the skin, occurring either in response to external changes of temperature or emotional conditions, are strongly suggestive of a central command of the vessels. This has been taken for granted in our own treatment of the matter of the maintenance of a normal body temperature. Much as the heart is reached by impulses which inhibit it and by others which spur it to a greater expenditure of energy, the small arteries and veins are subject to antagonistic influences. We speak of a vasoconstrictor effect when we mean a reinforcement of the existing tone, and we use the word vasodilator in the opposite sense, that is, to characterize changes in which the degree of contraction is lessened, with the result that the blood finds its way in greater quantity through the affected vessels.

The difference between the cardiac and the vasomotor factors in the control of the circulation can be made plain by means of an illustration borrowed from the laundry. Suppose that a supply-pipe runs along above a row of tubs and bears a faucet for each. Suppose, also, that there is a stop-cock on the pipe before it reaches the tubs. Fi-

nally, to make the correspondence closer, assume that the faucets can never be shut tight (for it is not likely that the blood-vessels can be). Now, by manipulating the cock (*H*) we can increase or diminish the outflow into all the tubs, but we cannot in this way hasten the filling of one more than another. This is obviously the type of cardiac regulation in the living system. The heart is appealed to

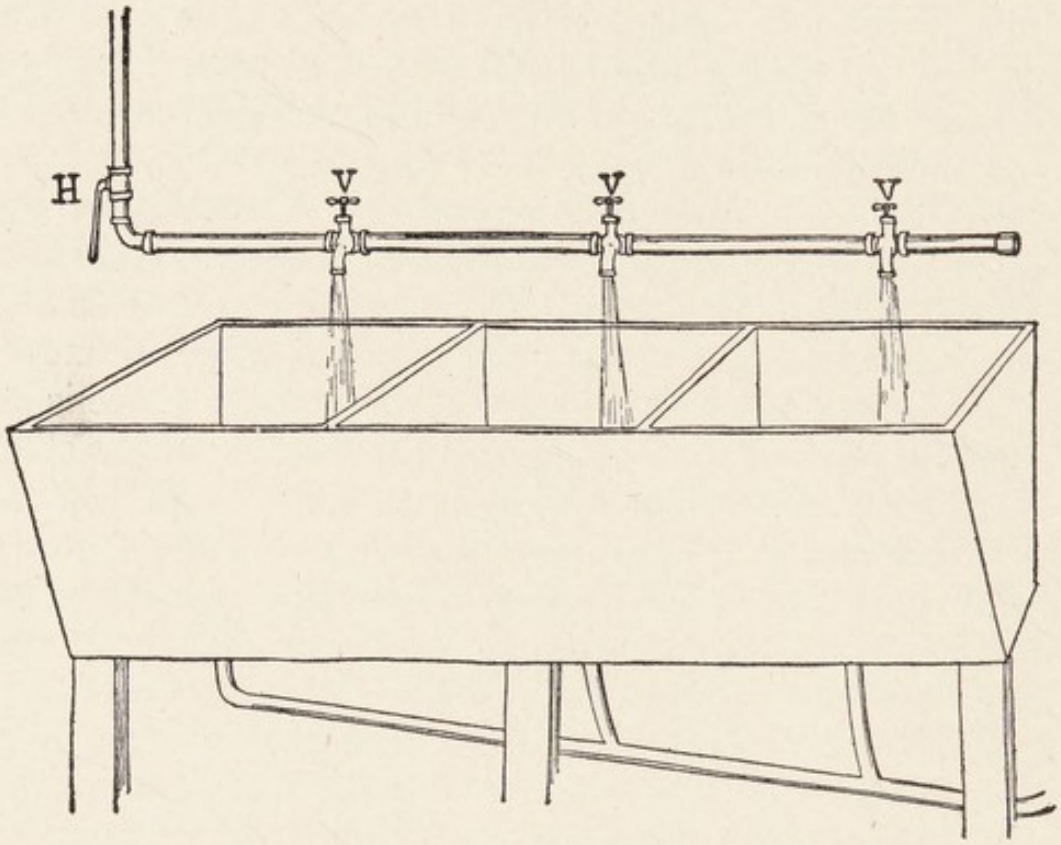


Fig. 23.—The supply to all the tubs is controlled at the "shut off" (*H*), while the share flowing into each compartment is regulated by its own faucet (*V*).

when there is a general and widespread demand for more blood per unit of time, muscular activity being by far the most important occasion.

The faucets over the several tubs are the symbols of vasomotor equipment. By using them we can change the share of the total stream which shall enter any compartment. If our only desire is to fill one tub, we can open widely that faucet and close the others as far as possible. The vasomotor system actually operates in that way to the

extent that a dilation in one large area seems often to be offset by a compensatory constriction in another. We count on this reciprocal relation in our medical and hygienic practice. For instance, we think that if we can encourage blood-flow at the surface we shall reduce it in the deeper parts. This is often an object, since congestions are important features of many disorders. We anticipate this balanced reaction when we make use of hot applications and when we give alcohol for a cold.

No one is likely to overestimate the services rendered by the vasomotor system. It has both a general and a local action. In the first sense it maintains a certain average state of contraction in the arteries—the arterial tone—which keeps up to a desirable level the pressure in the arterial trunks. It is this pressure which guarantees the prompt and sufficient supply of blood wherever the paths are opened. The principle is the same that is observed in the mains distributing water through the streets of a city. The pressure must be great enough to keep up the supply on the high ground as well as the low. Leakage or wasteful use of water will lower the pressure and the failure will be noted first on the hills. An unusual dilation of many blood-vessels, such as probably accompanies an attack of indigestion where the abdominal organs are engorged, may lessen the pressure and the volume of blood passing through the brain with the consequence that there is faintness. Partial relief is found in lying down because the factor of gravity is eliminated and the head given an equal chance with the rest of the body.

We notice the failure of the vasomotor system to do its duty in cases like the above. We ought also to appreciate how remarkable it is that the adjustments usually occur with such smoothness and success. It is really a wonderful thing that we can rear up the elongated human form from a horizontal to a vertical position without entirely deranging the circulatory mechanism. That the blood does not distend the vessels below the heart and forsake those above must be due in a great measure to vasomotor

correction. Doubtless, when one rises to his feet in the morning one is saved from falling in a faint by the promptness with which the arterial tone in the lower extremities and abdomen is raised by the nervous system to fight back the threatened excess of blood. It is easy to see what would happen in a lifeless model under similar conditions.

While our vasomotor reactions are usually executed without our conscious attention, it has always to be borne in mind that close ties exist between the higher and the lower regions of the nervous fabric. Emotions register themselves in changes of blood-flow. The obedience of the vasomotor center to hypnotic suggestion is almost unlimited. It would appear that this division of the nervous system is the chief mediator in the correction of the many ills which unquestionably yield to Christian Science and kindred ministrations. A normal circulation goes far to insure normal nutrition and irritability in each part, and these states are the fundamentals of health. Furthermore, the feeling of health—which is not always the same thing as the possession of health—must depend, in the absence of more positive sensations, on the character of the cerebral circulation. Assuming the blood to be chemically normal a moderate change in the amount passing through the brain may make all the difference between the sense of power and the feeling of utter helplessness.

Beside dictating the character of the breathing and determining the volume and distribution of the blood-flow, the lower part of the brain exercises control of the alimentary canal and, in varying degree, of the glands. To mention these facts is merely to recapitulate what has already been pointed out. It must be recalled that the government of the glands is partly through direct communication with their secreting cells and partly through vasomotor regulation of their blood-supply. In many cases of sustained glandular activity both features exist at the same time.

CHAPTER XXVIII

THE NERVOUS SYSTEM—ITS HIGHER WORK

"Our wills are ours, we know not how. . . ."

In the last chapter emphasis was constantly placed on the subconscious nature of the multifarious adjustments which are each moment secured through the action of the central nervous system. We are accustomed to think that the use of our sense-organs and the employment of our skeletal muscles are activities with which consciousness is far more closely concerned. While this is broadly true, we need to recognize that a great part of these reactions also goes on without our notice and beyond the reach of our intervention. This is readily admitted of the breathing. It will be found almost equally characteristic of the maintenance of the balance at rest and during locomotion.

The ability to stand is dependent on the occurrence of inconspicuous but indispensable reflexes which check each swaying movement of the body as it threatens a fall. When one walks the attention seems for the most part to be detached from the elaborate muscular performance and to be given to other matters. The contact of the feet with the ground, the gliding of one joint surface on another, the shifting of stresses from one muscle or tendon to a neighbor—these local changes become in a regular sequence the source of impulses which ascend to the brain and evoke appropriate responses. It has been generally believed that the division known as the cerebellum has a peculiar importance in this connection.

The position of the thinker himself with reference to the great afferent and efferent departments of his nervous

system may be likened to that of the general in command of a great army. From his headquarters he can see but a small proportion of his troops. Their line of battle stretches for miles beyond his sight. He issues the order for a general advance. His aides ride to the right and left, bearing the word to the commanders of corps and divisions. The simple act of the general has been followed by a train of events which becomes each moment more difficult to trace. The original order is transmitted to officers of lower rank and interpreted by them in conformity with local needs. When the private soldiers are at last put in motion it is at the word of colonels and captains. The impossibility of having the voice of the commander-in-chief the source of guidance in each company is perfectly evident. It is not merely that he is too far removed from most of his men, but that there are too many problems arising at one time. The minor ones must be solved at the discretion of his subordinates.

So in the living body the will to walk—which seems as simple as the dictation of the first order from headquarters—is promptly followed by the action of many nervous mechanisms whose function is to distribute impulses and to apply them in helpful sequence. We have no sense of the subdivision which is involved. We cannot analyze the groups of muscular movements which take place. Yet it is plain that there is an apportionment of stimulation, more to this muscle and less to that, without which the effective result could not be secured. How utterly we should fail in the attempt to regulate the part taken by each of a hundred co-operating muscles by giving attention to each in its turn! The efforts necessitated would be like those of the general deprived of his staff and messengers who should seek to ride swiftly from point to point in the endeavor to direct all his soldiers by his spoken word.

The comparison we have been using can be made to serve even further. We can find in it a place for the afferent side of nervous action. We have said that reflex elements can be found in almost any elaborate movement.

In walking, for example, the assumption of a given position by the body insures the return to the centers of impulses which cause the next appropriate change. We do not consciously resolve to take each step. The very idea is painful. One step accomplished makes the taking of another the natural sequel. Turning to our analogy, we readily see that when the grand advance is under way the continuance of the march will probably be intrusted to the direction of lower officers. Difficulties encountered they will report to the general if this seems necessary; minor obstacles they will meet upon their own responsibility. Thus when we walk we may be aware of gutters to be crossed, but we do not notice at all the incessant slight adjustments which are made for the lesser inequalities of the path.

The human brain contains at birth connections which make possible the execution of a moderate number of useful reflexes. Among these are sucking, winking, coughing, sneezing, and vomiting. Of course, there are also the requisite mechanisms for the government of breathing, the circulation, and the digestive tract. Such a brain appears to differ from that of one of the lower animals chiefly in its capacity for continued development. Loeb has shown that all that is acquired in the experiences which come to the child may be covered by the term "associative memory." The expression as used by him does not refer to the power to review past experience as a conscious process, but only to the power to acquire new reactions to environmental conditions. An early gain in this direction is the attainment of the ability to reach after and grasp an object which has stimulated the visual department of the nervous system. This seems to signify the opening of a pathway in the brain from the region receiving impulses from the retina to the region from which impulses go out to the muscles controlling the hand.

In similar fashion we can picture the acquirement of one accomplishment after another. All imitative action must be made possible by the establishment of bonds between

receiving and discharging stations in the surface gray matter of the cerebrum. As these connections are formed the conduct of the individual under given circumstances becomes predictable; in other words, we have here the physical basis of mannerisms and habits. It is even permissible to say that the foundations of character are defined in the direction which these association ties are found to take. All of education, so long as it is viewed from without and not from within, consists in the cultivation of response to varied influences. There can be no doubt that the anatomic accompaniment consists in the multiplication of brain pathways.

During the last hundred years the question has been much debated whether particular powers have definitely localized registration in the structure of the brain. In the first half of the nineteenth century the phrenologists attracted much favorable attention by their claims of very precise subdivision of the brain into "organs of different faculties." (Note the frequent references to these conceptions in "Jane Eyre.") The notion of "bumps" is still current, though it is usually referred to in a jocular spirit. The literature of phrenology is very large, and it is probable that it would repay a critical review, but the advocates of the cult went much farther than the facts warranted and their conceptions fell into disrepute. By 1850 the reaction had carried scientific opinion to the belief that there is little localization in the brain.

Since then a great many experimental studies, together with observations of the consequences of injuries suffered by human brains, have united to encourage the view that there is some degree of localization. The new doctrines have not followed the old traditions at all. Where the phrenologists sought to refer mental functions to particular regions of the brain surface, modern students have looked with more success for the central representation of bodily processes. They have shown that a certain area stands in definite relation with the skeletal muscles, that another area is the place for the reception of the visual impulses,

and so on. In most respects the human brain has been found to be organized in a manner closely corresponding with what is traceable in the brain of the ape and hinted at in the brain of the dog.

Yet the distinctive accomplishments in which man excels the lower animals must be coupled in some way with his cerebral equipment. One or two of these distinguishing features seem to have quite definite positions. This is especially clear in the case of the reputed "speech center." The belief is commonly held that the mechanisms which are correlated with such acquired powers as speech, reading, and writing are restricted to one-half of the brain, usually the left. The right hand, which in most subjects is so much superior in skill, is governed from the left side of the cerebrum. A charming account of the apparent relations between the human brain and human capacities is given in W. H. Thomson's "Brain and Personality." The claims made for precise localization in that book are regarded by many conservative writers as extreme. It is certainly fair to say that at present the most learned interpreters of brain physiology are placing emphasis on the development of paths between centers rather than on the organization of the centers themselves.[1]

The characteristic of early life is the ease and freedom with which these paths are opened and the comparative frequency with which they are changed. During the long period of mature efficiency they are less subject to multiplication and are used with increasing regularity and with rarer deviations. The man is becoming a creature of habit and acquiring "ruts." In old age, as has been finely said, the nervous system, instead of holding a prophecy of what may be, contains a record of the past. It is a fascinating fancy—though it is nothing more—that a physician of surpassing insight might look upon the warp and woof of fibers in a dead brain and tell us of the tastes,

[1] Reference: Berry, "Brain and Mind," Macmillan, New York, 1928.

talents, and pursuits of its former possessor. When we walk through the rooms of a deserted house we can tell by the worn places on the floors and thresholds and by the grimy edges of the doors just where the tenants came and went most often. The lifeless brain must bear a more subtle registry of the same order.

Afferent fibers reach the brain from all parts of the body. Many of these have had their origin within its tissues, where they are normally stimulated by conditions that belong to the organism itself rather than to its environment. The impulses that enter the brain from such sources are most of the time serving their purpose in promoting subconscious adaptive reflexes. When they affect consciousness it is to bring to the attention the so-called "general sensations"—those feelings which we refer to states of the organs. Such are hunger and thirst, many kinds of pain, satiety, nausea, faintness, fatigue, and the like. The majority of these general sensations seem to signify conditions that need to be rectified and they are mostly unpleasant.

Contrasted with these are the "special sensations," which are referred to causes acting upon the afferent apparatus from outside. Various terminal structures are developed at or near the surface of the body which serve to transmute different forms of environmental energy into nerve-impulses. Such structures are called sense organs or "receptors." A very suggestive distinction has been made between those receptors which are affected only by the literal contact of the stimulating substance, and the "distance-receptors," which respond to forms of energy radiating from places more or less remote. The nerve-endings in the skin which are acted upon by pressure and by temperature changes are of the first class. So are those in the tongue on which various dissolved substances take effect, giving the conscious subject sensations of taste. The olfactory endings high up in the nasal cavities are reckoned by most writers to belong to the same order.

The ear is a distance receptor. The energy which sets its intricate mechanism into vibration may have originated as far away as the thunder-cloud hanging near the horizon. The possession of an ear greatly extends the compass of the environment which can exert directing influences on the conduct of an animal. If this is true of the ear, how shall we estimate the widening of environment that comes with the addition to the receptor system of an eye! Our ability to see the stars means nothing less than this: that the reactions of the organism so endowed may be modified by energy proceeding from the incomprehensible distances of the stellar universe.

Throughout this book we have held steadily to the point of view defined in its very first paragraphs: that all living things are transformers of energy, and engaged so long as they live in reacting according to the principles of mechanics and chemistry in response to external changes. A presentation in this spirit provokes resentment and protest from many readers. It seems to leave out of account all that is instinctively held to be highest and finest in human life. To this remonstrance we are glad to give place. The scientist is, after all, a man, and no scientist was ever so ruthlessly logical as to convince himself that his friend was no more than a reflex mechanism. The impression that the study of science deprives one of the philosophic outlook and of the conviction of moral responsibility belongs to the earlier stages of the student's experience. Later it is seen that no incentive to right conduct and no worthy consolation is to be taken away.

A few years ago a brilliant astronomer—Percival Lowell—was concluding a course of lectures in which he had traced the long story of planetary evolution. He had pictured the ages of formative process, the slow condensation and cooling of the globe, the gradual approach to conditions suitable for organic life. He had sketched the brief flourishing of that life, the remorseless chilling of the planet, and its frigid and sterile old age. His hearers were

weighed down with the appalling sense of futility and insignificance. At the very last he asked abruptly: Which, after all, is the greater—these awful ranges of time and reaches of space, or the mind of man which comprehends and ponders them?

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