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HUMAN PHYSIOLOGY

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HUMAN PHYSIOLOGY

ESPECIALLY ADAPTED FOR
DENTAL STUDENTS

BY

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SECOND REVISED EDITION

FIFTY-NINE ILLUSTRATIONS, INCLUDING TEN COLOR PLATES

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PREFACE TO SECOND EDITION.

The gratifying reception which the first edition of this book has met with and the kindly criticism of our colleagues have encouraged us to revise it carefully, with the particular object of presenting in simpler form some of the more difficult, and yet essential principles upon which the modern science of physiology depends. This has been done without changing the paging of the book, and therefore without in anywise altering its general nature.

Although the book, as stated in the preface to the first edition, has been specially written to meet the requirements of the student of dentistry, the principle has been constantly kept in mind that the physiology which he should learn is essentially the same as that required by the student of medicine. To emphasize this point the title of the book has been somewhat altered in form.

The outlines of experiments found in the appendix are arranged to occupy about sixty hours of laboratory work. While the authors realize the impossibility of formulating experiments suitable to all laboratories, nevertheless they hope that these will be of some service.

The authors are deeply indebted to Miss Achsa Parker and Dr. E. P. Carter for pointing out many of the errors that appeared in the first edition.

R. G. PEARCE.

J. J. R. MACLEOD.

PREFACE TO FIRST EDITION.

A knowledge of the fundamentals of human physiology is essential in the training of the dental student, because physiology constitutes, along with anatomy, the basic science upon which all medical and surgical knowledge is founded; and dentistry is a highly specialized department of surgical practice. To operate on the teeth without knowing something about the physiology of the body as a whole, would reduce the dentist to the level of a craftsman who, although perhaps very highly skilled in his technical work, was yet quite ignorant of the nature of the machine upon a part of which his work had to be done.

But there are also practical reasons why the dentist should be familiar with physiology, for good health, and not good looks alone, depends very largely on sound teeth. The neglect of this fact may cause disturbances in bodily functions to which, at first sight, the teeth may apparently bear very little relationship; thus, extreme emaciation, with its consequent lowering of the normal resistance of the body towards disease and infection, is well-known to be frequently due to no other cause than some abnormal or pathological condition affecting the teeth; and, on the other hand, this very condition itself may become intractable to the most skilled dental treatment and hygiene, if measures are not taken at the same time to improve the general health. Although it is obviously beyond the province of the dentist to undertake the treatment of these general conditions, yet it is most important that he should be sufficiently familiar with the normal functioning of the human body to be able to recognize what is really at fault. A knowledge of the laws of nutrition and dietetics must therefore form a most important part of every course in dentistry, and these have received particular attention in this book.

The physiology of the digestive system, of the circulation of the blood and of the nervous system is scarcely less important.

The pain and shock produced by a dental operation may cause considerable disturbance in the action of the heart or in the distribution of blood in the body, and this disturbance, especially in cases in which the heart and the blood vessels are diseased, may become so pronounced as to render a certain amount of medical skill necessary. Or if, to avoid such pain, it be deemed advisable to administer anesthesia, then must the dentist be constantly on his guard that no more than the proper amount of anesthetic is given, which he can do intelligently only by observing the condition of the nervous and circulatory systems.

Besides knowing something about the physiology of the body as a whole, the dentist must be particularly familiar with the local physiology of the mouth, such as the finely coordinated nervous mechanisms involved in the acts of mastication and swallowing and the secretion of saliva. He must understand the nature of the sensations of the teeth and buccal mucosa, and be on the lookout for any lesions of the cranial nerves that supply the muscles and other tissues adjacent to the mouth cavity.

The chemistry of the saliva has demanded special attention because of the very interesting scientific investigations which are being prosecuted regarding the nature of the undoubted relationship that exists between changes in the saliva and the incidence of dental caries. To adequately describe the present status of this work we have found it necessary to devote some space (in the second chapter) to a review of the main physico-chemical principles which may regulate the reaction and neutralizing power of saliva.

Whenever the occasion presented itself to do so, we have given a brief description of the general nature of the diseases in which dental involvement is possible.

A few simple, but very instructive, laboratory demonstrations are described in an appendix at the close of the book. We have found that such demonstrations furnish an invaluable aid in the teaching of the subject.

To facilitate a clear understanding of the subject, diagrams have been used whenever necessary, and many of these have

been specially drawn for the work. To Prof. T. Wingate Todd and Mr. P. M. Spurney, the authors are deeply indebted for the valuable assistance which they gave in the preparation of these.

R. G. PEARCE.

J. J. R. MACLEOD.

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HUMAN PHYSIOLOGY

CHAPTER I.

THE CHEMICAL BASIS OF THE CELL.

The Scope of Physiology.—Physiology is the study of the phenomena of living things, just as anatomy or morphology is a study of their structure. The study of anatomy is most logically pursued by starting with the simplest organisms and gradually proceeding through the more complex forms until man is reached. Except for certain fundamental functions, such as nutrition, which are common to all cells, this method is not the most suitable one to pursue in physiology, because in the lowest organisms all of the functions are crowded together in a limited number of cells—indeed, it may be in one single cell. It is easier to study a function when it is performed by a tissue or organ that has been set apart for this particular purpose than when it is performed by cells that do many other things. Another reason for paying more attention to the functions of higher rather than lower animals is that the knowledge which we acquire may be more directly applicable in explaining the functions of man, and therefore in enabling us more readily to detect and rectify any abnormalities.

During the embryonic development of one of the higher animals, a single cell, the ovum, produces numerous other cells, which become more and more collected into groups, in many of which the cells undergo very marked changes in shape and structure, or produce materials, such as the skeleton or teeth, which show no cell structure whatsoever. Thus we have formed the tissues and organs, each having some particular function of

its own, although certain functions remain which are common to all. In other words, as the organism becomes more and more complex, there comes to be a division of labor on the part of the cells that comprise it. The conditions are exactly like those which obtain in the development of a community of men. In primeval communities there is little division of labor, every individual makes his own clothes, hunts his own food, manufactures and uses his own implements of war, but as civilization begins to appear, certain individuals specialize as hunters and fighters, others as makers of clothing, others as artisans. Although, in its first stages, this division of labor may be far from absolute, for every member of the community must still fight and take part in the building of his hut, yet it soon tends to become more and more so, until, as in the civilized communities of this twentieth century of ours, specialization has become the order of the day.

A good example of a one-celled animal is *the amœba*, which is often found floating in stagnant water, and which consists of nothing more than a mass of tissue, or protoplasm, as it is called, and yet this apparently simple structure can move from place to place, it can pick up and incorporate with its own substance particles of food with which it comes in contact, it can store up as granules certain of these foodstuffs, and get rid of others that it does not require; it grows as a result of this incorporation, until at last it splits in two and each half repeats the cycle. In other words, this single cell shows all of the so-called attributes of life: movement, digestion and assimilation of food, growth and reproduction. No one of these properties is necessarily confined to living structures alone, for some perfectly inanimate bodies may exhibit one or other of them, yet when all occur together, we consider the structure to be living.

In the higher animals, these functions are performed by the so-called systems, such as the digestive, the circulatory, the respiratory, the excretory, the motor, the nervous and the reproductive, each system being composed of certain organs and tissues which are designed for the special purpose of carrying out some particular function or functions. One function, however, is common to all of the organs and tissues, namely, that of nutrition,

which includes the process by which the digested food is built up into the protoplasm of the cells, or assimilation, and that by which the resulting substances are broken down again, or dissimilation. It is by these processes that the energy of life is set free; the energy by which the tissues perform their functions, and which appears as body heat. Every cell in the animal body is therefore a seat of energy production, and at the same time each is a machine for converting this energy into some definite form of work. In this regard the animal machine differs from a steam engine, in which energy liberation occurs in the furnace, and conversion of this energy to movement occurs in the pistons. The furnace and the machinery of the animal body are located in the tissue cells, and the digestive, circulatory, respiratory and excretory systems are provided for the purpose of transporting, to and from the living cells, the fuel (i. e., the food), along with the oxygen to burn it and the gases produced by its combustion. These processes of assimilation and dissimilation constitute the study of metabolism, the practical side of which is included in the science of nutrition.

The Physico-Chemical Basis of Life.

With the object of ascertaining to what extent the known laws of physics and chemistry can explain the fundamental processes that are common to all cells, we must make ourselves familiar, first of all, with the chemical and physical nature of the constituents of the cell, and secondly with the physico-chemical laws which govern the reactions that take place between these constituents. The same laws will control the reactions which take place in the juices secreted by cells; for example, in the blood and in the secretions, such as the saliva.

The Chemical Basis of Animal Tissues.—Certain substances are found in every living cell and in approximately equal quantities; hence these may be considered the *primary constituents* of protoplasm. In general they consist of the proteins, lipoids, inorganic salts, water, and probably the carbohydrates. Protoplasm is the substance composed of these primary constituents. By its

activity the protoplasm produces the *secondary constituents* of the cell, which are not the same in all cells, and which include the granules of pigment or other material, the masses of glycogen, the globules of fat or the vesicles of fluid which are found embedded in the protoplasm.

By whatever process we attempt to isolate its constituents, we of course kill the cell, so that we can never learn by analysis what may have been the real manner of union of these substances in the living condition. All we can find out is the nature of the building material after the structure (the cell) into which it is built has been pulled to pieces. If the chemical process by which we disintegrate the cell is a very energetic one, for example, combustion, we always find the elements, carbon, hydrogen, nitrogen, oxygen, sulphur, phosphorus, sodium, potassium, calcium, chlorine, and usually traces of other elements, such as iodine, iron, etc. If the decomposition be less complete, definite chemical compounds are obtained, namely, water, proteins, lipoids, carbohydrates, and the phosphates and chlorides of sodium, potassium and calcium. We shall proceed to consider briefly the main characteristics of each of these substances and their place in the animal economy.

WATER.—This is the principal constituent of active living organisms, and is the vehicle in which the absorbed foodstuffs and the excretory products are dissolved. It may be said indeed that protoplasm is essentially an aqueous solution, in which other substances of vast complexity are suspended. Water, on account of its very unique physical and chemical properties, is of prime importance in all physiological reactions. These properties are: its chemical inactivity at body temperatures; its great solvent power (it is the best known universal solvent); its specific heat, or capacity of absorbing heat; and, depending on this, the large amount of heat which it takes to change water into a vapor—latent heat of steam. These last mentioned properties are made use of in the higher animals for regulating the body temperature.

Of great importance in the maintenance of the chemical balance of the body are the electric phenomena which attend the solution of certain substances in water. This will be discussed

later in connection with ionization. Water has also a very great surface tension. It is this property which determines the height to which water will rise in plants and in the soil, and which no doubt plays a role in the processes of absorption going on in various parts of the animal body.

PROTEINS.—The great importance of proteins in animal life is attested by the fact that they are absolutely indispensable ingredients of food. An animal fed on food containing no protein will die nearly as soon as if food had been withheld altogether. Proteins are complex bodies composed of carbon, hydrogen, oxygen, nitrogen, and, in nearly all cases, sulphur. Some may contain in addition phosphorus, iron, iodine, or certain other elements. The proportions in which the above elements are found in different proteins do not vary so much as the differences in the chemical behavior of the proteins would lead us to expect. In general the percentage composition by weight is:

Carbon	53 per cent
Hydrogen	7 per cent
Oxygen	22 per cent
Nitrogen	16 per cent
Sulphur	1 to 2 per cent

The essential differences in the structure of the molecules of different proteins have been brought to light by studies of the products obtained by partially splitting up the molecule. We are able to do this by subjecting protein to the action of superheated steam, or by boiling with acids or alkalis in various concentrations, or by the action of the ferments of digestive juices or by bacteria. The cleavage produced by ferments or bacteria is much more discriminate than that brought about by strong chemical reagents; that is to say, the chemical groupings are not so roughly torn asunder by the biological as by the chemical agencies.

At first the proteins break up into compounds still possessing many of the features of the protein molecule. These are the *protoses and peptones*, which consist of aggregates of smaller

molecules, capable of being further resolved into simple crystalline substances. These have been called the building stones of the protein molecule, and although they differ from one another in many respects, they have one feature in common, namely, that each consists of an organic acid having one or more of its hydrogen atoms substituted by the radicle, NH_2 . Such substances are called *amino bodies* or *amino acids*. For example, the formula of acetic acid is CH_3COOH . If for one of the H atoms there is substituted the NH_2 group, we have $\text{CH}_2\text{NH}_2\text{COOH}$, which is amino acetic acid, or glycocoll. The same sort of substitution may take place, not alone in the simple organic acids containing one acid group, but also in those containing two acid groups, as in amino-succinic acid, $\text{COOH} \cdot \text{CH}_2(\text{NH}_2)\text{COOH}$, or in acids containing the aromatic or benzene ring group, as in the case of tyrosine, $\text{C}_6\text{H}_4\text{OH} \cdot \text{C}_2\text{H}_3 \cdot \text{NH}_2\text{COOH}$, or again there may be two amino acid groups present, as in the diamino acid, ornithin or diamino-valeric acid, $\text{C}_4\text{H}_7(\text{NH}_2)_2\text{COOH}$.

That the large and complex protein molecule is really built up out of these amino bodies has been very conclusively shown by Emil Fischer, who succeeded in causing two or more of them to become united to form a body called a *polypeptid*. When several amino bodies were thus synthesized, the polypeptid was found to possess many of the properties of peptones, which we have just stated are the earliest decomposition products of protein.

Proteins differ from one another, not only in the nature of the amino bodies of which they are composed (although certain of these are common to all proteins), but also in the manner in which the amino bodies are linked together. We shall see the practical value of knowing what are the amino bodies in a given protein when we come to the subject of dietetics (see p. 99).

The proteins of the cell are classified into two groups. The first includes the simple proteins, such as egg and serum albumin; and the second, the compound proteins, from which non-protein groups can be split off. As primary cell constituents, the following simple and compound proteins are important: albumin, globulin, nucleoprotein, and the glycoproteins. They are all of the nature of colloidal substances (see p. 32), and therefore are

either precipitated or coagulated when solutions containing them are boiled or have inorganic salts dissolved in them.

Albumins are characterized chiefly by their great solubility in water. Three forms are of importance: egg albumin, lactalbumin of milk, and serum albumin.

Globulins occur principally in the muscle proteins, and are insoluble in water, but soluble in dilute neutral salt solutions. Many consider that the albumins and globulins are only nutritive materials out of which the protoplasm manufactures the compound proteins, these being the essential proteins of the cell.

Nucleoproteins, both in quantity and in relation to their activity, are probably the most important constituents of the cell. They have a very complex structure, and occur in many varieties. They consist of a combination between protein and a substance called nucleic acid, which, on being broken up by chemical means, yields phosphoric acid, a simple sugar called pentose, and nitrogenous substances known as purin bases, and pyrimidines. The purine bases are of great interest, because they are the antecedents in the body of uric acid, which, being relatively insoluble, may become deposited from the body fluids and cause gout or gravel. That it is possible to have an enormous variety of nucleoproteins can be imagined when we consider that there exist different sort of purin bases, of carbohydrates, and of amino bodies. The nucleus of the cell contains a nucleoprotein which is particularly rich in purin bases and is often called nuclein.

Phosphoproteins are compounds of phosphoric acid and simple proteins, without any nucleic acid. An example is the casein of milk (see p. 105).

Glycoproteins are compound of carbohydrates with proteins. The mucin of saliva is an example (see p. 46).

Insoluble proteins resemble the coagulated proteins, and are left behind after the extraction of the other proteins from the cell.

LIPIDS.—These include all the substances composing a cell which are soluble in fat solvents. Besides fats and fatty acids, the most important of these substances are lecithin and cholesterol.

Lecithin is widely distributed in the animal body, and is very important in the metabolism and in the physical structure of the cell. It consists chemically of glycerine, fatty acid, phosphoric acid, and a nitrogenous base called cholin.

Cholesterol is another widely distributed lipoid. It is not in reality a fatty body, but rather resembles the terpenes. Lecithin and cholesterol are abundant in brain tissue, in the envelopes of erythrocytes, and in bile.

The fats exist mainly as secondary constituents of the cell, being deposited in very large amounts in certain of the connective tissue cells of the body, in bone marrow and in the omental tissues. Chemically, the tissue fats are of three kinds: olein, palmitin, and stearin, each having a distinctive melting point. They are compounds of the tri-valent alcohol, glycerine, and one of the higher fatty acids, oleic, palmitic, or stearic acid. Besides those that are present in the animal tissues, fats made up of glycerine combined with various lower members of the fatty acid series occur in such secretions as milk. In order to understand the influence which fats have on general metabolism, it is important to remember that they differ from the carbohydrates in containing a very low percentage of oxygen and a relatively high percentage of hydrogen and carbon. Thus, the empirical formula of palmitin is $C_{51}H_{98}O_6$ or $C_3H_5(C_{16}H_{31}O_2)_3$, that of dextrose $C_6H_{12}O_6$, and of protein $C_{72}H_{112}N_{18}O_{22}S$.

THE CARBOHYDRATES are also mainly secondary cell constituents, although it is becoming more and more evident that they are also necessary as primary constituents. In general they may be defined chemically as consisting of the elements C, H, and O, the latter two being present in the molecule in the same proportion as in water; thus, the formula for dextrose is $C_6H_{12}O_6$.

The basic carbohydrates are the simple sugars or *monosaccharides*, such as grape sugar or dextrose. When two molecules of monosaccharide become fused together with the elimination of a molecule of water (thus giving the formula $C_{12}H_{22}O_{11}$), a secondary sugar or disaccharide results. Cane sugar, lactose (or milk sugar) and maltose (or malt sugar) are examples. If several nonsaccharide molecules similarly fuse together, *polysac-*

charides having the formula $(C_6H_{10}O_5)_n$ are formed. These include the dextrines or gums, glycogen or animal starch, the ordinary starches, and cellulose. Since so many molecules are fused together, it is not to be wondered at that there should be so many varieties of each of these classes of polysaccharides, for, as in the case of proteins, not only may the actual "building stones" of the molecule be different, but they may be built together in very diverse ways. The polysaccharides may be hydrolyzed (i. e., caused to take up water and split up) into disaccharides, and these into monosaccharides by boiling with acids or by the action of diastatic and invertive ferments (see p. 36).

The following formulæ illustrate these facts:

1. $C_6H_{12}O_6$ = a monosaccharide (dextrose).
2. $C_{12}H_{22}O_{11}$ = a disaccharide (cane sugar) composed of:
 $C_6H_{12}O_6 + C_6H_{12}O_6 - H_2O$.
3. $(C_6H_{10}O_5)_n$ = a polysaccharide (starch) composed of:
 $n C_6H_{12}O_6 - n H_2O$ where n signifies that an indefinite number of molecules are involved in the reaction.

CHAPTER II.

THE INFLUENCE OF PHYSICO-CHEMICAL LAWS ON PHYSIOLOGICAL PROCESSES: ENZYMES.

Having learned of what materials the cell is composed, we may proceed to enquire into the chemical and physical reactions by which it performs its functions. The cell, either of plants or of animals, may be considered as a chemical laboratory, in which are constantly going on reactions, that are guided, as to their direction and scope, by the physical conditions under which they occur. A study of the material outcome of these reactions constitutes the science of metabolism, to which special chapters are devoted further on. At present, however, we must briefly examine the physico-chemical conditions existing in the cell which may give the directive influence to the reactions. Why should certain cells, like those which line the intestine, absorb digested food and pass it on to the blood, whilst others, like those of the kidney, pick up the effete products from the blood and excrete them into the urine? We must ascertain whether these are processes depending on purely physico-chemical causes, or whether they are a function of the living protoplasm itself, a vital action, as we may call it. In general it may be said that the aim of most investigations of the activities of cells is to find a physico-chemical explanation for them, and it is one of the achievements of modern physiology that some should have been thus explainable. A large number, however, do not permit of such an explanation, and this has induced certain investigators to believe that there are some animal functions which are strictly vital and can never be accounted for on a physical basis. The "physical" and the "vital schools" of physiologists are therefore always with us.

From the standpoint of physical chemistry, the cell may be considered as a collection of two classes of chemical substances,

called crystalloids and colloids, dissolved in water, or in the lipoids, or in each other, and surrounded by a membrane which is permeable towards certain substances but not towards others (semipermeable, as it is called). On a larger scale, the same general conditions exist in all of the animal fluids, such as the blood, the lymph, the secretions and the excretions. We may therefore study the above laws with a view to applying them to both cells and body fluids.

Properties of Crystalloids.—As their name implies, these form crystals under suitable conditions. When present in solution they diffuse quickly throughout the solution, and can readily

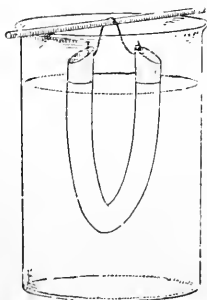


Fig. 1.—Dialyser made of tube of parchment paper suspended in a vessel of distilled water. The fluid to be dialysed is placed in the tube, and the distilled water must be frequently changed.

pass through membranes, such as a piece of parchment, placed between the solution containing them and another solution. This process is called *dialysis*, and the apparatus used for observing it, a *dialyser* (see Fig. 1). Dialysis differs from filtration, the latter process consisting in the passage of fluids, and the substances dissolved in them, through more or less pervious membranes as a result of differences of pressure on the two sides of the membrane. If instead of using a simple membrane, such as parchment, we choose one which does not permit the crystalloid itself to diffuse, but permits the solvent to do so—a *semipermeable membrane*, as it is called,—a very interesting property of dissolved crystalloids comes to light, namely, their tendency to os-

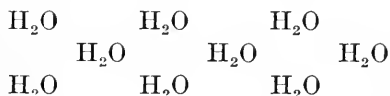
occupy more room in the solvent, that is, to cause dilution by attracting the solvent through the membrane. Cell membranes are semipermeable, but they are too small and delicate for most experimental purposes. For this purpose we use an artificial membrane composed of a precipitate of copper ferrocyanide supported in the pores of an unglazed clay vessel. If a solution of crystalloid—say, cane sugar—be placed in such a semipermeable membrane and this then submerged in water, it will be found that the cane sugar solution quickly increases in volume, or if expansion be impossible, a remarkably high pressure will be developed. This is called *osmotic pressure*, and it is a measure of the tendency of dissolved crystalloids to expand in the solvent.

It has been found that the laws which govern osmotic pressure are identical with those governing the behavior of gases. Therefore, osmotic pressure ought to be proportional to the number of molecules of dissolved crystalloid. This is the case for the sugars, but it is not so for the saline crystalloids, such as the alkaline chlorides, nitrates, etc., for these cause a greater osmotic pressure than we should expect from their molecular weights. Why is this? The answer is revealed by observing the behavior of the two classes of crystalloids towards the electric current. Solutions of sugars or urea do not conduct the current any better than water, whereas solutions of saline crystalloids conduct very readily. The former are therefore called *non-electrolytes* and the latter *electrolytes*. It has been found that the reason for this is that molecules of electrolytes when they are dissolved break into parts called "ions," each ion being charged with electricity of a certain sign, i. e., positive or negative. Whenever an electric current is passed through the solution, the ions, hitherto distributed throughout the solution in pairs carrying electrical charges of opposite signs, now line themselves up so that the ions with one kind of charge form a chain across the solution along which that kind of electricity readily passes, and in so doing carries the ions with it.

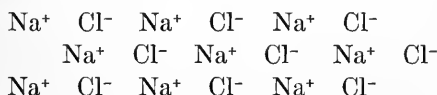
This splitting of electrolytes into ions is called *dissociation* or *ionization*. The ions which carry a charge of positive electricity and which therefore travel towards the cathode or nega-

tive pole, (since unlike electricities attract each other) are called *kathions*, and the negatively charged ions that travel to the anode, *anions*. Hydrogen and the metallic elements belong to the group of kathions; oxygen, the halogens and all acid groups, to the anions. These facts may be more clearly understood from the following equations:

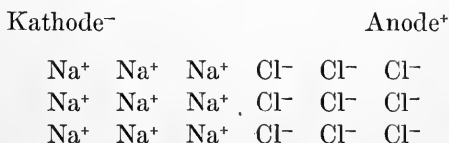
In water, or in a solution of a non-electrolyte, molecules of H_2O or non-electrolyte may be represented as existing thus:



In a solution of an electrolyte, the molecules split into ions thus:



When an electric current passes through a solution of an electrolyte, the ions arrange themselves thus:



To return to osmotic pressure, the ions influence this as if they were molecules, so that when we dissolve, say, sodium chloride in water, the osmotic pressure is almost twice what it should be, because every molecule has split into two ions.

Osmotic Phenomena in Cells.—Over and over again we shall have to refer to these physico-chemical processes in explaining physiological phenomena. For the present it may make matters clearer if we consider how osmosis explains the *behavior of cells when suspended in different solutions*. The cell wall acts as a semipermeable membrane. Thus, if we examine red blood corpuscles suspended in different saline solutions under the microscope, we shall observe that they shrink or crenate when the solu-

tions are strong, and expand and become globular in shape when these are weak. The shrinkage is due to diffusion of water out of the corpuscle and the swelling, to its diffusion in; that is to say, in the former case the osmotic pressure of the surrounding fluid is greater than that of the corpuscular contents and *vice versa* in the latter case. In this way we have a simple and convenient method of comparing the relative osmotic pressure of different solutions. When the solution has a higher pressure, it is called *hypertonic*, when less, *hypotonic*, when the same, *isotonic*. It is evident that the body fluids must always be isotonic with the cell contents, and that we must be careful never to introduce fluids into the blood vessels that are not isotonic with the blood. A one per cent solution of common salt is almost isotonic with blood, and is accordingly used for intravenous or subcutaneous injections, or for washing out body cavities or surfaces lined with delicate membranes, such as the conjunctiva or nares.

Reaction of Body Fluids.—Closely dependent upon these properties of ionization are the reactions which determine the *acidity* and *alkalinity of the body fluids*. When we speak of the degree of acidity or alkalinity of a solution in chemistry, we mean the amount of alkali or acid, respectively, which it is necessary to add in order that the solution may become neutral towards an indicator, such as litmus. This titrable reaction is however a very different thing from the real strength of the acid or alkali; for example, we may have solutions of lactic and hydrochloric acids that require the same amount of alkali to neutralize them, but the hydrochloric acid solution will have much more powerful acid properties (attack other substances, taste more acid, act much more powerfully as an antiseptic, etc.). The reason for the difference is the degree of ionization; the strong acids ionize much more completely than the weak. As a result of this ionization, each molecule of the acid splits into H-ions and an ion composed of the remainder. *To ascertain the real acidity we must therefore measure the concentration of H-ions.* (These considerations also apply in the case of alkalies, only in this case OH-ions determine the degree of alkalinity.) This can be done accurately by measuring the speed at which certain chemical

processes proceed, that depend on the concentration of H-ions. The conversion of cane sugar into invert sugar is a good process to employ for measuring the speed of reaction.

But even this refinement in technique does not enable us to measure the H-ion concentration—for now we must use this expression when speaking of acidity or alkalinity—of such important fluids as *blood* and *saliva*, in which there is an extremely low H-ion concentration. If either of these fluids be placed on litmus papers, the red litmus turns blue, but all that this signifies is that the litmus is a stronger acid than those present in blood or saliva, so that it decomposes the bases with which they were combined and changes the color. If we employ phenolphthalein, which is a much feebler acid, then blood serum reacts neutral and saliva often acid.

There are two methods open to us for measuring the H-ion concentration in such cases:

1. *The Hydrogen Electrode.*—Place the fluid (e. g., blood serum or saliva), with a platinum electrode dipping into it, in a small vessel filled with hydrogen. Connect this hydrogen electrode, as it is called, with a standard calomel electrode by means of wires in the course of which are suitably arranged electrical instruments for the measurement of electromotive force. From the difference in the electromotive force which is found to exist between the hydrogen and calomel electrodes, we can calculate the H-ion concentration. This method is being employed for measuring the reaction of saliva in relationship to its influence on caries of the teeth.

2. *The Use of Standardized Indicators.*—It has been found that different indicators change color at different H-ion concentrations. By measuring the H-ion concentration—by the electrical method—of solutions containing known proportions of acid and alkaline salts (such as NaH_2PO_4 and Na_2HPO_4 or NaHCO_3), and then observing their behavior with different indicators, it has been possible to evaluate the latter in terms of the H-ion concentration at which they change color. Expressing the results as the fraction of a normal solution of H-ion at which this change occurs, it has been found that paranitro-phenol turns

at about .000,001 (or 1×10^{-7}), which is the H-ion concentration of pure water, and is therefore the most practical point to choose as indicating neutrality. Methyl red and rosolic acid also change color about this point. Phenolphthalein, on the other hand, changes color at a H-ion concentration of 1×10^{-9} , i. e., it is very sensitive towards acids; methyl orange changes at 1×10^{-4} , i. e., it is relatively insensitive towards acids.

The indicators which change color at about the H-ion concentrations found in animal fluids are therefore rosolic acid, parantrophenol and methyl red. By comparing the color produced by adding one of these indicators to the unknown fluid with the color obtained by adding the same indicator to a series of solutions containing varying but known H-ion concentrations, we can accurately tell the H-ion concentration of the unknown solution, for the H-ion concentration of the solution whose tint matches with that of the unknown is the H-ion concentration of the latter. The series of standard solutions is made by mixing varying proportions of acid and alkaline phosphates.

Before leaving this subject, it is important to point out that the blood has an H-ion concentration which is practically the same as that of water, i. e., is as nearly neutral as it could be. It also has the power of maintaining this neutrality practically constant even when large amounts of acid or alkali are added to it. Although saliva and some other body fluids are not so nearly neutral as blood, yet they can also lock away much acid or alkali without materially changing the H-ion concentration. This property is due to the fact that the body fluids contain such salts as phosphates and carbonates, which exist as neutral and acid salts, and can change from the one state to the other without greatly altering the H-ion concentration, and yet, in so changing, can lock away or liberate H- or OH-ions. This has been called the "buffer" action, and is a most important factor in maintaining constant the neutrality of the animal body.

Colloids.—These are substances which do not diffuse through membranes when they are dissolved. Thus if blood serum be placed in a dialyser which is surrounded by distilled water, all

the crystalloids will diffuse out of it, leaving the colloids, which consist mainly of proteins. The physical reason for this failure to diffuse is the large size of the molecules, in comparison with the small size of those of the crystalloids. By causing a beam of light to pass through a colloidal solution and holding a microscope at right angles to this beam, the colloidal particles become evident, just as particles of dust become evident in a beam of daylight in a darkened room.

Filters can be made of unglazed porcelain impregnated with gelatin in which the pores are so very minute that colloids can not pass through them, though water and inorganic salts do so. When blood serum is filtered through such a filter, the filtrate contains no trace of protein. The colloidal molecules can very readily be caused to fuse together, thus forming aggregates of molecules which become so large that they either confer an opacity on the solution or actually form a precipitate.

This fusing together of colloidal particles can be brought about either by adding certain neutral salts or by mixing with certain other colloids. The explanation of these results is as follows: colloidal molecules carry either a positive or a negative electrical charge, and when this is neutralized, the colloidal molecules fuse together, i. e., become aggregated. This neutralization of electrical charge can be accomplished either by adding an electrolyte, one of whose ions will supply the proper electrical charge, or by a colloid having an opposite charge. Thus the SO_4 anion of Na_2SO_4 , in virtue of charges of negative electricity which it carries, will very readily precipitate such a colloid as colloidal iron (ferrum dialysatum, U. S. P.), which is charged with positive electricity; or again, this colloid itself will readily precipitate arsenious sulphide, another colloid carrying a negative charge. The physiological importance of these reactions lies in the fact that they probably explain many of the peculiarities of behavior of mixtures of different animal fluids, such as toxins and anti-toxins (see p. 149).

A property of colloids which is closely related to the above is that of *adsorption*. This means the tendency for dissolved substances to become condensed or concentrated at the surface of

colloidal molecules. An example is the well known action of charcoal when shaken with colored solutions. It removes the pigment by adsorbing it. Adsorption is due to *surface tension*, which is the tension created at the surface between a solid and a liquid, or between a liquid and a gas. It is in virtue of surface tension that a raindrop assumes a more or less spherical shape. Since colloids exist as particles, there must be an enormous number of surfaces throughout the solution, that is, an enormous surface tension. Now many substances, when in solution, have the power of decreasing the surface tension, and in doing so it has been found that they accumulate at the surface, that is to say, in a colloidal solution, at the surface of the colloidal molecules. The practical application of this is that it helps to explain the physical chemistry of the cell, the protoplasm of which is a colloidal solution containing among other things proteins and lipoids. The lipoids depress the surface tension and therefore collect on the surface of the cell and form its supposed membrane, whilst the proteins exist in colloidal solution inside. It is possibly by their solvent action on lipoids that ether and chloroform so disturb the condition of the nerve cells as to cause anaesthesia. A knowledge of colloidal chemistry is coming to be of great importance in physiology.

General Nature of Enzymes or Ferments.

To decompose proteins, fats or carbohydrates into simple molecules in the laboratory necessitates the use of powerful chemical or physico-chemical agencies. Thus, to decompose the protein molecule into amino bodies requires strong mineral acid and a high temperature. In the animal body similar processes occur readily at a comparatively low temperature and without the use of strong chemicals in the ordinary sense. The agencies which bring this about are the enzymes or ferments. These are all colloidal substances (see p. 32), so that they are *readily destroyed by heat* and are *precipitated by the same reagents as proteins*. They are capable of *acting in extremely small quantities*. Thus, a few drops of saliva can convert large quantities of starch solution into sugar. During their action, the enzymes do not them-

selves undergo any permanent change, for even after they have been acting for a long time, they can still go on doing their work if fresh material be supplied upon which to act. These properties are explained by the fact that they act *catalytically*, just as the oxides of nitrogen do in the manufacture of sulphuric acid. That is to say, they do not really contribute anything to a chemical reaction, but merely serve as accelerators of reactions, which however would occur, though very slowly, in their absence. Thus, to take our example of starch again, if this were left for several years in the presence of water, it would take up some of the water and split into several molecules of sugar (p. 34). The enzyme ptyalin in saliva merely acts by hurrying up or accelerating the reaction so that it occurs in a few minutes.

Enzymes differ from inorganic catalysers in the remarkable *specificity of their action*, there being a special enzyme for practically every chemical change that occurs in the animal body. Thus, if we act on any of the sugars called disaccharides (cane sugar, lactose and maltose) with an inorganic catalytic agent, such as hydrochloric acid, they will split up into their constituent monosaccharide molecules, whereas in the body, each disaccharide requires a special or specific enzyme for itself. The enzyme acting on one of them, in other words, will be absolutely inert towards the others. This specificity of action is explained by supposing that each substance to be acted on (called the *substrat*) is like a lock to open which the proper key (the enzyme) must be fitted.

Enzymes are *peculiarly sensitive* towards the chemical condition of the fluid in which they are acting, more particularly its reaction. Thus the enzyme of saliva acts best in neutral reaction, whereas the enzyme of gastric juice acts only in the presence of acid, and those of pancreatic juice, in the presence of alkali. Enzymes may unfold this action either inside or outside of the cells which produce them. Thus, the enzymes produced in the digestive tract act outside the gland cells, but the enzyme of the yeast cell acts in the cell itself and is never secreted. The former are called *extracellular* enzymes and the latter *intracellular*. The activities of intracellular enzymes are much more liable to be

interfered with by unfavorable conditions than those of extracellular enzymes. This is because the former become inactive whenever anything occurs to destroy the protoplasm of the cell in which they act. The living protoplasm is necessary to bring the substrat in contact with them. On this account enzymes used to be classified into *organized* and *unorganized*. We know that there really is no difference in the enzyme itself; the only difference is with regard to the place of activity. The cells that compose the tissues of animals perform their various chemical activities in virtue of the intracellular enzymes which they contain. These are, therefore, the chemical reagents of the laboratory of life. After the animal dies, the intracellular enzymes may go on acting for a time and digest the cells from within. This is called *autolysis*.

Enzymes are *classified into groups* according to the nature of the chemical action which they accelerate. Thus:

Hydrolytic enzymes—cause large molecules to take up water and split into small molecules. (Most of the digestive enzymes belong to this class.)

Oxidative enzymes (oxydases)—encourage oxidation.

Deamidating—remove NH_2 group.

Coagulative—convert soluble into insoluble proteins.

Each group is further subdivided according to the nature of the substrat on which the enzymes act; e. g., hydrolytic enzymes are subdivided into amylolases—acting on starch; invertases—acting on disaccharides; proteases—acting on proteins; ureases—acting on urea, etc.

When enzymes are repeatedly injected into the blood, or under certain other conditions, they have the power, like toxines, of producing *antienzymes*. As their name signifies, these are bodies which retard the action of enzymes. Thus, if some blood serum from an animal into which trypsin has been injected for some days previously be mixed with a trypsin solution, the mixture will digest protein very slowly, if at all, when compared with a mixture of the same amount of trypsin and protein (see also p. 78).

CHAPTER III.

DIGESTION.

Necessity and General Nature of Digestion: Digestion in the Mouth.

The never-ceasing process of combustion that goes on in the animal body, as well as the constant wear and tear of the tissues, makes it necessary that the supply of fuel and of building material be frequently renewed. For this purpose food is taken. This food is composed of fats and carbohydrates, which are mainly fuel materials, of inorganic salts and water, which are necessary to repair the worn tissues and of proteins which are both fuel and repair materials, and are therefore the most important of the organic foodstuffs. The blood transports the foodstuffs from the digestive canal to the tissues. In the digestive canal the foodstuffs are digested by hydrolyzing enzymes (see p. 36), which are furnished partly in the secretions of the digestive glands and partly from the numerous micro-organisms that swarm in the intestinal contents. The enzymes, as we have seen, are very discriminative in their action, for not only is the enzyme for protein without action on a fat or carbohydrate, but each of the different stages in protein break-down requires its own peculiar enzyme. It becomes necessary therefore that the enzymes be mixed with the food in proper sequence, and to render this possible the digestive canal is found to be divided into special compartments, such as the mouth, the stomach, the small intestines, etc., each provided with its own assortment of enzymes and with some mechanism by which the food, when it has been sufficiently digested, can be passed on to the next stage.

Such correlation between the different stages of digestion necessitates the existence, in the different levels of the gastrointestinal tract, of mechanisms which are specially developed to

bring about the right secretion at the right time. These mechanisms are of two essentially different types, a *nervous reflex control*, and a chemical or "*hormone*" control. The nervous control is exercised through a nerve center, which is called into activity by afferent stimuli proceeding from sensory nerve endings or receptors (see p. 244) that are especially sensitized so as to be stimulated by some property of food (its taste or smell, or its consistency or chemical nature). This type of control exists where prompt response of the glandular secretion is important, as in the mouth and in the early stages of digestion in the stomach. The hormone control consists in the action directly on the gland cells of substances which have been absorbed into the blood from the mucous membrane of the gastro-intestinal tract. The production of these substances depends upon the nature of the contents of the digestive tube. This is a more sluggish process of control than the nervous, but it is sufficient for the correlation of most of the digestive functions.

These considerations point the way to the scheme which we must adopt in studying the process of digestion; we must explain how each digestive juice comes to be secreted, what action it has on the foodstuffs, and what it is, after each stage in digestion is completed, that controls the movement onward of the food to the next stage. And when we have followed each foodstuff to its last stage in digestion, we may then proceed to study the means by which the digested foodstuffs are absorbed into the circulating fluids, and in what form they are carried to the tissues.

On account of the varying nature of their food we find that the digestive system differs considerably in different groups of animals. In the omnivora, such as man, the digestive canal begins with the mouth cavity, in which the food is broken up mechanically and is mixed with the saliva in sufficient amount to render it capable of being swallowed. The saliva, by containing starch-splitting ferment, also initiates the digestive process. The food is then carried by way of the œsophagus to the stomach, in the near or cardiac end of which it collects and becomes gradually permeated by the acid gastric juice. It is then caught up, portion by portion, by the peristaltic waves of the

further or pyloric end of the stomach and, after being thoroughly broken down by this movement and partially digested by the pepsin of gastric juice, is passed on in portions into the duodenum, where it meets with the secretions of the pancreas and liver. These secretions, acting along with auxiliary juices secreted by the intestine itself, ultimately bring most of it into a state suitable for absorption. What the digestive juices leave unacted on bacteria attack, especially in the cæcum, so that by the time the food has gained the large intestine it has been digested as far as it can be. In its further slow movement along the large intestine the process of absorption of water proceeds rapidly.

Disturbances in the digestive process may be due not only to possible inadequacy in the secretion of one or other of the digestive juices, but also to disturbances in the movements of the digestive canal. Such disturbances will not only prevent the forward movement of the food at the proper time, but, by failing to agitate the food, they will prevent its thorough admixture with the digestive juices, so that the enzymes which these contain will not become properly mixed with the food.

Digestion in the Mouth.

Salivary Secretion.—In the mouth, besides its preparation for swallowing, by mastication, etc., the food, mainly on account of its taste and smell, stimulates sensory nerve endings which, by acting on nerve centers, set agoing several of the digestive secretions. The first of these is the secretion of the salivary glands. On account of their ready accessibility to experimental investigation, very extended studies have been made of the salivary glands, and from these studies some of the most important physiological truths, concerning the nature of the nervous control of glands in general, have been drawn. Of the three salivary glands in man, the parotid secretes a watery saliva usually containing the enzyme, ptyalin, and the submaxillary and sublingual secrete a sticky saliva containing mucin, usually along with some ptyalin. When the glands are not secreting, the cells that

compose them are engaged in preparing material to be secreted. By microscopical examination, this material is seen in the protoplasm of the cells (Fig. 2) as granules, which are extremely small in the serous gland cells, but much larger in the mucous. In both types of gland the granules so crowd the cell that the nucleus becomes indistinct and the cell itself much swollen. After the gland has been active, the granules disappear, being evidently discharged from the cell into the duct of the gland. The granules are believed to represent the precursors of the ptyalin or mucin of saliva—hence their name of “zymogen” or “mother of ferment” granules—rather than these substances

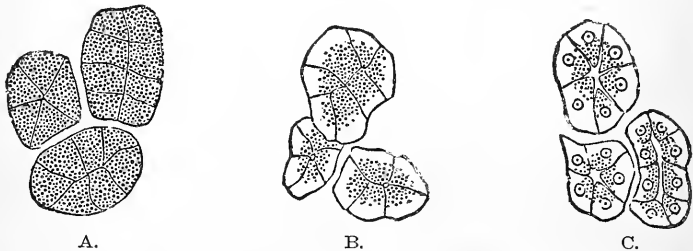


Fig. 2.—Cells of parotid gland showing zymogen granules: *A*, after prolonged rest; *B*, after a moderate secretion; *C*, after prolonged secretion. (Langley.)

themselves. Watery or saline extracts of the glands contain neither mucin nor ptyalin, nor does the addition of acetic acid to a mucous gland cause any precipitate of mucin; indeed, it has an entirely opposite action, it causes the granules to swell.

The Nerve Supply of the Salivary Glands.—The nerve fibers supplying the glands are of the autonomic or visceral type (see p. 277), and they include sympathetic and cerebro-spinal fibers. The sympathetic fibers are derived from cells in the lateral horns of the spinal cord, from which they emerge by the upper three or four thoracic roots, and after ascending as medullated fibers in the cervical sympathetic, terminate as synapses around the cells of the superior cervical ganglion. The axons of these cells proceed as non-medullated post-ganglionic fibers along the nearest vessels to the respective glands. The cerebral autonomic

fibers arise from a center in the medulla and proceed to the glands by various routes; those to the submaxillary and sublingual glands in the chorda tympani, and those to the parotid by way of the tympanic branch of the glosso-pharyngeal. The ganglion cells connected with the cerebral fibers are situated more or less peripherally; in the case of the submaxillary they are embedded in the substance of the gland; in the case of the sublingual gland, in the connective tissue of the so-called submaxillary triangle, and in the case of the parotid, in the otic ganglion (Fig. 3).

In both cerebral and sympathetic nerves there are two varieties of fibers, the one *vasomotor*, the other *secretory*. The for-

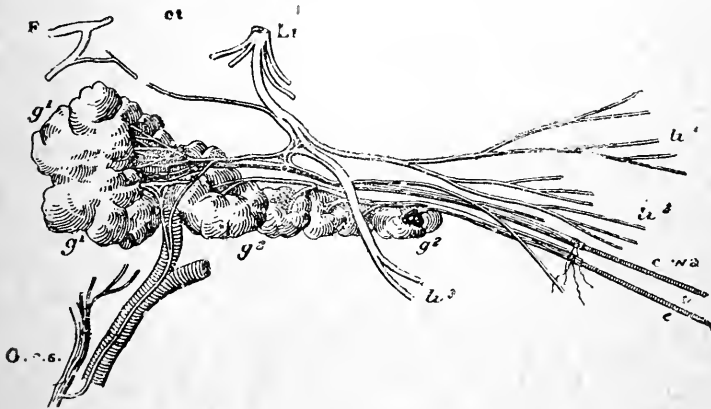


Fig. 3.—The nerve supply of the submaxillary gland: *Li*, lingual nerve; *c. t.*, chorda tympani; *g.* gland. Wharton's duct is ligated and it will be noticed that the chorda leaves the lingual nerve, just before this crosses the duct, thus forming the submaxillary triangle. (Claude Bernard.)

mer, in the case of the cerebral nerves, are dilator in their action, but in the sympathetic they are constrictor. On account of the association of secretory and vasodilator fibers, in the cerebral nerves, stimulation leads to the secretion of large quantities of saliva, the amount of which, as well as its percentage of organic and inorganic constituents, varies with certain limits with the strength of the stimulus. Although secretory activities also become excited when the sympathetic nerve is stimulated, as is

revealed by histological examination of the gland, there is only a slight flow of saliva from the duct because of the concomitant curtailment of the blood supply. In so far as actual secretion of saliva is concerned, the net result of stimulation of either nerve is therefore dependent upon whether dilatation or constriction of the blood vessels of the gland occurs, and this might lead us to conclude that the secretion is secondary to changes in the blood supply; in other words, that it is unnecessary to assume the independent existence of specific secretory nerve impulses. That such secretory fibers do exist, however, is established by many facts. Two of these are: (1) The vessels still dilate but no secretion occurs after a certain amount of atropin has been allowed to act on the gland. This alkaloid paralyzes the secretory nerve fibers, but has no action on those concerned in vasodilation. (2) If the secretions were merely the result of increased blood supply, in other words, were a filtrate from the blood, the pressure in the duct would at all times be less than that in the blood vessels; but this is not the case, for during stimulation of the cerebral nerves the duct pressure may rise far above that of the blood vessels.

But it must never be lost sight of that although both kinds of fibers do exist, they are very closely associated in their action.

The Reflex Nervous Control of Salivary Secretion.—The structural differences between the parotid and submaxillary glands suggest that their functions may not be the same; that their respective secretions must be required for different purposes. To put this supposition to the test, it becomes necessary to adopt some means by which the conditions calling forth the secretion of each gland may be separately studied. This can be accomplished by a small surgical operation in which the ducts are transplanted so as to discharge through fistulæ in the cheek, the secretion being easily collected, by allowing it to flow into a funnel which is tied in place.

^a In general, two distinct types of stimuli may call forth secretion of one or other gland, namely: (1) *direct stimulation of sensory nerve endings* in the mouth, and (2) *psychological stimuli* involving more or less of an association of ideas.

Of the stimuli which cause secretion by acting on sensory nerve endings in the mouth, some influence the parotid, others, the submaxillary gland, and different stimuli produce different effects. Even for pure mechanical stimulation of the buccal mucosa, a marked degree of discrimination is shown; thus, smooth clean pebbles may be rolled around in the mouth and yet cause no saliva to be secreted, whereas dry sand will immediately cause the parotid to discharge enormous quantities of thin watery juice. Similarly dry bread crumbs invoke copious parotid secretion, bread itself having little effect; water, ice, etc., are inert, but if they contain a trace of acid an abundant secretion is instantly poured out. It is plain in all these cases that the purpose of the secretion is to assist in the removal or neutralization of the substance which is present in the mouth. The thick mucous secretion of the submaxillary and sublingual glands seems to depend more on the chemical nature of the food than on its mechanical state, boiled potatoes, hard boiled eggs, meat, etc., causing the secretion of a thick slimy saliva, which by coating the food assists swallowing. The relish for the food seems to be of little account in influencing the secretion of saliva, for noxious substances, or those that are acid, or very salty, call forth much more secretion than do savory morsels. Although mere mechanical stimulation is not in itself an adequate stimulus, yet movement of the lower jaw is quite effective, as for example in chewing, or when the mouth is kept open, as by a gag in a dental operation.

The stimulus does not, however, require to be applied to the buccal mucosa itself; it may be *psychic or associational*, and here again a remarkable discrimination is evident, although the response is not so predictable as when the stimulus is local. Thus, when dry bread or sand is shown to a dog to which previously these substances have been given by mouth, salivation follows, but this is not the case when moist bread or pebbles are offered. Appetite plays an important part in this psychic reflex, for when dry food is shown to a fasting animal, salivation is marked, but may cause no secretion when it is offered to a well-fed animal. It is possible in this case, however, that there may

be inhibition of the glandular activities on account of the presence of food products in the blood. Perhaps the most interesting fact of all is that even a fasting animal will after a time fail to salivate if he be repeatedly shown food which causes a secretion, but which he is not permitted to get. The response is immediately established again, however, if some food, or indeed some other object, be placed in the mouth. A hungry animal will even salivate when he hears some sound which by previous experience he has learned to associate with feeding time. The psychic reflexes are evidently dependent upon an association of ideas (a nervous integration, see p. 242); they are conditioned reflexes, and are therefore the result of a certain degree of education. They are easily rendered ineffective by confusing the usual associations.

General Functions of Saliva.—These observations indicate that a very important function of the saliva is what we may call a *mechanical* one, namely, either to flood the mouth cavity with fluid and so to wash away objectionable objects in it, or to lubricate the food with mucin and so facilitate swallowing. The solvent action of saliva is also important for the act of tasting (see p. 295). Its *chemical* activities in many animals seem to be limited to the neutralizing properties of the alkali which is present in it, but in man and the herbivora it also contains a certain amount of a diastatic enzyme, ptyalin, which can quickly convert cooked starches into dextrines and maltose. Even when this action is most pronounced, however—for it varies considerably in different individuals—it cannot proceed to any extent in the mouth cavity, partly on account of the short time food remains here, and partly because many starches, as in biscuits, are taken more or less in a raw state. In some animals, such as the dog, the saliva has no diastatic action whatever. Although there can therefore be little diastatic digestion in the mouth, a good deal may go on in the stomach, for the saliva that is swallowed along with the food does not become destroyed by the gastric juice until some thirty minutes after the food has gained the stomach.

Although mastication of the food and its preparation for swallowing are undoubtedly the main functions of the mouth cav-

ity, another exists which is of very great importance for proper digestion; this is the stimulation of the taste nerve endings, and, for foods with a flavor, of those of the olfactory nerve in the posterior nares. Such stimulation not only gratifies the appetite, but it serves as the adequate stimulus to set agoing the secretion of the gastric juice. Without any relish for food, digestion as a whole materially suffers, and for this reason unpalatable food is always more or less indigestible.

Recent investigations point to another function of the saliva. Pepsin, a ferment which is important in the digestion of the proteins and which is found in the juice secreted by the glands of the stomach, is readily absorbed by starch when in the colloidal state as it is generally eaten. In this condition the ferment is not free to act upon the proteins and digestion is delayed. If the saliva be allowed to partially digest the starch into sugar before the food reaches the stomach, the colloidal state is changed by the action of the ptyalin of the saliva, and absorption of the ferment does not occur.

CHAPTER IV.

DIGESTION (Cont'd).

The Chemistry of Saliva and the Relationship of Saliva to Dental Caries.

A knowledge of the composition and chemical properties of saliva is of great importance because of the undoubted etiological relationship which exists between this secretion and dental caries. Mixed saliva when freshly secreted is a watery, more or less opalescent and sticky fluid, often containing small masses of mucin, but on standing it becomes cloudy because of precipitation of calcium carbonate. Its specific gravity is 1002-1006, and it contains about 0.05 per cent of solids. The saliva from the sublingual and submaxillary glands is very much richer in solids than that from the parotid. The parotid saliva also differs from that of the other glands in containing no mucin, although it is often rich in ferment. The solid constituents, with some of their properties, are as follows:

<i>Organic</i> . . .	{	Glycoprotein (mucin): precipitated by acid.	
		Other proteins: coagulated by heat.	
		Ptyalin: a starch-splitting enzyme.	
		Potassium sulphocyanide: gives a red color with ferric chloride.	
<i>Inorganic</i> . . .	{	Sodium chloride: } give a precipitate with sil-	
		Potassium chloride: } ver nitrate.	
		Calcium bicarbonate: in fresh saliva.	
		Calcium carbonate: precipitated in saliva after standing.	
		Calcium and magnesium phosphates: } Have an important re-	
		Sodium and potassium phosphates: } lationship to the neu-	
			tralizing properties
			of saliva.

Organic Constituents.—*Mucin* is the substance to which saliva owes its stickiness. Being a glycoprotein, it yields reduc-

ing sugar when it is hydrolyzed, as by boiling with acid. It was at one time suggested that sugar might sometimes appear in the saliva, as a result of bacterial action in the mouth, and be responsible for caries of the teeth. The amount thus produced is, however, so very small in comparison with the ingested carbohydrates that it can be entirely disregarded.

Ptyalin.—This belongs to the class of diastatic or amylolytic enzymes, converting starch into sugar. It is not so powerful as the similar enzyme in pancreatic juice (see p. 74), for it has no action on uncooked starch, which the latter has. It acts best in neutral reaction and in the presence of sodium chloride, but is little affected by a small degree of alkalinity. On the other hand, it is readily destroyed by acids and by higher degrees of alkalinity. These facts are of importance in connection with the continuance of action of saliva after it has been swallowed, for although the food remains in the mouth for much too brief a period to permit of more than a trace of sugar being formed here, yet, after the stomach is reached, ptyalin may continue to act for about half an hour. The ptyalin content, however, varies very considerably in different individuals.

Ptyalin converts starch into the sugar maltose, so called because it is also formed by the action of the diastase of malt. As intermediate substances are formed the dextrans, two of which are distinguishable on account of their behavior towards iodine; one of these, called erythrodextrin, gives a brown color with this reagent, while the other gives no color and is called achroodextrin.

It has been suggested that a deficiency of ptyalin may predispose to caries of the teeth because, under such circumstances, a large amount of dextrin is formed, which being very sticky in character adheres to the teeth and becomes a suitable nidus for bacterial growth.

Potassium Sulphocyanide (sulphocyanate).—This salt has the formula $KCNS$, and is usually present in human saliva to the extent of about 0.01 per cent. It is produced in the blood whenever cyanides or organic nitrites make their appearance in the organism, one source for these being possibly protein meta-

bolism (p. 108). It is excreted from the blood into the urine as well as the saliva. In contrast to cyanides it is non-poisonous, so that it represents the innocuous form into which these substances are converted.

The chemical test used for its detection is the red color which it gives with a solution of ferric chloride (FeCl_3). Sometimes, however, the reaction is not very definite, in which case the method of Bunting should be employed. This is performed as follows: Slowly evaporate 5 c. c. of saliva in a watch glass and while stirring with a glass rod add a few drops of a 25 per cent solution of FeCl_3 . Pour about 5 c. c. of a mixture of 5 parts amyl alcohol and 2 parts ether over the residue, and after stirring decant into a test tube. If sulphocyanide is present, the alcohol-ether will become red. Benzoate and aceto acetic acid may give a similar reaction, but most of the other substances which might interfere with the test, as when it is done by merely adding FeCl_3 to saliva, are eliminated by Bunting's method.

All this care and interest in the testing for KCNS has arisen because of the supposition that the amount of this substance in saliva might have some relationship to caries of the teeth. It was suggested that it might confer on the saliva somewhat of an antiseptic action and thus destroy the bacteria that are the cause of caries. Careful work by Bunting, by Gies and others has, however, shown that this hypothesis is untenable.

Inorganic Constituents.—Two important questions arise in connection with these, viz: (1) their relationship to the reaction of the saliva; (2) the conditions which control the precipitation of calcium carbonate and phosphate and the deposition of the precipitate on the teeth in the form of tartar.

THE REACTION OF THE SALIVA.—Tested with litmus paper, saliva is more or less alkaline and it is distinctly so towards lacmoid and Congo red, but it is acid when tested with phenolphthalein. It is thus said to be amphoteric, like blood and urine. Difficulty in deciding as to the reaction of saliva is partly due to the fact that it changes on standing because carbon-dioxide (CO_2) is dissipated, thus making it more alkaline. To succeed in determining the reaction of saliva, we must therefore under-

stand to what its amphoteric behavior is due and we must constantly bear in mind that the real reaction of a fluid is the ratio between free H- and OH-ions (see p. 30). By analysis saliva has been found to contain phosphates and carbonates, both of which are capable of existing either as acid or alkaline salts, that is to say, as NaH_2PO_4 and NaHCO_3 (acid salts) or Na_2HPO_4 and Na_2CO_3 (alkaline salts). Since the reaction given by solutions which contain such mixtures of acid and alkaline salts depends, first, on the relative proportions of these salts and, secondly, on the exact indicator employed to test the reaction (see p. 31), it is plain that the reaction of the saliva as ordinarily tested must be very haphazard.

To determine the H-ion concentration of saliva, some of this fluid is diluted about ten times with distilled water, which has been boiled and cooled so as to free it of carbon dioxide, and 0.5 c. c. of paranitrophenol solution is added. The resulting tint is then compared with that obtained by adding 0.5 c. c. of the same indicator to each of a series of test tubes containing varying proportions of acid and alkaline phosphate solutions ($1/15$ normal). The H-ion concentration of the saliva is equal to that of the phosphate solution which gives the same test.

THE METHOD OF MEASURING THE NEUTRALIZING POWER OF SALIVA.—Interesting though H-ion results may be, they do not appear to be of any practical value in connection with the relationship between the saliva and caries of the teeth. To study this question it has been found to be of more value to determine *the neutralizing power* of saliva; that is, to find out how much standard acid or alkali we must add to a measured quantity of saliva in order to get a change with one or more of the above indicators. In doing this, however, we are immediately struck with the fact that the reaction does not change in proportion to the amount of acid or alkali added, but that the saliva under such conditions possesses the property of changing very slowly in reaction. This same property also exists in the blood, and it depends on a series of changes which the phosphates and carbonates can undergo, when acids or alkalies are added to solutions containing them,

without causing any considerable amount of free H- or OH-ion to be set free. This has been called the "buffer action" of such salts. It endows the saliva with the power of locking away considerable quantities of acid or alkali.

In actually measuring the neutralizing power of saliva, it is best first of all to bring the saliva to some readily detectable H-ion concentration, on the acid side of neutrality, and then to find out how much alkali is required to bring it to another definite H-ion concentration, on the alkaline side.

The methods for applying the above principles are as follows:

10 c.c. saliva is diluted in an evaporating dish with 20 c.c. water which has been boiled to expel CO_2 and then cooled to 20°C . About eight drops of an aqueous solution of paranitrophenol is then added and N/200 HCl run in from a burette, with constant stirring until the yellow color due to the indicator just disappears. The amount of N/200 HCl is noted. N/200 NH_4HO is then added till the yellow color just returns.¹ The difference between the two readings gives the *alkalinity* in terms of c.c. of N/200 HCl.

The *acidity* may be directly measured by adding four drops of an alcoholic solution of phenolphthalein to another 10 c.c. sample of saliva and running in N/200 NaOH until a definite pink color results.

Addition of the acidity and alkalinity results gives the total neutralizing power of the saliva, or in other words *the power of maintaining neutrality*. This is a much more constant property of saliva than the acidity or alkalinity alone, and it has consequently been used, in the most recent work of Marshall,² for the purpose of ascertaining *whether the susceptibility to dental caries bears any relationship to the reaction of the saliva*. It was found that it does not. On the other hand, this author has shown

¹The reason for titrating back with N/200 NH_4HO till a yellow color again reappears, when measuring the alkalinity, is to increase the accuracy of the titration, it being often difficult to decide the point at which the color disappears when N/200 acid is added, but easy to decide when it reappears when N/200 NH_4HO is used. NaOH is employed in the acidity titration because phenolphthalein cannot be used with ammonia.

²Cf. J. A. Marshall, Amer. Jour. of Physiology, 1915, XXXVI, p. 260.

that the neutralizing power of saliva, collected without any effort or artificial stimulation of the mouth (resting saliva), is very distinctly less than that of saliva collected whilst chewing on a piece of paraffin (activated saliva), and that this difference *becomes very much less in those with carious teeth*. Marshall has suggested that we should express the ratio of the neutralizing power of resting saliva to that of activated saliva as a percentage ratio, which he calls the *salivary factor*. In persons immune from caries this factor amounted to 43-80; in those with caries it varied from 80-132. The following examples will illustrate these points:

Case	NORMAL RESTING SALIVA			ACTIVATED SALIVA			Salivary Factor
	c. c. N/200 HCl	c. c. N/200 NaOH	Neutralizing Power	c. c. N/200 HCl	c. c. N/200 NaOH	Neutralizing Power	
No caries	22.22	7.60	29.82	57.55	0.90	58.45	51
Carious	18.50	7.00	25.50	22.80	2.13	24.93	102

If these interesting observations should prove to be confirmed by other observers, a comparatively simple method will be available for solving what has hitherto been a most puzzling question. Several observers, particularly Bunting and Price, have employed the very delicate physico-chemical methods of the concentration cell (p. 31) and electrical conductivity in their attempts to solve it.

Before leaving the subject of the relationship between the character of the saliva and the occurrence of dental caries, it may be well to point out that other factors besides the neutralizing power of the saliva must be taken into consideration, namely, its amount and the presence of phosphates. A large and free flow of saliva, besides mechanically cleansing the teeth, will offer more neutralizing fluid. An excess of phosphates, on the other hand, will encourage fermentation of any carbohydrate which may be adherent to the teeth and, by forming acids, thus tend to erode the teeth and predispose to caries.

Tartar Formation and Salivary Calculi.—Under certain conditions a precipitate, varying in color from pale yellow to almost black, collects on the teeth, particularly on the lower incisors and molars. This precipitate is called *tartar*, and it may be either hard (as on the incisors) or soft (as on the molars). Its chemical composition varies considerably, but may be given as follows:

	I	II
Water and organic matter.....	32.24 per cent	31.48 per cent
Magnesium phosphate	0.98 per cent	4.91 per cent
Calcium phosphate	63.08 per cent	72.73 per cent
Calcium carbonate	3.7 per cent	—

(Talbot)

The organic matter consists of epithelial scales, other extraneous matter and leptothrix chains. The place and manner of deposition shows clearly that the tartar is largely derived from the saliva, the chemical explanation of the precipitation being probably as follows: Saliva, as it is produced in the gland, contains calcium bicarbonate, which is soluble in water, and is prevented from changing into the insoluble carbonate by the presence of free carbon dioxide in solution. When the saliva is discharged into the mouth some of the carbon dioxide escapes from it so that the bicarbonate changes to carbonate and becomes precipitated. The precipitate carries down with it phosphates as well as any organic debris or micro-organisms that may be present.

The precipitation of calcium carbonate may even take place in the salivary ducts (Wharton's), thus forming *salivary calculi*, which may reach the size of a pea or larger. Such calculi may contain as much as 3.8 per cent of organic matter, the remainder being largely calcium carbonate. The following table gives the composition of three such calculi:

	I	II	III
Calcium carbonate	81.2 per cent	79.4 per cent	80.7 per cent
Calcium phosphate	4.1 per cent	5.0 per cent	4.2 per cent
Magnesium phosphate ...		present	
Organic matter and other soluble solids	13.3 per cent	13.3 per cent	13.4 per cent
Water	1.3 per cent	2.3 per cent	1.7 per cent

(Talbot)

CHAPTER V.

DIGESTION (Cont'd).

Mastication: Deglutition: Vomiting.

Mastication.—By the movements of the lower jaw on the upper, the two rows of teeth come together so as to serve for biting or crushing the food. The resulting comminution of the food forms the first step in digestion. The manner of occlusion of the cusps of the teeth in the performance of this act is not a problem of Physiology, but rather of Anatomy and Orthodontics; nevertheless, the other factors which contribute to the efficiency of the process and the condition into which the food is brought by it are subjects to which we must devote some attention. The up and down motion of the lower jaw results in biting by the incisors, and after the mouthful has been taken, the side to side movements enable the grinding teeth to crush and break it up into fragments of the proper size for swallowing. The most suitable size of the mouthful is about five cubic centimeters, but this varies greatly with habit. After mastication, the mass weighs from 3.2 to 6.5 gram, about one-fourth of this weight being due to saliva. The food is now a semi-fluid mush containing particles which are usually less than 2 millimeters in diameter. Some, however, may measure 7 and even 12 millimeters.

Determination of the proper degree of fineness of the food is a function of the tongue, gums and cheeks, for which purpose the mucous membrane covering them is supplied with very sensitive touch nerve endings (see p. 244). The sensitiveness of the tongue, etc., in this regard explains why an object which can scarcely be felt by the fingers seems to be quite large in the mouth. If some particles of food that are too large for swallowing happen to be carried backward in the mouth, the tongue returns them for further mastication.

The saliva assists in mastication in several ways: (1) by dis-

solving some of the food constituents; (2) by partially digesting some of the starch; (3) by softening the mass of food so that it is more readily crushed; (4) by covering the bolus with mucus so as to make it more readily transferable from place to place. The secretion of saliva is therefore stimulated by the chewing movements, and its composition varies according to the nature of the food (p. 43). In some animals, such as the cat and dog, there is no mastication, the food being merely coated with saliva and then swallowed. In man the ability thus to bolt the food can readily be acquired, not however without some detriment to the efficiency of digestion as a whole. Soft starchy food is little chewed, the length of time required for the mastication of other foods depending mainly on their nature, but also to a certain degree on the appetite and the size of the mouthful.

The crushing force of the molars, as measured by a dynamometer, can be made to rise as high as 270 pounds, but this is far in excess of the force required to crush the ordinary food stuffs. Thus cooked meats have a crushing point which varies between 15 and 80 pounds on direct thrust, but is considerably less when there is a side to side movement, as there is in chewing. Candies have a crushing point of 30 to 110 pounds, and nuts 55 to 170 pounds. Admixture of the food with saliva greatly lowers the crushing point, especially in the case of such foods as soft bread. Without such admixture this hardens into a solid mass when it is crushed, whereas it readily breaks up into small particles in the presence of saliva.

It cannot be too strongly insisted upon that the act of mastication is of far more importance than merely to break up and prepare the food for swallowing. It causes the food to be moved about in the mouth so as to develop its full effect on the taste buds; the crushing also releases odors which stimulate the olfactory epithelium. On these stimuli depend the satisfaction and pleasure of eating, which in turn initiate the process of gastric digestion (see p. 60). Thus it has been observed in children with gastric fistulæ that the chewing of agreeable food caused the gastric juice to be actively secreted, which, however, was not the case when tasteless material was chewed.

The benefit to digestion as a whole of a large secretion of saliva, brought about by persistent chewing, has been assumed by some to be much greater than it really is, and there has existed, and indeed may still exist, a school of faddists who, by deliberately chewing far beyond the necessary time, imagine themselves to thrive better on less food than those who occupy their time with other more profitable pursuits.

Deglutition or Swallowing.—After being masticated the food is rolled up by the tongue, acting against the palate, into a bolus, and this, after being lubricated by saliva, is moved, by elevation

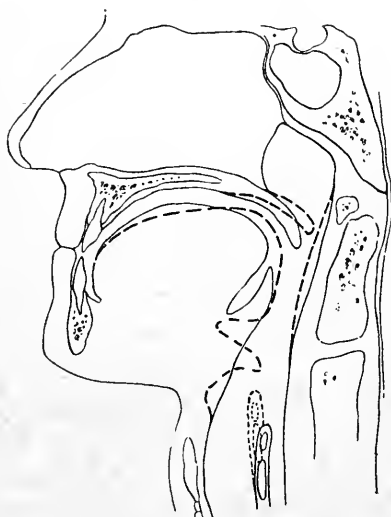


Fig. 4.—The changes which take place in the position of the root of the tongue, the soft palate, the epiglottis and the larynx during the second stage of swallowing. The thick dotted line indicates the position during swallowing.

of the front of the tongue, towards the back of the mouth. This constitutes the *first stage* of swallowing, and is, so far, a voluntary act. About this time a slight inspiratory contraction of the diaphragm occurs—the so-called respiration of swallowing—and the mylohyoid muscle of the floor of the mouth quickly contracts with the consequence that the bolus passes between the

pillars of the fauces. This marks the beginning of the *second stage*, the first event of which is that the bolus, by stimulating sensory nerve endings, acts on nerve centers situated in the medulla oblongata so as to cause a coordinated series of movements of the muscles of the pharynx and larynx and an inhibition for a moment of the respiratory center (p. 219). The movements alter the shape of the pharynx and of the various openings into it in such a manner as to compel the bolus of food to pass into the œsophagus: (see Fig. 4) thus, (1) the soft palate becomes elevated and the posterior wall of the pharynx bulges forward so as to shut off the posterior nares, (2) the posterior pillars of the fauces approximate so as to shut off the mouth cavity, and (3) in about a tenth of a second after the mylohyoid has contracted, the larynx is pulled upwards and forwards under the root of the tongue, which by being drawn backwards becomes banked up over the laryngeal opening. This pulling up of the larynx brings the opening into it near to the lower half of the dorsal side of the epiglottis, but the upper half of this structure projects beyond and serves as a ledge to guide the bolus safely past this critical part of its course. (4) To further safeguard any entry of food into the air passages, the laryngeal opening is narrowed by approximation of the true and false vocal cords.

The force which propels the bolus, so far, is mainly the contraction of the mylohyoid, assisted by the movements of the root of the tongue. When it has reached the lower end of the pharynx, however, the bolus readily falls into the œsophagus, which has become dilated on account of a reflex inhibition of the constrictor muscles of its upper end. This so-called second stage of swallowing is therefore a complex coordinated movement initiated by afferent stimuli and involving reciprocal action of various groups of muscles: inhibition of the respiratory muscles and of those that constrict the œsophagus, and stimulation of those that elevate the palate, the root of the tongue and the larynx. It is purely an involuntary process.

The *third stage of deglutition* consists in the passage of the swallowed food along the œsophagus. The way in which this is done depends very much on the physical consistence of the food.

A *solid bolus*, that more or less fills the œsophagus, excites a typical peristaltic wave, which is characterized by a dilatation of the œsophagus immediately in front of, and a constriction over and behind the bolus. This wave travels down the œsophagus at such a rate that it reaches the cardiac sphincter in about five or six seconds. On arriving here the cardiac sphincter, ordinarily contracted, relaxes for a moment so that the bolus passes into the stomach. The peristaltic wave travels much more rapidly in the upper portion of the œsophagus than lower down because of differences in the nature of the muscular coat, this being of the striated variety above, and of the non-striated, below. The purpose of more rapid movement in the upper portion is no doubt that the bolus may be hurried past the regions, where, by distending the œsophagus, it might interfere with the function of neighboring structures, such as the heart. The peristaltic wave of the œsophagus, unlike that of the intestines (see p. 79), is transmitted by nerves, namely, by the œsophageal branches of the vagus. If these be severed, but the muscular coat left intact, the œsophagus becomes dilated above the level of the section and contracted below, and no peristaltic wave can pass along it; on the other hand, the muscular coat may be severed (by crushing, etc.) but the peristaltic wave will jump the breach, provided no damage has been done to the nerves.

The propagation of the wave by nerves indicates that the second and third stages of deglutition must be rehearsed, as it were, in the nerve centers from which arise the fibers to the pharynx and the different levels of the œsophagus. *The afferent stimuli which initiate this process* arise, not as might be expected, in the œsophagus itself, but in the pharynx, and they are carried to the brain by the fifth, superior laryngeal and vagus nerves; thus, a foreign body placed directly in the œsophagus does not begin to move until the pharynx is stimulated, as by touching it. The afferent fibers in the glossopharyngeal nerve exercise a powerful *inhibitory* influence on the deglutition center as well as on that of respiration. Thus, if swallowing movements be excited by stimulating the central end of the superior laryngeal nerve, they can be instantly inhibited by stimulating the

glossopharyngeal, and the respiratory movements stop in whatever position they may have been at the time.

This inhibition of the œsophagus is indeed a most important part of the process when *liquid or semi-liquid food* is swallowed. By the contraction of the mylohyoid muscle, fluids are quickly shot down the distended œsophagus, at the lower end of which, on account of the cardiac sphincter being closed, they accumulate until the arrival of the peristaltic wave which has meanwhile been set up by stimulation of the pharynx. If the swallowing is immediately repeated, as is usually the case in drinking, the œsophagus remains dilated because peristalsis is inhibited, and the fluid lies outside the cardiac orifice until the last mouthful has been taken.

These facts have been revealed by listening with a stethoscope to the sounds produced by swallowing, and by observing with an X-ray lamp the shadows produced along the course of the œsophagus when food, impregnated with bismuth subnitrate, is taken. When a solid bolus is swallowed, one sound is usually heard, but with liquid food there are two, one at the upper end, due to the rush of the fluid and air, and the other occurring four or six seconds later at the lower end (heard over the epigastrium), and due to the arrival of the peristaltic wave with the accompanying opening of the cardiac sphincter and the escape of the fluid and air into the stomach. Sometimes, as when the person is in the horizontal position, this second sound may be broken up into several, indicating that, unassisted by gravity, the fluid does not so readily pass through the sphincter. The X-ray shadows yield results in conformity with the above. After swallowing milk and bismuth, for example, the shadow falls quickly to the lower end of the œsophagus and then slowly into the stomach. When the passage of a solid bolus is watched by the X-ray method, its rate of descent will be found to depend on whether or not it is well lubricated with saliva; if not so, it may take as long as fifteen minutes to reach the stomach; if moist, but from eight to eighteen seconds.

The Act of Vomiting.—This is usually preceded by a feeling of sickness or nausea and is initiated by a very active secretion

of saliva. The saliva, mixed with air, accumulates to a considerable extent at the lower end of the œsophagus and thus distends it. A forced inspiration is now made, during the first stage of which the glottis is open so that the air enters the lungs, but later the glottis closes so that the inspired air is sucked into the œsophagus, which, already somewhat distended by saliva, now becomes markedly so. The abdominal muscles then contract so as to compress the stomach against the diaphragm and, simultaneously, the cardiac sphincter relaxes, the head is held forward and the contents of the stomach are ejected through the previously distended œsophagus. The compression of the stomach by the contracting abdominal muscles is assisted by an actual contraction of the stomach itself, as has been clearly demonstrated by the X-ray method. (See p. 58.) After the contents of the stomach itself have been evacuated, the pyloric sphincter may also relax and thus permit the contents (bile, etc.) of the duodenum to be vomited.

The act of vomiting is controlled by a center located in the medulla, and the *afferent fibers* to this center may come from many different regions of the body. Perhaps the most potent of them come from the sensory nerve endings of the fauces and pharynx. This explains the tendency to vomit when the mucosa of this region is mechanically stimulated. Other afferent impulses come from the mucosa of the stomach itself, and these are stimulated by swallowing certain drugs called emetics, important among which are strong salt solution, mustard water, zinc sulphate, etc. When some poisonous substance has been swallowed, the immediate treatment is to give one of these emetics and thus cause the poison to be vomited. Certain other emetics, particularly tartar emetic and apomorphine, act on the vomiting center itself, and can therefore act when given subcutaneously. Afferent vomiting impulses also arise from the abdominal viscera, thus explaining the vomiting which occurs in strangulated hernia, and in other irritative lesions involving this region.

CHAPTER VI.

DIGESTION (Cont'd).

Digestion in the Stomach.

The Secretion of Gastric Juice.—After passing the cardiac sphincter, the food collects in the fundus of the stomach. When it is solid in consistency it becomes disposed in definite layers, the first swallowed near the mucosa, the last swallowed in the center. When, as is usual in man, the food is more or less fluid, it collects in the most dependent part of the body of the stomach and the layer formation is less evident (see Fig. 5). Within a few minutes of the entry of the first portion of food, the glands of the gastric mucosa begin to secrete their digestive juices. The immediate exciting cause of this secretion is not the contact of food with the mucosa—although this acts later—but is a nervous stimulus transmitted to the stomach through the vagus nerve¹ and coming from a nerve center situated in the medulla.

The activities of this gastric center are called into operation by afferent impulses in the nerves that terminate in the taste buds and olfactory epithelium. The process of gastric secretion is therefore initiated in the mouth, and the stimulus that is responsible for it is the good taste and the flavor of the food. Just as in the case of the salivary glands, the food, in order to excite the secretion, need not actually enter the mouth, for a psychological stimulus may also act on the gastric center. Thus, the sight or smell of savory food, or even the hearing of some sound that is known by experience to be associated with the gratification of the appetite can call it forth. These important facts were first of all revealed by observations through a gastric fistula (artificial opening) in the case of a boy who, because of stricture of the œsophagus, was unable to take food by the mouth. This

¹After the vagi are cut, this secretion of gastric juice does not occur.

boy had to be fed through the gastric fistula, but it was noticed that when he was allowed to chew food for which he had a relish and then spit it out, gastric secretion occurred. This observation suggested to Pavlov the establishment of analogous conditions in dogs, with the modification that, besides the fistula in the stomach, another was made in the œsophagus. The animal could therefore swallow interminably without ever becoming satisfied, because the food escaped by the œsophageal fistula.

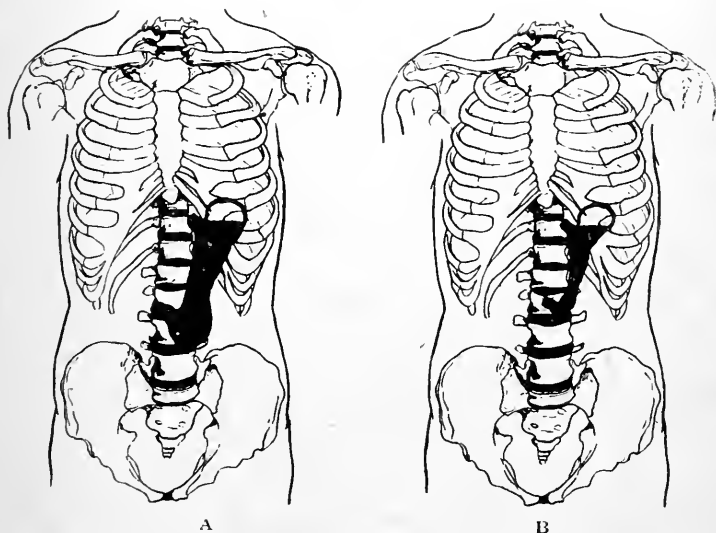


Fig. 5.—Diagrams of outline and position of stomach as indicated by skiagrams taken on man in the erect position at intervals after swallowing food impregnated with bismuth subnitrate. *A*, moderately full; *B*, practically empty. The clear space at the upper end of the stomach is due to gas, and it will be noticed that this "stomach bladder" lies close to the heart. (T. Wingate Todd.)

Nevertheless the gastric juice flowed abundantly, provided this "sham feeding" was with appetizing food. Stones, bread, acid or irritating substances, although they might cause much saliva to be secreted and swallowed (see p. 43), had no influence whatsoever on the flow of gastric juice. The only adequate stimulus was gratification of the appetite.

In passing, it may be well to call attention to the practical importance of these observations in connection with the feeding of debilitated persons; by frequent feeding with appetizing food the nutritional condition is likely to improve much more rapidly than by occasional stuffing with uncongenial mixtures, however rich these may be in calories and nitrogen.

The secretion is therefore well named the *appetite juice*, and it lasts sometimes for nearly two hours after sham feeding has been discontinued. Yet this is only about one-half as long as the time during which gastric juice is secreted when the food is ac-

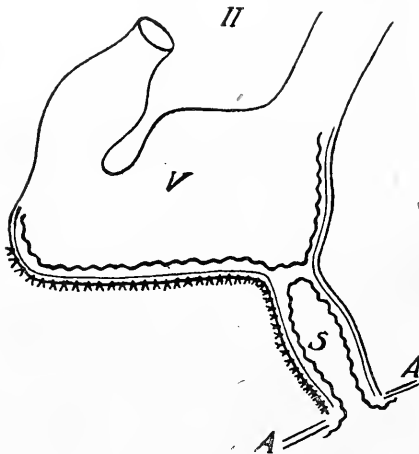


Fig. 6.—Diagram of stomach showing miniature stomach (S) separated from the main stomach (V) by a double layer of mucous membrane. A.A. is the opening of the pouch on the abdominal wall. (Pavlov.)

tually permitted to enter the stomach. In order to investigate *the cause of the continued secretion*, it was necessary to devise some means by which the gastric juice could be collected, unmixed with food, while normal digestion was in progress. As there is no duct, the only means by which this could be done was by isolating a portion of the stomach as a pouch with an opening exteriorly through which the secretions collecting in it could be removed. An operation for making such a pouch, or “miniature stomach,” as it is called, without injuring any of the nerves of

the stomach has been devised by Pavlov (see Fig. 6). By simultaneously collecting the secretions from the main stomach and the miniature stomach after sham feeding, it was found that they ran strictly parallel with each other, in amount as well as in strength of secretion. The secretion in the miniature stomach therefore accurately mirrors the secretion occurring in the main stomach, and so permits us to study this during the actual digestion of food.

By introducing food directly into the main stomach through a fistula, it was found, by observations on the secretions from the miniature stomach, that very little secretion occurred until after some time, provided of course that precautions had been taken, as by experimenting on a sleeping animal, not to excite the appetite juice. There was found to be great discrimination in the nature of the adequate stimulus for this local secretion; mechanical stimulation of the gastric mucosa, contact with alkaline fluids, such as saliva, or with white of egg, failed to produce any secretion; water had a slight effect, milk still more, whereas a marked secretion occurred when a decoction of meat or meat extract, or a solution containing the half-digested products of peptic digestion (such as Witte's peptone) was placed in the main stomach. It was further observed, when meat was directly placed in the stomach, that the juice which collected in the pouch increased, both in quantity and in strength, after the first hour, and that it continued to flow even after four hours, thus indicating that the primary stimulus had come from the extractives in the meat, further stimulation being due to the proteose and peptones liberated as the protein of the meat became digested.

This *local stimulation* is independent of the medullary nerve center that controls secretion of the appetite juice, for it still occurred after both vagi had been divided or even after destruction of the sympathetic nerve plexuses in the abdomen. It might, however, still be a nervous reflex involving the local nerve structures (plexus of Auerbach) in the walls of the stomach, although this is not so probable as that it is dependent upon some chemical excitation of the gland cells by substances appearing in the blood

as a result of absorption from the stomach. This "hormone" (see p. 124) is not merely absorbed food, for no gastric secretion occurred when solutions of meat extract, or of peptone were injected intravenously. It must therefore be some substance which is absorbed into the blood from the mucous membrane of the stomach, and which is produced in this as a result of the action of the gastric contents on its cells. In confirmation of this view it has been shown that boiled extracts of the mucous membrane of the pyloric region of the stomach (made with water or weak acid or solutions of peptone or dextrin) cause some gastric juice to be secreted when they are injected in small quantities every ten minutes into a vein, similar injections of the extracting fluids themselves being without effect.

We are now provided with the necessary facts from which to draw a completed account of the mechanism of gastric secretion. The satisfaction of taking food causes appetite juice to flow and this soon digests some of the protein. The products of this digestion, along with the extractive substances of the food, after some time (which is probably quite short in the case of man), gain the pylorus, where they act on the mucosa to produce some hormone, which becomes absorbed into the blood and stimulates further secretion of the juice. As digestion proceeds juice therefore continues to be secreted. The appetite juice sets the process agoing; it initiates gastric digestion.

The Active Constituents of Gastric Juice.—When there is no food in the stomach, a certain amount of mucous secretion is present in it, and most of the gland cells are filled with zymogen granules (see p. 40). An extract (made with glycerine) of the mucosa in this resting condition exhibits no digestive powers; but if the mucosa be first of all macerated with weak hydrochloric acid, the extract becomes highly active, because it contains large amounts of the proteolytic ferment *pepsin*. Other cells in the stomach produce the necessary *hydrochloric acid*. It may be concluded, therefore, that during the process of secretion the zymogen granules are activated by hydrochloric acid and converted to pepsin. In conformity with this, it has been found that the secretion of a pouch of stomach pre-

pared from the pyloric region possesses no digestive activity, since in this region no hydrochloric acid is secreted. The activation of the zymogen can also be accomplished by tissue extracts and by the products of micro-organismal growth. Because of such growth in the stomach contents, it is often found, in diseased conditions in which there is no acid secretion, that active pepsin, nevertheless, is present. Accompanying the pepsin, if indeed not identical with it, the gastric juice contains the milk-curdling ferment, *rennin*. It also contains a fat-splitting ferment, *lipase*, whose activities are, however, limited to emulsified fats.

The most remarkable constituent of the gastric secretion is *hydrochloric acid*, which in some animals, such as the dog, may attain a percentage of 0.6, being usually about 0.4 in the case of man. It is derived from the parietal cells of the glands in the cardiac region of the stomach, none being present in the secretion of the pyloric region, where there are no parietal cells.

The source of the acid is of course the blood, for although this is practically neutral, yet it contains, on the one hand, substances such as sodium bicarbonate which readily yield hydrogen ions, and on the other, chlorides which, by dissociation, make chlorine ions readily available. Although it is thus possible, in the light of modern physico-chemical teaching, to formulate an equation for the reaction, yet we are at a loss to explain why just at this particular place (i. e., in the gland cells of the stomach) in the animal body, and nowhere else, the Cl- and H-ions should be picked out of the blood and secreted as HCl.

Little as we know about the cause and mechanism of the secretion of hydrochloric acid, we do know something regarding its *value and use in the process of digestion*, and in general we may state that this is partly regulatory and partly digestive. It is *regulatory* in that it serves as the exciting cause of subsequent events in the digestive process, and *digestive* not only in that it actually assists in the break-down of protein, but also because it may cause a certain amount of acid hydrolysis of sugar after enough has been secreted so that some is free. Its action on protein is, however, the most important, for it initiates pro-

teolytic break-down by producing so-called acid—protein on which the pepsin—itself also dependent, as we have seen, on a preliminary activation by acid—then unfolds its action. As the protein becomes progressively broken down, the proteose and peptone which are produced absorb still more of the acid, so that it is some considerable time after gastric digestion has started before any acid is allowed to exist in the free state.

It is only after there is some free acid that it can hydrolyse sugars or perform another important function, namely, *act as an antiseptic*. In this regard, however, it must be remembered that it is only towards certain organisms that such antiseptic action is displayed, for there may be bacteria in the gastric contents even in cases of excessive secretion of hydrochloric acid. The undoubted tendency for intestinal putrefaction to increase when there is a deficient secretion of hydrochloric acid is probably dependent more upon the delay in digestion which this occasions, than upon any specific antiseptic power of hydrochloric acid. During the time that elapses before a sufficiency of hydrochloric acid has accumulated to perform this function, bacterial fermentation occurs in the stomach contents. Carbohydrates are broken down by this process, at first into simple sugars and then into lactic acid, which may come to be present in considerable amount before the fermentation process is terminated. For these reasons we find that there is relatively much more lactic acid detectable in the gastric contents removed by the stomach tube at an early stage in gastric digestion than later.

The so-called acid albumin which results from the action of the acid, becomes attacked by the pepsin, which still further breaks it down into so-called proteose and peptones, which do not coagulate by heat and which become progressively more diffusible through animal membranes. Although pepsin is capable of carrying the digestive process far beyond the stage of peptones, this does not occur in the comparatively short time (about six hours) during which the food remains in the stomach. Slight as is this action of pepsin in the stomach, it nevertheless appears to be of considerable importance for the subsequent digestion of protein by the other proteolytic ferments, trypsin and erepsin (see p. 75), which operate in the small intestine. Thus, a given

amount of blood serum becomes digested much farther in a given time by a given amount of trypsin if it receives a preliminary digestion by means of pepsin, than when it is acted on by trypsin alone, and erepsin will cause no digestion of most proteins unless these are first of all acted on by either pepsin or trypsin. But peptic digestion is not essential for life, for several cases are now on record in which individuals have thrived after the stomach has been removed.

The milk curdling action of gastric juice is due partly to the hydrochloric acid and partly to pepsin. Curiously enough the curdled milk undergoes little further change until it reaches the small intestine.

The lipase in gastric juice can act only on emulsified fat and in a neutral or alkaline reaction. Fat digestion cannot therefore be an important gastric process.

It has been supposed that there is a certain specific adaptation between the chemical nature of the food and the amount and strength of the gastric secretion. For example, it has been found, by observations on the gastric juice flowing from a miniature stomach (see Fig. 6), that feeding with bread causes a maximal secretion during the first hour, whereas with an equivalent amount of flesh the maximum occurs during the first and second hours, and with milk it is delayed till the third or fourth. In proteolytic power the bread juice is much the strongest of the three, but it contains a lower percentage of acid than the others.

The Movements of the Stomach.—Solid food after being swallowed accumulates in the body of the stomach, where on account of an absence of movements it is not uniformly acted on by the gastric juice, its outer layers only becoming digested. In the case of man, however, some of the food, because of its semi-fluid nature, passes beyond the so-called transverse band and into the pyloric region, in which waves of contraction make their appearance. Starting very faintly at this point, these waves travel towards the pylorus and become gradually more marked until they may become so deep as practically to cut off a portion of the pyloric region from the rest of the stomach. This last portion of the pylorus, sometimes called the *pyloric canal*,

gradually contracts on the food which has been forced into it, thus tending to eject it through the pyloric sphincter, or, if this is closed, to cause it to pass back again as an axial stream into the proximal part of the pylorus, which has been called the *pyloric vestibule*. These waves occur every fifteen to twenty seconds, three or four being present in the pyloric vestibule at one time. They become more marked as digestion proceeds, and are accompanied by a gradual diminution in size of the body of the stomach (see Fig. 5). Their function, besides carrying the food towards the outlet of the stomach, is to keep it properly mixed with the gastric juice.

The Opening of the Pyloric Sphincter.—The mere pressure with which the contents of the vestibule are thus driven, with each peristaltic wave, against the pyloric sphincter does not alone succeed in opening it; for half an hour after feeding with protein, for example, no food may pass the sphincter, although during this time there may have been well over a hundred peristaltic waves. Nor is it the consistency of the food which controls the opening. It must therefore be some chemical property which the food acquires during its stay in the stomach. This has definitely been shown by Cannon to be the presence of free acid. By measuring the length of the skiagram shadow in the intestines after feeding cats with bismuth-impregnated foods rendered acid or alkaline, it could be clearly shown that acid hastened the initial discharge, whereas alkalis retarded it, and observations through a fistula in the vestibule showed that any delay in the appearance of acid in the contents was associated with a delay in the opening of the sphincter.

But the sphincter does not remain open; it quickly closes after a little chyme, as the half digested food is called, has passed through it. This closure is due to stimulation of afferent nerve endings in the duodenum by the free acid in the chyme. The sphincter remains closed so long as there is any free acid in the duodenum. Whenever this acidity has become neutralized by the alkali present in the bile and pancreatic juice, the acid on the stomach side again becomes operative and the sphincter opens.

The pyloric sphincter is thus under the control of a nerve reflex, called the duodenal reflex, which transmits influences that tend to relax the sphincter when the afferent nerve fibers from the stomach side are excited by acid, but which cause it still more powerfully to contract when the acid acts on afferent fibers having their terminations in the duodenum. When both afferent paths are simultaneously stimulated, the duodenal predominates over the gastric, so that the sphincter remains closed until the acidity of the chyme in the duodenum has all been neutralized, and this seems to be true however faint the acidity may be on the duodenal side and however strong on the stomach side. The reflex arc is situated in the walls of the stomach and duodenum, for it operates after complete isolation of these from the central nervous system. It is a function of the nerve plexus found present in the walls—the myenteric plexus.

Rate of Discharge of Food from the Stomach.—The acidity of the gastric contents, as we have just seen, must attain a certain degree before it becomes an adequate stimulus for the opening of the pyloric sphincter, and consequently the rate at which the different foodstuffs leave the stomach is to a large extent proportional to their power of combination with the acid. Proteins combine with large amounts of acid, so that their initial discharge is delayed and their subsequent passage slow. Carbohydrates absorb but little acid, so that they begin to leave early and the stomach is soon emptied of them. The passage of fats is peculiar; when taken alone, which, however, is scarcely ever the case, they seem to bring about a partial relaxation of the pyloric sphincter, so that bile and pancreatic juice regurgitate into the stomach and some fat may pass out; but the subsequent discharge into the intestines is very slow, so slow indeed that each discharged portion seems to become completely absorbed before any further discharge occurs. When fats are mixed with other foods, they materially delay the discharge. These effects are no doubt due in part to the inhibitory influence which fats have on gastric secretion; and in part to the liberation of fatty acid in the duodenum by the action of pancreatic lipase. This fatty acid

seems to be liberated so quickly that it is not immediately neutralized by alkali.

Water alone begins to leave the stomach almost immediately after it is taken, because in this case the sphincter opens before an acid reaction has been acquired, and remains open on account of there being no acid in the duodenum to effect its closure. Water does not remain for a sufficient time in the stomach to excite any gastric secretion, and consequently it readily carries infection into the intestine. The discharge of raw egg albumin is peculiar. Like water it begins to pass the pylorus immediately after ingestion, its reaction for some time being alkaline; it becomes acid later, so that the discharge becomes intermittent because of the duodenal reflex. The consistency of food itself does not affect the rate of discharge unless hard particles are present in it, when a marked retardation occurs.

It is well known that the gastric contents are but slowly discharged into the duodenum when there is excessive gas accumulation in the stomach. This is due to the atony of the stomach which accompanies pathological gas accumulation.

CHAPTER VII.

DIGESTION (Cont'd).

Intestinal Digestion: The Movements of the Intestines: Absorption.

The Secretion of Bile and Pancreatic Juice.—Besides causing reflex closure of the pyloric sphincter, the contact of the *chyme*, which is the name given to the semi-digested food as it leaves the stomach, with the duodenal mucosa inaugurates the processes of intestinal digestion by exciting the secretion of bile and pancreatic juice. Neither of these juices is secreted into the intestine during fasting; but both begin to flow very soon after taking food, and they gradually increase in amount for about three hours, and then rapidly decline. The bile at first comes mainly from the gall bladder, in which it has accumulated during fasting. When the gall bladder supply has been exhausted, the bile comes directly from the liver without entering the gall bladder. This direct secretion becomes more and more marked as digestion proceeds.

Bile is partly an excretory product of the liver, and is thus being constantly secreted into the bile ducts. On account of its value as a digestive fluid it is not, however, allowed to run to waste, but is stored up in the gall bladder until food arrives in the duodenum, when the bile is immediately discharged as above described.

The sudden discharge of bile from the gall bladder is dependent upon a nerve reflex excited by the contact of the acid chyme with the duodenum. The increased secretion of bile which occurs later in digestion, like the secretion of pancreatic juice, is, however, independent of nerves, for it has been found that it occurs when acid is placed in the duodenum after all the nerves, but not the blood vessels of the duodenum, have been cut. The only way by which such a result can be explained is by assuming that the acid causes some chemical sub-

stance to be added to the blood, which then carries it to the pancreas and liver, upon the cells of which it exercises a stimulating influence. This explanation was shown to be correct by studying the effect which is produced on the secretion of pancreatic juice and bile by intravenous injections of decoctions of intestinal mucosa made with weak acid and subsequently neutralized. An immediate secretion resulted. The acid extract contains some hormone whose production, in the normal process of digestion, is evidently occasioned by the contact of the acid chyme with the duodenal mucosa. This hormone is called *secretin* but we know very little of its exact chemical nature. It is not a ferment, for it withstands heat; it is not a protein, for it can be extracted by boiling the mucous membrane with weak acids after treatment with alcohol. It is readily oxidized in the presence of alkalis, and is of the same nature in all animals. It is useless to give secretin as a drug with the hope that it will stimulate pancreatic secretion, for it is not absorbed from the lumen of the intestine.

Although most abundant in the mucosa of the duodenum and jejunum, secretin is also present in the mucosa of the lower end of the small, and to a lesser degree, in that of the large intestine. Soap solutions act like acid in producing secretin. A fatty meal, therefore, excites the flow of much pancreatic juice and bile, because the fatty acid which is split off unites with alkali and forms soap.

It may be that the first portion of pancreatic juice to be secreted after a meal, is the result, not of secretin formation, but of reflex nervous stimulation of the pancreas. In comparison with the hormone control the nervous control is, however, quite unimportant in pancreatic secretion, for there is no necessity in the intestine, as in the mouth, or to a less degree in the stomach, for a quick response to the stimulus which is set up by the presence of food. The histological changes produced in the gland cells of the pancreas by secretory activity are much the same as in the parotid glands.

Functions of the Bile and Pancreatic Juice.—These two juices are very closely associated in their activities. This fact

is perhaps most strikingly demonstrated in the digestion and absorption of fat; for, in the absence of either secretion, large amounts of unabsorbed fat appear in the fæces. Both juices contain relatively large amounts of *alkali*, which neutralizes the acidity of the chyme. In the pancreatic juice alone, for example, there is a sufficient concentration of sodium carbonate to neutralize the acid in an equal volume of gastric juice. Whenever the chyme becomes alkaline the pepsin present in it ceases to act and conditions thus become suitable for the activities of the pancreatic enzymes. Besides its neutralizing action, the bile causes the chyme to assume a somewhat greater consistency, by precipitating incompletely peptonized protein, as well as pepsin. The precipitate becomes redissolved when excess of bile has become mixed with the chyme and the significance of the precipitation may be that it causes a temporary delay in the movement of the chyme along the duodenum, thus allowing it to become properly mixed with pancreatic juice before it moves further along the intestine.

Composition, Properties and Functions of the Bile.—

Water.	85.9
Total Solids	14.1

of which :

Organic	{	Bile Salts	9.14
		Lecithin and Cholesterol	1.10
		Mucinoid Substance	}..... 2.98
		Pigment	

Inorganic Salts	0.78
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The bile is a greenish-yellow fluid of sticky consistency and bitter taste. Its most interesting constituents are the bile salts, which are complex organic substances, having an important function to perform in assisting the lipase and amylopsin of pancreatic juice in their digestive activities. Otherwise the bile contains no digestive enzymes. The cholesterol is not a readily soluble substance, so that it is apt to become precipitated in the

bile duct and cause *gall stones*. The distention of the ducts by the gall stones may cause great pain (biliary colic). The formation of gall stones is encouraged by inflammatory processes of the mucous membrane of the ducts. When bile fails to reach the intestine, because of blocking the ducts, either by gall stones or by inflammatory swelling of the mucous membrane, the digestion, especially of fats, is much interfered with, and the fæces become foul smelling and pale in color.

The Composition and Properties of Pancreatic Juice.—The pancreatic juice contains three important enzymes: *lipase* (acting on fats), *amylopsin* (acting on starch), and *trypsinogen* (acting on protein). Lipase and amylopsin are secreted in an active condition, but trypsinogen is without any action until it has become changed into *trypsin*. This does not occur until the pancreatic juice has reached the intestine, when the activation is brought about by a ferment present in the intestinal juice (secretion of Lieberkühn's follicles) called *enterokinase*. The intestinal juice contains this activator only when there is some trypsinogen present in the intestine. There is no enterokinase, for example, in the juice that is secreted as a result of mechanical stimulation of the intestinal mucosa, but it immediately appears when some pancreatic secretion is brought in contact with the mucosa.

Enterokinase is not the only substance which can activate trypsinogen; the addition to the pancreatic juice of calcium salts, or the contact of the juice with leucocytes, as in granulation tissue, or even mere standing of the juice, has a similar activating effect. If the pancreatic juice, in escaping from the duct, should run over granulation tissue, as occurs when a fistula (i. e., an opening made by surgical operation) of the duct is made, it becomes activated and unless precautions are taken it will excoriate the wound. Should it escape into the peritoneum, as when a cyst bursts, it also becomes activated.

It will be remembered that the amount of gastric juice secreted varies with different foods, being relatively more abundant on a diet of bread than on one of milk, or even meat (p. 63). Simi-

lar quantitative differences exist in the secretion of pancreatic juice and this is probably to be explained by the varying quantities of acid chyme coming in contact with the duodenal mucosa.

Chemical Changes Produced by Intestinal Digestion.—In the lower portion of the duodenum and in the jejunum, the digestive enzymes of the pancreatic juice act on the food in full intensity. The trypsin rapidly hydrolyzes the proteins to peptone, which if it is not immediately absorbed may become further broken down to amino acids and aromatic compounds. The lipase hydrolyses fat to glycerine and fatty acid, which are absorbed, the former as such, the latter, after combining with alkali to form soap, or, if no alkali be available, with bile salts to form compounds which like soap are soluble in water. Amylopsin converts into maltose any starch or dextrines which the ptyalin of saliva has failed to act on. The maltose thus formed, and the other disaccharides, cane sugar and lactose, although soluble in water, do not become absorbed into the blood as such but become further hydrolyzed by the action of so-called inverting enzymes, of which there is one for each disaccharide (see p. 25). These inverting enzymes are more plentiful in extracts of the mucosa than in the intestinal juice itself, from which we conclude that it is only after they have been absorbed into the cells of the intestines that the disaccharides are inverted. The process, in other words, is an intracellular one.

One other enzyme exists in the intestinal juice, namely, *crepsin*. It acts on partially hydrolyzed proteins and on caseinogen, so as to hydrolyze them completely into the amino acids. Erepsin is a widely distributed enzyme in the animal body, being present in practically every tissue, although it is absent from blood plasma. It is present in much greater concentration in extracts of the intestinal mucosa than in the succus entericus, so that, like the inverting enzymes, it possibly displays its action while the protein is being absorbed as proteoses and peptones. It serves as the last barrier against the entry into the blood of protein in any other form than as a mixture of amino acids. Less completely digested protein is poisonous when added to the blood (p. 152).

Most of the food is now in a suitable condition for absorption. Before we proceed to study the nature of this process, however, there are one or two further digestive changes that we must consider.

The Digestive Function of Intestinal Bacteria.—On account of the antiseptic action of free hydrochloric acid, there is, ordinarily, no bacterial growth in the stomach, but the neutralization of acid by the pancreatic juice and bile in the intestine provides a perfect medium for such growth. The extent and nature of the bacterial growth varies very greatly according to the nature of the diet.

There can be no doubt that the micro-organisms are a valuable aid to digestion in the case of most animals, especially of those whose diet includes cellulose. Indeed, in such animals as the herbivora special provision is made to encourage bacterial growth by the great length of the large intestine, for without bacteria, digestion of cellulose is impossible. Thus if newly-hatched chicks be fed with sterilized grain they succumb in about two weeks, but if a small amount of the excrement of the fowl be mixed with the grain, they thrive as ordinarily. On the other hand, if the food contains no cellulose, animals may develop and grow with sterile intestinal contents; thus guinea pigs have been removed from the uterus under aseptic conditions and kept in a sterile place on sterilized milk and have thrived and grown as normal guinea pigs. The organisms in the intestine of man are probably much more useful than harmful. No doubt they are parasites, but they are useful parasites; they work for their living, not only by assisting when necessary in the digestion of food but also by destroying certain substances which, if absorbed, would have a toxic action on the host. Thus cholin, a substance produced by the digestion of lecithin, is distinctly poisonous, but it really never gets into the blood because the bacteria destroy it.

In the case of man bacterial digestion occurs in both the small and the large intestines, and there are varieties of bacteria capable of acting on all the foodstuffs. They may break up the sugars into lactic acid or even further so as to form CO_2 and H. It has been claimed that this formation of lactic acid in the intestine is

of benefit to the health of man because when it occurs other bacteria which are more harmful than useful become destroyed. To encourage this growth of lactic acid bacteria, it has been recommended that large quantities of sour milk should be taken. It is undoubtedly true that such treatment is of benefit in many persons who suffer from excessive intestinal putrefaction, but that such treatment should prolong the life of otherwise healthy individuals is visionary. As in herbivora, there are also bacteria in man which break up cellulose, producing methane and CO_2 . After diets containing much vegetable matter, therefore, a large amount of gas is likely to accumulate in the intestines. From fats, the intestinal bacteria produce lower fatty acids, which tend to cause the contents in the lower portion of the small intestines to become acid in reaction.

Although capable of hydrolyzing native protein from the very start, bacteria act most readily on protein that has been partially digested by the proteolytic enzymes of the stomach and intestines. The products of this action are more or less characteristic because of the peculiar manner in which the aromatic groups of the protein molecule are attacked, producing from it such substances as phenol, skatol, indol, etc., to which the characteristic odor of the faeces is due. When protein has been adequately digested in the stomach, it is so rapidly acted on by the trypsin (and erepsin) of the small gut and is so quickly absorbed that bacteria have no chance to act on it. When protein has been inadequately digested in the stomach, however, the trypsin fails to digest it quickly enough, so that bacterial putrefaction sets in which may be quite marked in the small intestine, although much more so in the colon. Even when they do not find a suitable substrat in the food, the bacteria attack the proteins of the intestinal secretions themselves, which accounts for the well-known occurrence of this process during starvation.

The Immunity of the Walls of the Digestive Organs Toward the Enzymes Which Act within Them.—The immunity of the mucosa of the stomach and intestines seems to be due in main to the presence in the cells of the mucosa of anti-enzymes, that is, of substances which can inhibit the action of the various enzymes

(antipepsin, antitrypsin, etc.). As we should expect, very strong anti-enzymes can be prepared from tapeworms and other intestinal worms. It is by virtue of possessing these, that the worms are not digested. The immunity of the gland cells and ducts, as of the pancreas, to the proteolytic enzymes which they produce is possibly to be explained in another way, namely, by the existence of the enzyme as an inactive precursor (e. g., trypsinogen) until after the secretion has been carried to a region whose walls contain the specific anti-body. A certain degree of immunity to the destructive action of the intestinal bacteria on the mucous membrane may be conferred by the mucin, which is quite abundant, at least in the empty stomach and in the large intestine. The relatively poor growth of bacteria which occurs on inoculating faecal matter in culture media—although many bacteria can be seen by microscopic examination to be present—is probably to be explained by their having been killed by the mucin.

The Movements of the Intestines.

The Movements of the Small Intestine have two functions: (1) to macerate and mix up the food and (2) to move it along towards the lower end of the gut. These two functions are subserved by two different types of movement, the so-called pendular and the peristaltic. The *pendular movements* are rendered evident by allowing the intestine to float out in a bath of isotonic saline (p. 30), when the various loops sway from side to side like a pendulum. By closer examination it can be seen that the movements are produced by faint waves of contraction of both muscular coats, which sweep with considerable rapidity along the gut. When the waves arrive at a part of the intestine containing any solid substance, they become accentuated, and this becomes most marked at the middle of the solid mass of food, thus tending, on account of the contraction of the circular fibers, to divide the mass into two. These movements are therefore sometimes called *segmenting movements*. Their function is evidently to break up the food masses and thus mix the food with the digestive juices. This can be very well shown in skiagram shadows of the ab-

domen some time after taking food mixed with bismuth. A column of food can be seen to divide into several segments, each of which in a few seconds breaks into two, the neighboring halves then joining together, and the process repeating itself.

Two varieties of *peristaltic waves* are usually described, both of which are characterized by a marked constriction preceded by a distinct dilatation of the gut, which may extend for a considerable distance down it (two feet). The one variety of wave travels slowly ($\frac{1}{2}$ cm. per minute), and has the function of carrying along the food; the other travels very rapidly (peristaltic rush), and is evidently for the purpose of hurrying along irritating substances.

Besides being set up by the presence of food in the intestine, these waves may be influenced through the nervous system; stimulation of the vagus excites them, whereas stimulation of the sympathetic brings about a marked inhibition, in which the whole gut becomes profoundly relaxed with the exception of the ileo-colic sphincter, which contracts. This influence of the splanchnic may be excited reflexly, as by pain or fear.

The Movements of the Large Intestine are more difficult to study than those of the small intestine. They vary considerably in different animals, as indeed is to be expected when we remember that the function of this part of the alimentary tract depends upon the nature of the food. In herbivora, for example, food may lie in the capacious cæcum for days, and even in carnivora, in which this part of the gut is rudimentary, it may remain for twenty-four hours. In man the conditions seem to be intermediate between those in the herbivora and carnivora, and the movements are believed to be as follows: As the semi-fluid food enters the cæcum through the ileo-cæcal valve and collects in the cæcum and proximal colon, it excites the occurrence of waves of constriction, which start probably about the hepatic flexure and travel in a *central* direction towards the cæcum, into which the food is thus forced back.

Occasionally the arrival of the wave at the cæcum starts a true peristaltic wave, which travels *distally*, getting feebler as it proceeds, and which may carry some of the contents into the

transverse colon. Here the contents assume more or less of the consistency of fæces, and more powerful peristaltic waves make their appearances so that the solid masses are carried on towards the rectum. These waves are sufficiently energetic to keep the descending colon comparatively empty, and the faecal masses gradually accumulate in the sigmoid flexure and rectum until evacuated by the act of defæcation.

Examination of the accompanying diagram (Fig. 7) will show how long food takes to pass along the various parts of the gastrointestinal tract.

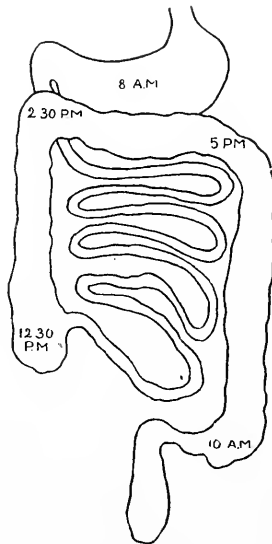


Fig. 7.—Diagram of time it takes for a capsule containing bismuth to reach the various parts of the large intestine.

The Absorption of Food.

As has been explained, the whole object of digestion is to break up the large molecules of which food is composed into smaller ones so that they can be absorbed into the blood or lymph which circulates in the mucous membrane of the intestines. Except under unusual circumstances, no absorption occurs until the small intestine is reached. Here sugars are absorbed into the blood

as dextrose, and proteins as amino acids, whilst fats are absorbed into the lymphatic vessels, as fatty acids and glycerine. These substances are absorbed in solution, which would lead us to expect that, because of the water absorbed along with them, the contents of the small intestine would be more solid at its lower than at its upper end; but this is not the case, for the digestive juices which have been secreted make up for the loss of water. It is in the large intestine that the water is finally absorbed.

Attempts have been made to explain the mechanism of absorption in terms of the known laws of filtration, osmosis, surface tension, and imbibition, but little further progress has been made than to establish the fact that although these processes may play a role, they are not alone responsible. Thus, if blood serum be placed in an isolated loop of intestine, it will become entirely absorbed, even although identical in all the above properties with the blood of the animal. That osmosis does have some influence, however, is evidenced by the well-known effect of a strong saline solution in the intestine; it attracts water from the blood, thus diluting the intestinal contents and stimulating peristaltic contractions. It is in this way that saline cathartics act.

Regarding the absorption of fats, it is now definitely known that these are first of all split into fatty acid and glycerine by the action of the lipase of pancreatic juice. The fatty acid then unites with alkali to form a soap, or with bile salts to form a soluble compound. In either case, the dissolved fatty acid passes into the intestinal epithelium, into which is also absorbed the glycerine, the two re-uniting after their absorption so as to form neutral fat again. The neutral fat then passes into the central lacteal of the villus, whence it is transported by the abdominal lymphatics to the thoracic duct, which discharges it into the subclavian vein on the left side of the root of the neck.

Hunger sensations coincide with stomach contractions, but these differ from those which occur during digestion. *Thirst* is due to dryness of the throat. It is temporarily relieved by moistening the throat, but unless liquid is swallowed permanent thirst develops because the tissues become dry.

Resumé of Actions of Digestive Enzymes.

SECRETION	ENZYME OR ADJUVANT AGENCY	ACTION
<i>Saliva</i>	Ptyalin Alkalies	Converts boiled starch into maltose. Favors action of ptyalin.
<i>Gastric juice</i>	Pepsin HCl	(1) Converts metaproteins (acid albumin, etc.) into proteoses and peptones. (2) Clots milk. (1) Produces metaproteins. (2) Acts as antiseptic. (3) Stops action of ptyalin.
<i>Pancreatic juice</i>	Lipase Trypsinogen Lipase Amylopsin Alkali	Acts on emulsified fats. Inactive until acted on by enterokinase. Splits neutral fat into fatty acid and glycerine. Converts all starches into maltose. (1) Helps to neutralize HCl of chyme. (2) Combines with fatty acid to form soaps.
<i>Bile</i>	Bile salts Alkali	(1) Augment the action of lipase and amylopsin. (2) Precipitate pepsin and peptones in chyme. (3) Combines with fatty acids. (1) Helps to neutralize HCl of chyme. (2) Combines with fatty acid to form soaps.
<i>Intestinal juice</i>	Enterokinase Erepsin Inverting enzymes	Converts trypsinogen into trypsin, which splits proteins into amino bodies. Converts caseinogen and peptones into simple amino bodies. One for each disaccharide, splitting them into monosaccharides.
<i>Bacteria</i>	Acting on carbohydrates Acting on fats Acting on proteins	(Both the last two enzymes are more plentiful in the epithelium than in the intestinal juice.) (1) Digest cellulose. (2) Splits monosaccharides into lactic and lower acids. Split higher, into lower fatty acids. Split off aromatic groups, as phenol, cresol, etc. (Besides these specific actions, bacteria may perform many of the digestive functions of the juices.)

CHAPTER VIII.

METABOLISM.

The Energy Balance.

Introductory.—The object of digestion, as we have seen, is to render the food capable of absorption into the circulatory fluids, the blood and lymph. The absorbed food products are then transported to the various organs and tissues of the body, where they may be either used or stored away against future requirements. After being used, certain substances are produced as waste products, and these pass back into the blood to be carried to the organs of excretion, by which they are expelled from the body. By comparison of the amount of these excretory products with that of the constituents of food, we can tell how much of the latter has been retained in the body, or lost from it. This constitutes the subject of *general metabolism*. On the other hand, we may direct our attention, not to the balance between intake and output, but to the chemical changes through which each foodstuff must pass between its absorption and excretion. This is the subject of *special metabolism*. In the one case we content ourselves with a comparison of the raw material which is acquired and the finished product which is produced by the animal factory; in the other, we seek to learn something of the particular changes to which each crude product is subjected before it can be used for the purpose of driving the machinery of life or of repairing the worn out parts of the body.

In drawing up such a balance sheet of general metabolism, we must select for comparison substances which are common to both intake and output. In general the intake comprises, besides oxygen, the proteins, fats and carbohydrates, and the output, carbon dioxide, water and the various nitrogenous constituents of urine. This dissimilarity in chemical structure between the substances ingested and those excreted limits us, in balancing the one

against the other, to a comparison of the smallest fragments into which each can be broken. Such fragments are the elements, and of these carbon and nitrogen alone can be measured with accuracy in both intake and output. From the balance sheets of intake and output of carbon and nitrogen, and from information obtained by observing the ratio between the amounts of oxygen consumed by the animal and of carbonic acid (CO_2) excreted, we can draw far-reaching conclusions regarding the relative amounts of protein, fat and carbohydrate which have participated in the metabolism.

As has already been stated, the essential nature of the metabolic process in animals is one of oxidation, that is, one by which large unstable molecules are broken down to those that are simple and stable. During this process of *katabolism*, as it is called, the potential energy locked away in the large molecules becomes liberated as actual or kinetic energy, which takes the form of movement and heat. It therefore becomes of importance to compare the actual energy which an animal expends in a given time with the energy which has meanwhile been rendered available by metabolism. This is called the *energy balance*. We shall first of all consider this and then proceed to examine somewhat more in detail the *material balance of the body*.

Energy Balance.

The unit of energy is the large calorie (written C), which is the amount of heat required to raise the temperature of one kilogramme of water through one degree (Centigrade) of temperature.¹ We can determine the caloric value by allowing a measured quantity of a substance to burn in compressed oxygen in a steel bomb which is placed in a known volume of water at a certain temperature. Whenever combustion is completed, we ascertain the increase in temperature of the water in degrees (Centigrade), and multiply this by the volume of water in

¹The distinction between a calorie and a degree of temperature must be clearly understood. The former expresses *quantity* of actual heat energy; the latter merely tells us the intensity at which the heat energy is being given out.

liters. Measured in such a calorimeter, as this apparatus is called, it has been found that the number of calories liberated by burning one gramme of each of the proximate principles of food is as follows:

Carbohydrates	{ Starch	4.1
	{ Sugar	4.0
Protein		5.0
Fat		9.3

The same number of calories will be liberated at whatever rate the combustion proceeds, provided it results in the same end products. When a substance, such as sugar or fat, is burned in the presence of oxygen, it yields carbon dioxide and water, which are also the end products of the metabolism of these foodstuffs in the animal body; therefore, when a gramme of sugar or fat is rapidly burned in a calorimeter, it releases the same amount of energy as when it is slowly oxidized in the animal body. But the case is different for proteins, because these yield less completely oxidized end-products in the animal body than they yield when burned in oxygen; so that, to ascertain the physiological energy-value of protein, we must deduct from its physical heat value (calories) the physical heat-value of the incompletely oxidized end-products of its metabolism. It is obvious that we can compute the total available energy of our diet by multiplying the quantity of each foodstuff by its caloric value.

In order to measure the energy which is actually liberated in the animal body, we must also use a calorimeter, but of somewhat different construction from that used by the chemist, for we have to provide for long continued observations and for an uninterrupted supply of oxygen to the animal. *Animal calorimeters* are also usually provided with means for the measurement of the amounts of carbon dioxide (and water) discharged and of oxygen absorbed by the animal during the observation. Such respiration calorimeters have been made for all sorts of animals, the most perfect for use on man having been constructed in America (see Fig. 8). As illustrating the extreme accuracy of even the largest of these, it is interesting to note that the actual heat given out when a definite amount of alcohol or ether is

burned in one of them exactly corresponds to the amount as measured by the smaller bomb calorimeter. All of the energy liberated in the body does not, however, take the form of heat. A variable amount appears as mechanical work, so that to measure in calories all of the energy which an animal expends, one must add to the actual calories given out, the caloric equivalent of

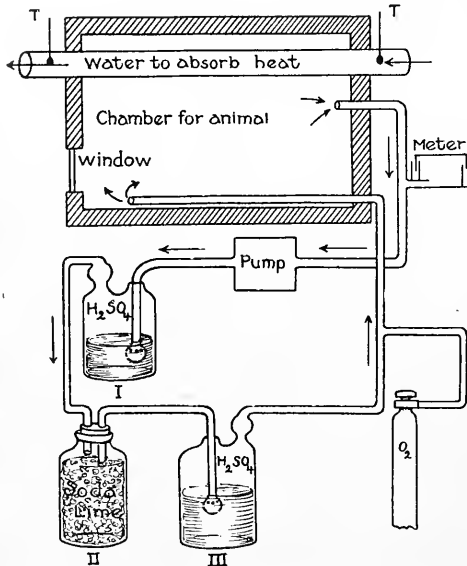


Fig. 8.—Diagram of Atwater-Benedict *Respiration Calorimeter*. As the animal uses up the O_2 , the total volume of air shrinks. This shrinkage is indicated by the meter, and a corresponding amount of O_2 is delivered from the weighed O_2 -cylinder. The increase in weight of bottles II and III gives the CO_2 .

the muscular work which has been performed by the animal during the period of observation. This can be measured by means of an ergometer, a calorie corresponding to 425 kilogrammeters² of work. That it has been possible to strike an accurate balance between the intake and the output of energy of the animal body, is one of the achievements of modern experimental biology. It can be done in the case of the human ani-

² A kilogrammeter is the product of the load in kilograms multiplied by the distance in meters through which it is lifted.

mal; thus, a man doing work on a bicycle ergometer in the Benedict calorimeter gave out as actual heat, 4,833 C., and did work equalling 602 C., giving a total of 5,435 C. By drawing up a balance sheet of his intake and output of food material during this period, it was found that the man had consumed an amount capable of yielding 5,459 C., which may be considered as exactly balancing the actual output.

Having thus satisfied ourselves as to the extreme accuracy of the method for measuring energy output, we shall now consider some of the conditions which control it. To study these we must first of all determine the *basal heat production*, that is, the smallest energy output which is compatible with health. This is ascertained by allowing the man to sleep in the calorimeter and then measuring his calorie output while he is still resting in bed in the morning, and fifteen hours after the last meal. When the results thus obtained on a number of individuals are calculated so as to represent the calorie output per kilogram of body weight in each case, it will be found that 1 C. per kilo per hour is discharged. That is to say, the total energy expenditure in 24 hours in a man of 70 kilos, which is a good average weight, will be $70 \times 24 = 1,680$ C.

When food is taken the heat production rises, the increase over the basal heat production amounting, for an ordinary diet, to about ten per cent. Besides being the ultimate source of all the body heat, food is therefore a direct stimulant of heat production. This *specific dynamic* action, as it is called, is not, however, the same for all groups of foodstuffs, being greatest for proteins and least for carbohydrates. Thus, if a starving animal is given an amount of protein which is equal in caloric value to the calorie output during starvation, the calorie output will increase by 30 per cent, whereas with carbohydrates it will increase only by 6 per cent. Evidently, then, protein liberates much free heat during its assimilation in the animal body; it burns with a hotter flame than fats or carbohydrates, although, as in the case of fats, at least, before it is completely burnt, it may not yield so much energy. This peculiar property of proteins accounts for their well-known heating qualities. It explains why protein com-

poses so large a proportion of the diet of peoples living in cold regions, and why it is cut down in the diet of those who dwell near the tropics. Individuals maintained on a low protein diet may suffer intensely from the cold.

If we add to the basal heat production of 1,680 C. another 168 C. (or 10 per cent) on account of food, the total 1,848 C. nevertheless falls far short of that which we know must be liberated when we calculate the available energy of the diet. What becomes of the extra fuel? The answer is that it is used for *muscular work*. Thus it has been found that if the observed person, instead of lying down in the calorimeter, is made to sit in a chair, the heat production is raised by 8 per cent, or if he performs such movements as would be necessary for ordinary work (writing at a desk), it may rise 29 per cent, that is to say, to 90 C. per hour. Allowing 8 hours for sleep and 16 hours for work, we can thus account for 2,168 C., the remaining 300 odd C. which is required to bring the total to that which we know, from statistical tables of the diets of such workers, to be the actual daily expenditure, being due to the exercise of walking. If the exercise be more strenuous, still more calories will be expended; thus, to ascend a hill of 1,650 feet at the rate of 2.7 miles an hour requires 407 extra calories. Field workers may expend, in 24 hours, almost twice as many calories as those engaged in sedentary occupations.

Another factor which controls the energy output is the *cooling influence of the atmosphere*. When this is marked, more heat must be liberated in order to maintain the body temperature (see p. 135). In other words, the necessary heat loss must be compensated by an increased heat production, just as we must burn more coal to keep the house at a given temperature on a cold, than on a warm, day. This adjustment of energy liberation to the rate of cooling at the surface of the body explains, among other things, why it should be that small animals give out much more energy, per unit of body weight, than those that are larger. The small animal has relatively the greater surface area, just as two cubes of equal weight when brought together have a combined weight which is double that of either cube, but a surface

area which is less than double (two surfaces having been brought together). Greater tendency to surface cooling explains why small animals should so much more quickly succumb to cold than those that are larger, and why slim persons should feel the cold more keenly than those that are stout.

Other things, such as diet, external temperature, etc., being the same, it is therefore *surface area and not body weight which determines the energy production*, a fact which is clearly demonstrated by finding that the calorie output for different animals is constant when it is calculated for each square meter of surface. Thus, a horse produces only 14.5 C. per kg. of body weight in 24 hours, whereas a mouse produces 452 C., but if we calculate according to square meter of surface the differences practically vanish. These facts, however, do not apply when the differences in size are due to age. This has been most strikingly demonstrated in the case of man, for it has been found that the calorie requirement per unit of surface is very distinctly greater in the early years of life than later. Thus, taking the discharge of carbon dioxide as a criterion of the energy discharge, the following results have been obtained from individuals sitting down:

Average age (years)	Average weight (kilograms)	Carbon dioxide discharged, per square meter of surface and hour (grams)
<i>Males</i>		
9 2/3	28	29.9
12 1/2	34	26.5
15 1/2	51	23.5
19 1/2	60	21.8
25	68	18.5
35	68	16.9
45	77	16.3
58	85	14.2
<i>Females</i>		
8	22	26.6
12	36	20.1
15	49	16.0
17 2/3	54	14.8
30	54	16.3
45	67	17.9

This table shows us clearly that over and above the greater combustion necessary on account of their relatively greater surface, children require calories for growth. They must be fed more liberally than adults, otherwise they starve. The table further shows that boys must be more liberally fed than girls of equal age and body weight, probably because of their greater restlessness. It is on account of these greater food requirements that children are the first to die in famine.

Recent work has shown that the above conclusions are not strictly warranted by the facts, for there appear to be other factors than surface and mass of the body affecting the energy requirement of the growing organism.

CHAPTER IX.

METABOLISM (Cont'd).

The Material Balance of the Body.

We must distinguish between the balances of the organic and the inorganic foodstuffs. From a study of the former we shall gain information regarding the *sources* of the energy production whose behavior under various conditions we have just studied. From a study of the inorganic balance, although we shall learn nothing regarding energy exchange—for such substances can yield no energy—we shall become acquainted with several facts of extreme importance in the maintenance of nutrition and growth.

To draw up a balance sheet of organic intake and output requires an accurate chemical analysis of the food and of the excreta (urine and expired air). Furnished with such analyses we proceed to ascertain the total amount of nitrogen and carbon in the excreta in a given time and to calculate, from the known percentage of nitrogen in protein, how much protein must have undergone metabolism. We then compute how much carbon this quantity of protein would account for, and we deduct this from the total carbon excretion. The remainder of carbon must have come from the metabolism of fats and carbohydrates, and although we cannot tell exactly its source, yet we can arrive at a close approximation by observing the respiratory quotient (R. Q.), which is the ratio of the volume of carbon dioxide exhaled

to that of oxygen retained by the body in a given time, i. e., $\frac{\text{CO}_2}{\text{O}_2}$

When carbohydrates are the only foodstuff undergoing metabolism, the quotient is one, that is to say, the CO_2 excretion and O_2 intake are equal in volume. The reason for this is that a molecule of carbohydrate consists of C along with H and O in the same proportions as they exist in water; therefore oxygen is required

to oxidize the C., but not the H., and, since equimolecular quantities of all gases occupy equal volumes (at the same temperature and pressure), the volume of CO_2 produced equals the volume of C. required to produce it. The conditions are otherwise in the case of fats and proteins, for besides C. these molecules contain an excess of H., so that O. is required to oxidize some of the H., as well as all of the C. A greater volume of O_2 is therefore absorbed during their combustion than the volume of CO_2 that is produced, and R. Q. is about 0.7. By observing this quotient, therefore, we can approximately determine the source from which the non-protein carbon excretion is derived. Having in the above manner computed how much of each of the proximate principles has undergone metabolism, we next proceed to compare intake and output with a view to finding whether there is an equilibrium between the two, or whether retention or loss is occurring.

Starvation.—In order to furnish us with a standard condition with which we may compare others, we will first of all study the metabolism during starvation. When an animal is starved, it has to live on its own tissues, but in doing so, it saves its protein so that the excretion of nitrogen falls after a few days to a low level, the energy requirements being meanwhile supplied, as much as possible, from stored carbohydrate and fat. Although always small in comparison with fat, the stores of carbohydrate vary considerably in different animals. They are much larger in man and the herbivora than in the carnivora. *During the first few days of starvation* it is common, in the herbivora, to find that the excretion of nitrogen is actually greater than it was before starvation, because the custom has become established in the metabolism of these animals of using carbohydrates as the main fuel material, so that when this fuel is withheld, as in starvation, proteins are used more than before and the nitrogen excretion becomes greater. We may say that the herbivorous animal has become carnivorous. The same thing may occur in man when the previous diet was largely carbohydrate.

During the greater part of starvation, however, most of the energy required to maintain life is derived from fat, as little

as possible being derived from protein. This type of metabolism lasts until all the available resources of fat have become exhausted, when a more extensive metabolism of protein sets in with the consequence that the nitrogen excretion rises. This is really the harbinger of death—it is often called the *premortal rise in nitrogen excretion*. It means that all the ordinary fuel of the animal economy has been used up, and that it has become necessary to burn the very tissues themselves in order to obtain sufficient energy to maintain life. Working capital being all exhausted, an attempt is made to keep things going for a little longer time by liquidation of permanent assets. But these assets, as represented by protein, are of little real value in yielding the desired energy because, as we have seen, only 4.1 calories are available against 9.3, obtainable from fats. These facts explain why during starvation a fat man excretes daily less nitrogen than a lean man, and why the fat man can stand the starvation for a longer time.

Not only is there this general saving of protein during starvation, but there is also a discriminate utilization of what has to be used by the different organs according to their relative activities. This is very clearly shown by comparison of the loss of weight which each organ undergoes during starvation. The heart and brain, which must be active if life is to be maintained, lose only about 3 per cent of their original weight, whereas the voluntary muscles, the liver and the spleen lose 31, 54 and 67 per cent, respectively. No doubt some of this loss is to be accounted for as due to the disappearance of fat, but a sufficient remainder represents protein to make it plain that there must have been a mobilization of this substance from tissues where it was not absolutely necessary, such as the liver and voluntary muscles, to organs, such as the heart, in which energy transformation is *sine qua non* of life. The vital organs live at the expense of those whose functions are accessory.

When we compare the excretion of carbon dioxide from day to day during starvation, it will be found to remain practically constant, when calculated for each kilogram of body weight. The same is true for the calorie output. Certain unusual substances

such as creatin also make their appearance in the urine, and there is an increase in the excretion of ammonia, indicating that larger quantities of free acid are being set free in the organism.

Starvation ends in death in an adult man in somewhat over four weeks, but much sooner in children, because of their more active metabolism. At the time of death the body weight may be reduced by 50 per cent. The body temperature does not change until within a few days of death, when it begins to fall, and it is undoubtedly true that if means be taken to prevent cooling of the animal at this stage, life will be prolonged.

Normal Metabolism.—Apart from the practical importance of knowing something about the behavior of an animal during starvation, such knowledge is of great value since it furnishes a standard with which to compare *the metabolism of animals under normal conditions*. Taking again the nitrogen balance as indicating the extent of protein wear and tear in the body, let us consider first of all the conditions under which equilibrium may be regained. It would be quite natural to suppose that if an amount of protein containing the same amount of nitrogen as is excreted during starvation were given to a starving animal, the intake and output of nitrogen would balance. We are led to make this assumption because we know that any business balance sheet showing an excess of expenditure over income could be met by such an adjustment. But it is a very different matter with the *nitrogen balance sheet* of the body; for, if we give the starving animal just enough protein to cover the nitrogen loss, we shall cause the excretion to rise to a total which is practically equal to the starvation amount *plus* all that we have given as food, and although by daily giving this amount of protein there may be a slight decline in the excretion, it will never come near to being the same as that of the intake. Such feeding will prolong life for a few days only.

To strike *equilibrium* we must give an amount of protein whose nitrogen content is at least two and one-half times that of the starvation level. For a few days following the establishment of this more liberal diet, the nitrogen excretion will be far in excess of the income, but it will gradually decline until it corre-

sponds to the intake. Having once gained an equilibrium, we may raise its level by gradually increasing the protein intake. During this progressive raising of the protein intake, it will be found, at least in the carnivora (cat and dog), that for a day or so immediately following each increase in protein intake, a certain amount of nitrogen is retained by the body. The excretion of nitrogen, in other words, does not immediately become adjusted so as to correspond to the intake. The amount of nitrogen thus retained is too great to be accounted as a retention of disintegration products of protein; it must therefore be due to an actual building up of new protein tissue, that is, growth of muscles.

Such results undoubtedly obtain in the cat, and less markedly in the dog. In man and the herbivorous animals, this is not the case, for in these we can never give a sufficiency of protein alone to maintain nitrogen equilibrium; there will always be an excess of excretion over intake. But indeed it scarcely requires any experiment to prove this, for it is self-evident when we consider that there are only 400 C. in a pound of lean meat, and there are few who could eat more than 4 pounds a day, an amount which however would only furnish about half of the required calories. A person fed exclusively on flesh is therefore being partly starved, although he may think that he is eating abundantly and be quite comfortable and active. This fact has a practical application in the so-called *Banting cure for obesity*, which consists essentially in limiting the diet to flesh and green vegetables, allowing only a very small quota of carbohydrates or fats.

Protein Sparers.—Very different results are obtained when carbohydrates or fats are freely given with the protein. Nitrogen equilibrium can then be regained on very much less protein; so we speak of fats and carbohydrates as being "*protein sparers.*" Carbohydrates are much better protein sparers than fats; indeed they are so efficient in this regard that it is now believed that carbohydrates are essential for life, so that when the food contains no carbohydrates, a part of the carbon of protein is converted into this substance. This important truth is supported by evidence derived from other fields of investigation (e. g., the

behavior of diabetic patients, where the power to use carbohydrates is much depressed). The marked protein-sparing action of carbohydrates is illustrated in another way, namely, by the fact that we can greatly diminish the protein break-down during starvation by giving carbohydrates. In this way we can indeed reduce the daily nitrogen excretion to about one-third what it is in complete starvation.

The Protein Minimum.—In the case of man living on an average diet, although the daily nitrogen excretion is about 15 grams, it can be lowered to about 6 grams, provided that, in place of the protein that has been removed from the diet, enough carbohydrate is given to bring the total calories up to the normal daily requirement. If an excess of carbohydrate over these energy requirements be given, the protein may be still further reduced and yet equilibrium maintained. To do this, however, it is not the amount of carbohydrate alone that determines the ease with which the *irreducible protein minimum* can be reached; the kind of protein itself makes a very great difference. This has been very beautifully shown by one investigator, who first of all, determined his nitrogen excretion while living on nothing but starch and sugar, and then proceeded to see how little of different kinds of protein he had to take in order to bring himself into nitrogenous equilibrium. He found that he had to take the following amounts: 30 gm. meat protein, 31 gm. milk protein, 34 gm. rice protein, 38 gm. potato protein, 54 gm. bean protein, 76 gm. bread protein, and 102 gm. Indian corn protein. The organism is evidently able to satisfy its protein demands when it takes meat protein much more readily than with vegetable proteins.

To understand *why proteins should vary so much in their nutritive value*, we must examine their ultimate structure very closely. When the protein molecule is disintegrated, as by digestion, it yields a great number of nitrogen-containing acids, the amino acids, as well as several bases and aromatic substances. The most important of these acids are glycine, alanine, serine, valine, leucine, proline, aspartic and glutamic acids, the bases being lysine, histidine and arginine and the aromatic bodies, phenylalanine, tyrosine and tryptophan. These substances constitute the available

“units” or “building stones” of protein molecules, but in no two proteins are the materials used exactly in the same proportions, some proteins having a preponderance of one or more and an absence of others, just as in a row of houses there may be no two that are exactly alike, although for all of them the same building materials were available. Albumin and globulin are the most important proteins of blood and tissues, so that the food must contain the necessary units for their construction. If it fails in this regard, even to the extent of lacking only one of them, the organism will either be unable to construct that protein, and will therefore suffer from partial starvation, or it will have to construct for itself this missing unit, a process which it can accomplish for some but not all of the units.

It is therefore apparent that those proteins are most valuable as foods that contain an array of units which can be reunited to form *all* the varieties of protein entering into the structure of the body proteins. Naturally, the protein which most nearly meets the requirement is meat protein, so that we are not surprised to find that less of it than of any other protein has to be taken to gain nitrogen equilibrium. Casein, the protein of milk, although it does not contain one of the most important units, namely, glycine, is almost as good as meat protein, because the organism is itself able to manufacture glycine. When, on the contrary, proteins (such as zein from corn) are given, in which certain units are missing, starvation inevitably ensues. But it does not do so if the missing units, (which in the case of zein is tryptophan) are added to the diet.

These most important facts have been ascertained by experiments carried out in New Haven by Osborne and Mendel. Young albino rats, just weaned, were fed on a basal diet consisting of the sugar, fat and salts of milk to which was added the protein whose nutrition value it was desired to study. The rats were weighed from day to day, and the results plotted as a curve—the *curve of growth*. A gradually rising curve was obtained when casein or the albumin of milk or eggs, or the edestin of hemp seed, or the glutenin of wheat was fed, but this was not the case with the gliadin of wheat or, as

above mentioned, with zein of corn. It will be seen, therefore, that of the two proteins in wheat one, glutenin, contains all the necessary units for building up the growing tissues, but that in the other protein, gliadin, some essential unit is absent; by analysis this was found to be lysin. By adding lysin to gliadin a normal curve of growth resulted, thus showing that this was really the missing unit. The result was made even more spectacular by feeding a batch of young rats on gliadin alone, so that they remained undeveloped and stunted, and then adding lysin to their diet, when they very quickly made up for lost time, and soon reached, if not quite, yet almost as good a development as their more fortunate brothers who had been fed on glutenin or casein from the first.

The animal economy itself can therefore produce certain of the amino bodies—thus, as we have seen, it can produce glycin—this power being much more developed, in the case of herbivorous, as compared with carnivorous animals. In the vegetable food on which oxen live, several of the prominent amino bodies of muscle protein are missing, but they are constructed in the organism by altering the arrangement of the molecules of those amino bodies which are present, so that a protein is built up which is very like that present in the tissue of the carnivorous animals. Even in the case of the herbivora, however, there are limitations to the power of forming new amino bodies. Tryptophan, for example, cannot be formed in this way.

CHAPTER X.

THE SCIENCE OF DIETETICS.

In order that a proper assortment of amino bodies may be assured in the diet, protein is taken in excess of the quantity necessary to repair the tissues. It has been thought by some that the surplus thus taken by the average individual is much more than need be, and that an unnecessary strain is thus thrown on the organs which have to dispose of the excess. It has been claimed by the adherents of this view that many of the obscure symptoms—headaches, muscular and back pains, sleepiness, etc.—that city folk are liable to suffer from, are due to the presence in the blood of unnecessary by-products of excessive protein metabolism. Such opinions seemed to receive very weighty indorsement some years ago when Chittenden published a long series of observations showing that men in various callings in life, could perform their daily work quite satisfactorily and apparently maintain their health after reducing the protein of their diets to less than half of the usual amount. No direct benefit could be claimed for this reduction except that some of the men believed that they felt better and fitter and more inclined for work, an improvement which admits of no quantitative measurement because of the psychological elements involved. Although these observations were conducted with all the care and accuracy of the highly trained scientist, they have been considered quite inadequate to justify the claim that man takes too much protein. The observations have, nevertheless, been of immense value in compelling a careful review of the evidence that the proportion of protein which habit has prescribed as being the proper one for us to take, is really the most suitable for our daily needs.

There are, however, *differences in the protein content of the diet according to the race and environment.* This has been ascertained by compiling the standard diet for a community, that

is, measuring the exact quantities of protein and carbohydrate in the diets which the people are accustomed to live on, and averaging the results. One remarkable outcome of such statistical work has been to show that for peoples living under approximately the same conditions as regards climate and amount of daily muscular work, the average daily requirement of calories, carbon and nitrogen works out pretty much the same, although there may be some diversity in the proportions of protein and carbohydrate. The following table shows this:

Type of individuals.	Protein gm.	Fat gm.	Carbo. gm.	Total Cal.	C. gm.	N. gm.
Average workman in Germany, 20 years age.	118	56	500	3,045	328	18.8
German soldier in the field	151	46	522	3,190	340	24
British soldier in peace...	133	115	429	3,400	...	21.3
Russian soldier in war (Man- churian campaign)	187	27	775	4,900	...	30
Professional man	100	100	240	2,324	230	16

Such figures can be compiled with tolerable accuracy because the diet is under control. It is of course more difficult to collect sufficiently accurate data regarding the diets of civilians, but it is safe to say that the average city dweller in temperate zones derives his daily requirement of 15 gm. nitrogen in 95 gm. of protein, which also yields 60 gm. of the required 250 gm. carbon. This deficit he might supply either from fats or carbohydrates, the actual proportion depending on availability and price. It should be particularly noted that the proportion of protein is very much increased whenever strenuous muscular work has to be performed. Now the question is, do such statistical studies substantiate Chittenden's claim that the protein which we are accustomed to consume could profitably be reduced? They certainly do not. Let us for a moment consider the health condition and physical development of communities such as the Bengalis of Lower Bengal, who live largely on rice and take only a little less in the way of protein than the amount Chittenden would have us take. Their body weight, chest measurement and muscular development are distinctly inferior to those of the natives of

Eastern Bengal, who, nevertheless, belong to the same race as the lower Bengalis, but differ from them in taking more protein in their food. Not only this, but the lower Bengalis are in every sense of the word half starved, and are very prone to disease, especially of the kidneys, the very type of disease to which we are told excessive protein consumption must predispose. Diabetes is also very prevalent amongst these people, probably because of the enormous quantities of sugar-yielding food (carbohydrates) which they are compelled to eat in order to provide sufficient calories for life. Mentally, they are a very inferior race. This, then, is an experiment on a much grander scale than Chittenden's, and what of the results? It is fortunate that most of Chittenden's subjects "through force of circumstances" have returned to their old dietetic habits.

Exactly concordant results have been obtained when attempts have been made to reduce the protein in the dietaries of public institutions such as prisons, alms houses, etc. There has invariably been a distinct increase in the sick list, especially of such diseases as pneumonia, tuberculosis, etc. And if we seek for evidence of an opposite nature, we do not find that excessive protein ingestion is fraught with any evil consequences to the community. Thus the Eskimo takes five times more protein than the Bengali and two and one-half times more than the European, yet he is peculiarly free from "uric acid" diseases; and his physical endurance and his power of withstanding cold are extraordinary.

There are a great many secondary factors, such as availability, taste, etc., that determine the average diet of a community, but the main determining factors are instinct and experience. In the struggle for supremacy of one race over another, we may assume that adequacy of diet has been a determining factor, and that the average which is taken usually represents that which conduces to the greatest efficiency.

We have dealt at some length on these questions because of their great practical importance, and because they show us that in the matter of the protein content of our diet, as in that of all other animal functions, there comes into play the principle of

the "factor of safety." We have two lungs, although it is quite possible to live with one only, two kidneys, although one will usually suffice; and so with our food; we could get along for some time with about half of the protein which we take, but at the constant risk of a deficiency, for should physical exhaustion occur, a reserve of building stones ought to be available to restore the tissue which has been consumed. Instead of the excess of protein throwing a strain on the organism, the contrary is the case, for it is indisputably a greater strain for the tissues to have to construct new building stones than to use those supplied ready made in the food.

Another deduction which we may draw from these observations is that more protein should be taken when its source is mainly vegetable food than when it is animal. On the other hand, there is nothing to indicate that one kind of animal protein possesses any advantages over another; flesh protein, milk protein, egg protein are practically of equal dietetic value, and with regard to which varieties of meats—whether light or dark—are most nutritious, all we can say is that any differences that may be thought to exist are not due to differences in the chemical nature of the proteins which they contain, but depend on their flavor and digestibility. There are more fads and fancies about which meats are nutritious and which are not so than would fill a volume, but after all the whole question is one of flavor. Man digests best what he likes best, and he thrives best when digestion is good. A sound knowledge of the principles of dietetics is of no less importance for the dentist than the physician; but there are no simple rules by which the most suitable diet for each individual can be prescribed. Many factors besides the nutritive values of the food must be considered, and the old adage should never be forgotten, that "one man's food is another man's poison."

Very practical conclusions may be drawn from these observations regarding **the most suitable diet for the city dweller**. It is evident that we are now-a-days in possession of a sufficient amount of scientific information regarding both the daily requirements of the body and the ability of the various foodstuffs to

fulfill these requirements, to compute, from the market prices of foods, how much it should take per diem for an individual, or a family of individuals, to live healthfully and economically. The day will surely come when, through the medium of schools and the press, everyone will know what we may call the *fundamentals of dietetics*, namely: (1) that a man of sedentary occupation (the ordinary city clerk) requires daily 2,600 calories, and a laboring man, at least 3,000 calories. (2) That at least 5 per cent of the calories should be provided in protein food of animal origin (meats, milk) with 10 per cent or more as other protein (bread, oatmeal, etc.).

To enable the housewife to purvey the necessary food to meet these requirements, she must therefore become familiar with the caloric value and the percentage of protein in the different classes of protein foods, and of the caloric values of other great staples of diet. Canned foods will no doubt some day have printed on the label: "This can contains calories, of which per cent are in proteins of grade" And this is no utopian idea; it is practical common sense. The adoption of such a scheme is far more likely to be the solution of the problem of the high cost of living than anything else, for, indeed, it is not so much the high cost of living as it is the cost of high living that troubles us. We demand business efficiency in our manufacturing organizations, and yet we are inclined to ridicule as impractical any attempts at nutritive efficiency in the animal organization which is our own body. Not only the principles of dietetics, but the details as well are now so thoroughly understood that their application in the feeding of the masses is only a matter of education. Dietary impostures of the meanest description, often hiding behind a "bluff" of scientific knowledge, are of course the most serious enemies we shall have to face in spreading the knowledge. It will be the duty of physicians, of dentists, and of the educated classes to offset this commercial brigandage by spreading the gospel of food efficiency.

As illustrating the food efficiency, in relationship to cost we may take the following table from the menu of a well-known restaurant company:

	Cost in cents per portion	Calories Total	% in protein	Calories for 5 cents	Cost in cents per 1000 calories
Bread	5	933	12	933	5
Apple pie	5	343	5	337	15
Boston pork and beans	15	868	12	276	18
Ham sandwich	5	212	20	198	30
Corn beef hash	15	538	14	170	30
Beef stew	15	641	25	199	32
Club sandwich	25	438	20	82	61
Sliced pineapple	5	36	8	36	138
Mayonaise	20	53	16	13	35

(Lusk)

The above table is not by any means from a cheap restaurant. By economy and judicious purchasing it is possible even in New York to purchase, for 8 cents, 1,000 calories having the proper proportion of protein, so that a working man may easily cover his dietetic requirements for 25 cents a day, exclusive of the cost of cooking. All he spends above this is for personal taste and relish.

Chemistry of the Commoner Foodstuffs.

The accompanying diagram (Fig. 9) indicates the composition of some of the commoner foods and is self-explanatory. There are certain foodstuffs concerning which a little more detail may however be advisable.

Wheat Flour, besides a large amount of starch, contains two proteins, gluten and gliadin. When the flour is mixed with water and then kneaded, it forms dough, because the proteins change into a sticky substance called gluten. As dough the flour is not a suitable food, because the digestive juices cannot penetrate it. To render it digestible the dough must be made porous and this is accomplished by causing bubbles of carbon dioxide gas to develop in it, either by mixing it with baking powder which is composed of a bicarbonate and an organic acid (tartaric) or by keeping it in a warm place with yeast, which ferments the sugar that is present. The sugar is developed from the starch by the action of the diastase (see p. 44) present in the flour.



Fig. 9.—Dietetic chart, showing the percentage amounts of the various proximate principles (indicated by the shaded areas) and the calories (indicated in red) yielded by burning 1 lb. of the commoner foodstuffs. The numbers to the left represent the caloric values and the names to the right, the food in question.

When the yeast has been allowed to act for some time, or if baking powder was used, when the gas formation has ceased, suitable portions (loaves) of dough are placed in the oven. The heat causes the inclosed bubbles of gas to expand so that the whole mass becomes aerated and further increase of temperature acts on the proteins and starches on the surface coagulating the former and converting the latter into dextrins. The crust is thus formed. Brown bread is made from wheat from which all the husk has not been removed. There are two possible advantages of this over white bread, namely, the husks act as a mild laxative and they seem to contain traces of vitamins (see p. 121).

Other Cereals.—These include maize or Indian corn, oatmeal and rice, and differ from wheat in that their proteins do not form gluten when mixed with water. They cannot therefore be formed into bread unless they be mixed with some wheat flour. They are relatively rich in ash, and maize contains a large proportion of fat. When rice composes a large proportion of the diet, as is the case in tropical countries, the unpolished variety should be used to supply the vitamins. When the diet is a mixed one, however, danger of an insufficiency of vitamins cannot exist. As has been already explained, the protein of cereals is not of first quality, because it does not contain all of the amino acids (building stones) of tissue proteins.

Milk and Milk Preparations.—Whole milk is as nearly as possible a perfect food, for its protein is of the first quality and it contains a sufficiency of fats and carbohydrates for the growth of the tissues. Where muscular exercise must also be performed, carbohydrates should be added to the milk, and this is best accomplished by the use of cereals. Milk is an economical food, for one quart nearly equals in nutritive value a pound of steak or eight or nine eggs, and is easily digested and assimilated, but somewhat constipating. The chief protein of milk is caseinogen (phospho protein) and is characterized by being precipitated by weak acids and by the action of gastric juice. When milk sours some of the milk sugar, or lactose, becomes converted by bacterial action into lactic acid and this precipitates caseinogen. When an extract of the mucous membrane of the stomach is added to

milk and the mixture kept warm, the clot which forms is called casein. By separating the casein and allowing it to stand for some time ferments, derived from moulds and bacteria, act on it to produce *cheese*. The cheese, besides casein, contains much fat and mineral matter. Cheddar cheese is especially rich in fat. Cheese is a very concentrated article of diet and when taken in moderation is thoroughly digested and assimilated.

Cream consists of the milk fats with some of the constituents of milk. It is the most easily assimilated of all the fats and is hence very nutritious. When sweetened, flavored and frozen it forms ice cream, which should not be regarded, as it usually is, as a luxury, but as a highly nutritious food. It should not therefore surprise the indulgent parent when a child refuses food after visiting the corner pharmacy. On standing, cream ripens (undergoes change due to bacterial growth), and the fat can be made to separate as *butter*. There is no foodstuff that contains more calories than butter, and it also contains certain vitamins. The fluid from which the butter separates, *butter-milk*, contains practically no fat and is acid to the taste because of bacterial action on the lactose producing lactic acid. Its influence on the nature of bacterial growth in the intestines has already been referred to.

Eggs.—The only point we need emphasize is the much greater percentage of fat substances (lipoids) in the yolk than in the white. One dozen eggs equals in food value two pounds of meat. Eggs are therefore more costly than milk.

Meats.—The building stones of the protein molecule of meat, for reasons which are obvious, are more nearly identical with those of the tissues of man than are those of any other food. The carbohydrate is however insufficient in amount, for which reason we take potatoes with meat. The flavors of different meats depend largely on the extractive substances which they contain. These include creatin and purin substances. When a decoction of meat is evaporated to small bulk, after precipitating all of the protein, *meat extract* is prepared, which, like coffee or tea, has no nutritive value but acts as a mild stimulant (cafein and their are chemically very closely related to the purin bodies of meat

extract). Clear soups are mainly dilute solutions of meat extractives, but in beef tea, if properly made, there is much meat protein.

Other Foods and Condiments.—Although green vegetables and salads consist very largely of water, they are very important articles of diet, because they contain cellulose, which serves to increase the bulk of the intestinal contents—to serve as ballast, as it were—and prevent constipation by keeping the intestinal musculature active. Some vegetables, such as spinach, are especially important since they contain iron. Salads have a further importance because of the oil taken with them. The relishes and the condiment flavors are by no means insignificant adjuncts of diet, for they give the relish to food without which digestion is likely to be inefficient. This most important property of diet has been sufficiently insisted upon elsewhere.

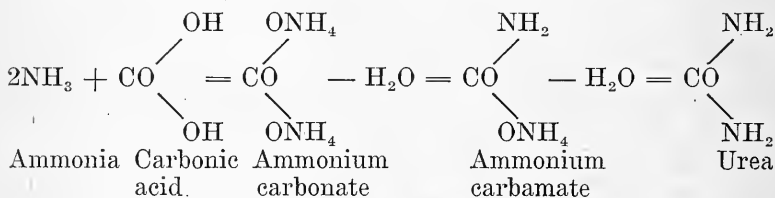
CHAPTER XI.

SPECIAL METABOLISM.

But we must now return to the more theoretical aspects of our subject. We will proceed to trace out very briefly the intermediary stages in metabolism through which proteins, fats and carbohydrates have to pass in order to yield the energy required to drive the animal machine and to supply material with which to repair the broken-down tissues.

Metabolism of Proteins.—We must follow the amino acids after their absorption into the blood until they ultimately reappear, the nitrogen among the nitrogenous constituents of urine and the carbon as part of the carbon dioxide of expired air. In order to do this it is necessary for us to become familiar with *the nature and source of the urinary substances which contain nitrogen*, and to consider some of the most important chemical relationships of these substances, so that we may understand how they become formed in the body. The substances in question are: urea, ammonia, creatinin, the purin bodies, and undetermined nitrogenous substances. Urea and ammonia may be considered together.

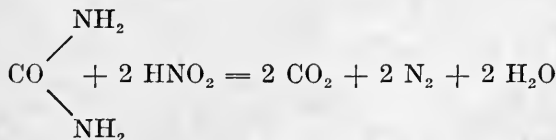
UREA AND AMMONIA.—There is no doubt that it is as ammonia that the nitrogen of the amino acids is set free in the organism. The free ammonia would, however, be highly poisonous, so that it immediately becomes combined with acid substances to form harmless neutral salts. The acid which is ordinarily used for this purpose is carbonic, of which there is always plenty in the blood and tissue juices. The ammonium carbonate thus formed becomes changed into urea by removal of the elements of water from the molecule, thus:



The conversion of ammonium carbonate occurs largely in the liver. Our evidence for this is: (1) If solutions containing ammonium carbonate be made to circulate through an excised liver, urea is formed. (2) If this organ be seriously damaged, either experimentally or by disease, less urea and more ammonia appear in the urine. We see therefore that urea is formed in order to prevent the poisonous action of ammonia. But the ammonia may be more usefully employed; instead of being combined with carbonic acid in order that it may be got rid of, it may be employed to neutralize, and thus render harmless, any other acids that make their appearance. Thus, it may be employed to neutralize the acids which sometimes result during the metabolism of fat, as in the disease diabetes; or the lactic acid that appears in the muscles during strenuous muscular exercise; or the acids produced on account of inadequate oxygenation. Taking acids by the mouth has a similar effect; thus the ammonia excretion rises after drinking solutions containing weak mineral acids.

Ammonia is, of course, not the only alkali which is available in the organism for the purpose of neutralizing acids. The fixed alkalies, sodium and potassium, are also used. Thus, when we greatly increase the proportion of these, as by taking alkaline drinks, or by eating vegetable foods, the ammonia excretion diminishes.

Urea is an inert substance, capable of uniting with acids to form unstable salts (urea nitrate and oxalate), and like other amino acids, being decomposed by nitrous acid so as to yield free nitrogen. This latter reaction is used for the quantitative estimation of urea, the evolved nitrogen being proportional to the amount of urea, thus:



Certain bacteria are capable of causing urea to take up 2 molecules of water so as to form ammonium carbonate, a process

really the reverse of that which occurs in the organism and represented by the above formulæ. This change occurs in urine and accounts for the ammoniacal odor which develops when this fluid is allowed to stand.

CREATININ.—This is very closely related to creatin, which is the most abundant extractive substance in muscle, and which yields urea when it is boiled with weak alkali. These chemical facts would lead us to expect that some relationship must exist between the creatin of muscle and the creatinin and urea of urine, but, so far, it has been impossible to show what this relationship is. One very important fact has, however, been brought to light, namely, that creatin makes its appearance in the urine when carbohydrate substances are not being oxidized in the body, as in starvation, and in the disease diabetes. This is one reason for the growing belief that carbohydrates are something more than mere energy materials (see p. 113). The excretion of creatinin is so remarkably independent of the amount of protein in the food that it is believed to represent more especially the end product of the protein break-down of the tissues themselves, in contrast to urea, which partly represents the cast-off nitrogen of the protein of the food.

PURIN BODIES.—These are of particular interest because they include uric acid, about which more nonsense has been written than about any other product of animal metabolism. The so-called uric acid diathesis is very largely a medical myth—a cloak for ignorance. Uric acid is the end oxidation product of the purin bodies, which include the hypoxanthin and xanthin of muscle and their amino derivatives, the adenin and guanin of nuclein.

These relationships are seen in the following formulæ:

Oxy purins of muscle.....	{	Hypoxanthin	$C_5H_4N_4O$
		Xanthin	$C_5H_4N_4O_2$
Amino purins of nuclein..	{	Adenin	$C_5H_4N_4NH$
		Guanin	$C_5H_4N_4ONH$
		Uric acid	$C_5H_4N_4O_2$

There are therefore two sources for uric acid in the animal

body, namely, the muscles and the nuclei of the cells. This explains why the uric acid excretion increases after strenuous muscular work, and why it is much above the normal when cellular break-down is very excessive, as in the disease called leucocythemia, in which there is an excess of leucocytes in the blood (see p. 145). Another source of uric acid is the food when it contains either muscle (flesh) or glands (sweetbreads), for a large proportion (about half) of the ingested purins do not become destroyed in their passage through the organism, but become oxidized to uric acid, which is excreted in the urine. This is called the exogenous in contrast to purin produced in the tissues, which is called endogenous.

There is only a trace of uric acid in the urine of mammals, but in birds and reptiles most of the nitrogen is present in this form. The reason is that in these animals it is important to have semi-solid, instead of fluid excreta, so that the urea which results from protein metabolism becomes converted into uric acid, which, either free or as salts, is relatively insoluble. Uric acid is chemically a diureide, that is to say, it consists of two urea molecules linked together by a chain of carbon atoms. The chain of carbon atoms is furnished by substances not unlike lactic acid and the synthesis occurs in the liver. If this organ be removed from the circulation in birds, such as geese, in which the operation is comparatively easy, a very large part of the uric acid in the urine becomes replaced by ammonium lactate.

The relative insolubility of uric acid and its salts, which we have already referred to, makes it apt to become precipitated in urine, especially on standing. It forms the orange reddish deposit, so frequently observed in summer, when on account of perspiration the urine does not contain as much water as usual. Such deposits do not therefore indicate that there is an excess of uric acid in the blood, but merely that enough water is not being excreted to dissolve the usual amount of urates. Sometimes the urate becomes deposited in the joint cartilages, particularly in those of the great toe, causing local swelling and redness and great pain. This is gout, and it may be most effectually treated by drinking large quantities of alkaline fluids, and eliminating

from the dietary such foodstuffs as meats and sweetbreads, which yield exogenous purins. As we have said, there is no reason to believe that any other diseases besides gout are due to an excess of uric acid in the blood.

Besides the above there are traces of *other nitrogenous substances* in the urine, such as:

1. Hippuric acid, which, as its name signifies, is very abundant in the urine of the horse and other herbivora, and which is the excretory product of the aromatic substances which the food of these animals contains.

2. Cystin, an amino acid containing sulphur.

3. Pigments and mucin.

The exact *significance of the end products of nitrogenous metabolism* has been very beautifully demonstrated by Folin, of Harvard. The observations were made on several men who lived for some days on a diet rich in protein (but containing no purin-containing foodstuffs), and then on one which was very poor in protein. The problem was to see how each of the nitrogenous constituents behaved during the two periods, both absolutely and in relation to the total amount of nitrogen excreted. In order to show the latter relationship the results are given, as in the following table, not as urea, etc., but as urea-nitrogen, etc.:

	On the protein-rich diet	On the protein- poor diet
Quantity of urine	1170 c. c.	385 c. c.
Total nitrogen	16.8 gm.	3.6 gm.
Urea-nitrogen	14.7 gm. (87.5)	2.2 gm. (61.7)
Ammonia-nitrogen	0.49 gm. (3.0)	0.42 gm. (11.3)
Uric acid-nitrogen	0.18 gm. (1.1)	0.09 gm. (2.5)
Creatinin-nitrogen	0.58 gm. (3.6)	0.60 gm. (17.2)
Undetermined nitrogen.	0.85 gm. (4.9)	0.27 gm. (7.3)

The figures in parentheses represent the percentage which the nitrogen of each substance furnishes of the total amount of nitrogen excreted. It will be seen that urea decreases on the poor diet relatively more than total nitrogen, thus indicating that it comes partly from proteins in the food (exogenous) and partly

from the organism itself (endogenous). This result leads us to infer that most of the amino substances of protein foods which are not required as building stones for the tissues are broken down so as to yield ammonia, which is excreted as exogenous urea in the urine, but that the amino acids that are really appropriated by the tissues, although they may also produce some urea (endogenous), cause other end-products to be formed. The most important of these endogenous bodies is evidently *creatinin*, for, as will be seen from the above table, this substance is excreted in the same absolute amount during both the starvation and the protein-rich periods.

Direct evidence that this conclusion is correct has been obtained by examination of the blood and muscles for amino bodies, ammonia and urea. The results have shown that the amino acids absorbed from the intestine are carried through the liver into the systemic blood, which transports them to the muscles, where those that are not required for building up the tissues are broken down into ammonia and a carbonaceous residue, which is then burned just exactly as if it were carbohydrate or fat. The useless ammonia becomes converted into urea in the manner already described, either in the muscles themselves, or by being carried to the liver, which, as we have seen, possesses to a very high degree the power of producing urea.

The Relative Importance of Proteins, Fats and Carbohydrates in Metabolism.—The metabolism of fats and carbohydrates, with regard both to their importance as builders of living tissues and the type of their metabolism, is very different from that of proteins. That carbohydrates and fats are less important in the animal economy than proteins is evidenced by the fact that we can live perfectly well on protein food alone, but not on either of the others. This does not, however, justify us in concluding that carbohydrates and fats are merely materials which are oxidized by the tissues for the purpose of producing energy, fuel as it were, and which can be dispensed with. They are more than this, for no cell, in however starved a condition it may be, is entirely free from either of them, thus indicating that they must have been produced out of protein itself. Pro-

teins are no doubt the most important ingredients of cells, but fats and carbohydrates are indispensable also.

As *reserve materials*, striking differences exist among the three foodstuffs. Proteins are of little value in this regard for, as we have seen, very little, if any, can become laid down in the tissues when excess is taken as food; on the contrary, all that is not required is thrown out of the body, and when the food supply is cut off, as in starvation, the protein is spared as much as possible (see p. 92). Carbohydrates are very readily deposited as a starch-like substance, called glycogen, and this reserve is the first to be called on, not only in starvation, but also when muscular work is performed. It may be considered as the most immediately available material for combustion in the organism, but the limits of its storage are restricted in man to some hundreds of grams, which, as we have seen, soon become used up in starvation. Fat is pre-eminently the storage material, and the supply may serve in man to furnish, along with a little protein, enough fuel for several weeks' existence.

The relative importance of the three foodstuffs is shown in the extent to which each is used in the *metabolism during muscular exercise*. When there is an abundant store of glycogen, the energy is entirely derived from this source; when there is little glycogen but much fat, it is fat that is burned, and when neither of these is abundant but much protein is being taken with the food, or the animal is reduced to living on its own tissues, as in starvation, it is protein. In other words, the type of metabolism occurring during muscular work is the same as that which immediately preceded it; the only change is in the extent of the combustion, not in the nature of the fuel employed.

CHAPTER XII.

SPECIAL METABOLISM (Cont'd).

Metabolism of Fats.—Fats are absorbed by the lacteals and discharged into the blood of the left subclavian vein through the thoracic duct. They are carried to various parts of the body and gain entry into the cells, in the protoplasm of which they become deposited. This process occurs extensively in the subcutaneous connective tissues, between the muscles, and retroperitoneally around the kidney (the suet). The fat which is thus deposited possesses more or less the same qualities as the fat of the food. Thus, when the only fat taken over a long period of time is one with a very low melting-point, such as oil, the fat deposited in the tissues is likely to be oily in character, whereas it is stiff after feeding with a high melting-point fat, such as mutton fat. This similarity between the tissue fat and that of the food becomes very striking when the animal has been subjected to a preliminary period of starvation and then fed for some weeks with a large excess of the particular fat and as little carbohydrate and protein as possible. Fat in the food is of course not the only source of the fat in the tissues. It is also formed out of carbohydrates, a fact which is well known to farmers, who fatten their stock by feeding them with maize and other starchy grains, and to physicians, who reduce their corpulent patients by restricting carbohydrate foods. The fat thus deposited has the chemical characteristics of the fat which is peculiar to that animal. It is almost certain that there is ordinarily no formation of fat out of protein in the higher animals.

The fat thus deposited in the tissues may remain for a long time, but ultimately it is again taken up by the blood and carried to whatever active tissue requires it as fuel. Before being thus burnt, it splits into glycerine and fat acid (see p. 75). The fat acid possibly undergoes some preliminary change in the

liver; in any case, the long chain of carbon atoms of which we have seen the fat molecule to be composed (see p. 24) becomes oxidized (burnt), not all at once but piece by piece, two carbon atoms being split off at a time. If the fat acid chain originally contained an even number of carbon atoms, the oxidation process may stop short when there are yet four carbon atoms in the chain, thus producing oxybutyric acid ($\text{CH}_3\text{CHOHCH}_2\text{COOH}$). This imperfect metabolism of fat occurs in severe cases of diabetes and often causes death. It also occurs in carbohydrate starvation, and indicates, more clearly than any thing else, that even carbohydrates are essential for life.

Metabolism of Carbohydrates.—It will be remembered that these include the starches and the sugars, and that during digestion they are all hydrolyzed to dextrose or lævulose, as which they are absorbed into the blood of the portal vein. This absorption is rapid, so that a striking increase in the percentage of sugar occurs in the blood of the portal vein shortly after the food has been taken. Most of this excess of sugar does not immediately gain entry to the blood of the systemic circulation, however, because it is retained by the liver. For this purpose the liver cells convert the sugar into the starch-like substance, *glycogen*, which becomes deposited in their protoplasm as irregular colloidal masses, which stain with iodine and carmine. The liver does not manage in this way to remove all of the excess of sugar from the portal blood, so that, even in a healthy animal, there is a distinct postprandial increase of sugar, or hyperglycæmia, as it is called, in the systemic blood. If too much sugar passes the liver it causes so marked a postprandial hyperglycæmia that some sugar escapes into the urine, thus causing *glycosuria*. This is one of the early symptoms of diabetes, and its occurrence furnishes us with a warning that less carbohydrates should be given in the food. If the warning be heeded, the severer form of the disease will very probably be staved off.

The glycogen deposited in the liver stays there until the percentage of sugar in the systemic blood begins to fall below the normal level (which in man is about 0.1 per cent), when it becomes reconverted into sugar, which is added to the blood.

The reason why the sugar in the systemic blood tends to fall is that the tissues, especially the muscles, are using it up as fuel. If so much sugar is taken that the storage capacity of the liver is overstepped, the excess of sugar is carried by the systemic blood to the tissues, where much of it may be changed into fat. The *glycogenic function* of the liver, as the above process is called, is analogous to the starch-forming function of many plants, such as potatoes. Of the sugar which is formed in the green leaves of these plants, some is immediately used for building up other substances, the remainder being converted into starch, which becomes deposited in the roots, etc., until it is required (as during the second year's growth), when it is gradually reconverted into sugar.

Besides carbohydrates it is known that proteins form glycogen; fats, however, cannot form it. In severe cases of diabetes it is therefore usual to find that although carbohydrate foods are entirely withheld, dextrose continues to be eliminated in the urine. It may come partly from the protein of the food and partly from that of the tissues.

The adjustment between the rate at which the glycogen of the liver becomes converted into dextrose and the percentage of sugar in the systemic blood is effected partly through the nervous system and partly by means of substances called chemical messengers or hormones (see p. 124) secreted into the blood from the ductless glands, such as the pancreas and the adrenals. The very first *symptoms of diabetes*, which we have seen to consist in an excessive postprandial rise in the systemic blood-sugar and a consequent glycosuria, must therefore be due to defects in one or other of these regulatory mechanisms. It is therefore of great interest to know that glycosuria can be induced in the lower animals by stimulation of the nerves of the liver or by interfering with the function of the pancreas or the adrenal glands. The nerves of the liver may be stimulated either directly or through a nerve center located in the medulla oblongata (see p. 246). Complete removal of the pancreas is followed in a few hours by a very acute form of diabetes, which is invariably fatal in a few weeks, whatever the treatment may be. Injection of extract

of the adrenal gland (adrenalin) causes a transient hyperglycæmia and glycosuria.

These laboratory discoveries have in their turn caused clinical investigators to pay close attention to the *nature of the causes of diabetes*. It has been found, as a result, that oft-repeated overstimulation of the nervous system—nerve strain, as it is called—greatly predisposes to this disease. For example, it has been found that a considerable proportion of students who underwent a severe examination for a university degree had sugar in the urine which was passed immediately after leaving the examination room. Even more interesting was the observation of that of a number of men waiting on the side lines as reserves in one of the large football games, about one-half of them passed sugar, due to nervous excitation of the glycogenic function. Besides these types of nerve strain, nervous glycosuria may also be brought on by fright and terror. This has perhaps been most definitely shown by frightening a tom-cat by allowing a dog to bark at it; the cat shortly afterward passed urine containing much sugar. Now, whereas occasional attacks of such nervous glycosuria are harmless, yet their repeated occurrence undoubtedly weakens the ability of the liver to control properly the percentage of sugar in the blood, with the consequence that post-prandial hyperglycæmia becomes more and more marked and takes longer to disappear, so that there comes to be a permanent increase in the percentage of sugar in the blood. This persistent excess of sugar acts as a poison and causes deterioration of many of the tissues, and if unchecked will lead to severe diabetes.

It is for these reasons that diabetes is relatively common amongst locomotive engineers and ship captains; it is also said to be distinctly on the increase amongst business men. A most important element in the treatment of diabetes is therefore removal of the possible causes of nerve strain. Rest and quiet and freedom from worry, coupled with removal of sufficient amounts of carbohydrates from the diet so as to keep the urine free of sugar, is the correct treatment. One common symptom of diabetes is loosening of the teeth. When this is observed the urine passed an hour or so after lunch should be examined for

sugar. Properly conducted treatment will often cause the teeth to tighten up again.

A very common cause of death in diabetes is coma, which is due to the poisoning of the animal by acid substances (oxybutyric acid) resulting from the imperfect oxidation of fat (see p. 116). While these acid substances are gradually accumulating in the blood, the organism attempts to neutralize them by diverting ammonia from its normal course into urea (see p. 108); hence the ammonia content in the urine is very high in severe cases of diabetes. Along with these acids and ammonia, acetone also appears in the urine and breath, so that one can often diagnose a severe case of diabetes by the smell of these substances in the breath. Diabetes is therefore a disease which the dentist should always be on the lookout for.

Metabolism of the Inorganic Salts.—Being already completely oxidized, inorganic salts cannot yield any energy during their passage through the animal body but nevertheless they are essential to life. They are used not only for the building up of bones and teeth, but also for the proper carrying out of the metabolic processes. In this respect they are like the lubricant of a piece of machinery, the organic foodstuffs being like the fuel.

Their indispensability is very clearly shown by the fact that animals die sooner when they are fed on food from which all traces of inorganic salts have been extracted than when they are deprived of food altogether. This result shows us that during the metabolism of organic foods substances must be produced which act as poisons in the absence of inorganic salts. Some of these poisonous substances are no doubt acid in reaction because life can be prolonged for some time by merely adding sodium carbonate to the salt-free food. But salts not having any neutralizing powers are also necessary to keep the animal alive.

The chief salts which we take with our food are the chlorides, carbonates and organic acid salts (e. g., citrates, tartarates, etc.) of sodium and potassium and of calcium. We also take some iron and traces of iodine. All of these are already present in sufficient amount in the ordinary foodstuffs, except sodium chloride,

or common salt. This we must add to our food. The extent to which the addition of common salt is made varies very strikingly according to the nature of the organic food. When this is mainly vegetable in origin, much common salt is required, the reason being apparently that vegetables contain large quantities of potassium salts which would be harmful unless a proper proportion of sodium is also taken. The demand for sodium by herbivorous animals often inclines these to wander for hundreds of miles from their feeding grounds to salt licks. Here they take enough sodium chloride to last them for some time. The carnivorous animals do not visit salt licks unless it be for the purpose of preying on the herbivorous visitors. The *salt hunger* from which they suffer compels the herbivora to go to the salt licks even in the face of this danger of destruction by the carnivora. The same relationship between the desire for salt and the diet is seen in man, the salt consumption per capita being much greater in rural than in urban communities.

Usually enough *iron* is taken either in meats or in certain vegetables, as spinach. The body is very careful of its supply of iron (which is the most important constituent of hæmoglobin), but if it loses it more quickly than the loss can be made good from the food, anemia results and it becomes necessary to prescribe iron salts as medicine.

Similarly with *calcium*, there is usually enough in the food even of growing animals to meet the demands which bone and teeth formation entails. Rickets is not usually due to a deficiency of calcium in the food, but to a depraved condition of the general nutrition, making it impossible for the available calcium to be properly used. Good food, air and exercise, rather than drugs, is the correct treatment for rickets.

Our knowledge of just what each particular inorganic salt does in the metabolism of an animal is not yet very far developed, but some most important discoveries have been made in this connection during recent years. Thus, by observing the isolated beating heart of the frog or turtle it has been found that a certain proportion of sodium, calcium and potassium salts is essential to the maintenance of a proper beat. With sodium chloride

alone the beat soon stops, with excess of potassium an immediate paralysis occurs, and with excess of calcium an immediate rigor or permanent contraction. Analogous results are obtained with other muscles. Salts in certain proportions may even cause processes of cell division to start in the ova of some of the lower animals. In other words, a process of embryo development which is usually induced by impregnation by the male elements may be made to start by the action of salts.

Vitamines.—Another class of bodies called vitamins is of great importance as adjuncts of diet. Without them metabolism becomes upset, and serious symptoms make their appearance with perhaps death as the ultimate result; and this happens even although the protein, fat, carbohydrate and inorganic salts of the diet be in proper proportion. The first indication of the importance of vitamins was furnished by observations on a disease called *Beri-Beri*, which occurs among peoples of tropical countries, and is characterized by severe neuralgic pains, muscular weakness and paralysis; symptoms which are due to inflammation of the nerves (neuritis). It was noted that it occurred most frequently in the case of people whose main article of diet was polished rice, but was infrequent in the case of those using the unpolished grain. The difference between these two grades of rice is that the one (the unpolished) still contains some of the brownish husk; the other is free of it. This observation suggested the experiment of adding some of the ground-up rice husks to the polished rice diet of those suffering from the disease, with the result that the symptoms soon disappeared. Moreover, when unpolished rice was supplied, in place of polished rice, to natives among whom *Beri-Beri* was very prevalent, the disease disappeared entirely. Other foodstuffs contain this vitamin, so that *Beri-Beri* does not occur with mixed diets.

In order to learn something more about these remarkable substances it was necessary to seek for some animal in which symptoms similar to those of *Beri-Beri* could be induced by feeding with polished rice. Pigeons were found most suitable. When these birds are kept exclusively on such a diet, they develop the

most alarming symptoms of neuritis (paralysis, weakness, etc.), which however disappear in a few hours, not only when unpolished rice or rice polishings (or husks) are given, but also when meat, or beans, or a small piece of yeast is mixed with the rice. Attempts have naturally been made to isolate the substance which is responsible for this remarkable action, and indeed some success can already be reported. For example, it has been possible to separate from rice polishings and from yeast small traces of crystalline substances having a most powerful action in preventing neuritis.

Even such success in investigating the cause of Beri-Beri in rice-feeders would scarcely warrant us in asserting that vitamins are essential constituents of our own varied diets. To show that they are, however, has been no very difficult task. Thus, it is known that although young rats thrive admirably on milk diet, they fail to do so on one of artificial milk, that is, of milk made in the laboratory by mixing together, in proper proportions, the same proteins, fats, carbohydrates and salts that occur in milk. In this chemical mixture, something is wanting which exists only when the ingredients of milk are compounded by the mammary glands. The addition to synthetic milk of desiccated milk from which most of the proteins had been removed bestowed on it full nutritive value.

The practical importance of this observation in the feeding of infants, we need not insist on. Suffice it to say that it is quite possible that prolonged boiling of milk, as for its sterilization, may deprive it of vitamins and thus render the child liable to such diseases as rickets and infantile scurvy, or at least interfere materially with its proper development and growth. Among the symptoms thus produced, especially in the case of infantile scurvy, ulcers may develop on the gums, or the teeth may become loosened. Change of diet may in a few days restore perfect health, or even the addition of a few teaspoonfuls of orange or lemon juice to the original diet may suffice. It is often miraculous how quickly such treatment may change a fretful, pain-stricken child to one of perfect health and cheerfulness.

Innumerable other examples of the wonderful influence of

these mysterious vitamins in nutrition might be cited. The practical point to bear in mind is that, however correctly our diet may be composed with regard to caloric and chemical requirements, it is likely to be unsuitable unless it contains a certain, though perhaps extremely minute, amount of the drug-like substances called vitamins.

CHAPTER XIII.

THE DUCTLESS GLANDS.

Introductory.—We have no more than touched the very fringe of the subject of metabolism, and yet we have learned enough to impress us with the fact that although the chemical processes occurring in the body are extremely complicated, they are nevertheless under perfect control. We must now learn something regarding the nature of this control.

If we take such a metabolic process as that which carbohydrates undergo, we should expect that the conditions which determine whether glycogen shall be formed or broken down would be chemical in nature. We should expect, in other words, that some change in the chemical composition of the blood—either its reaction or the amount of sugar in it, or the appearance in it of some decomposition product of sugar—would determine whether or not glycogen should be mobilized as sugar. In muscular work, for example, sugar is required by the contracting muscles, and we find that the glycogen stores in the liver become very quickly depleted to meet the demand. The question is, how do the muscles transmit their requirements to the liver so as to cause this organ to mobilize the dextrose? Our natural assumption would be that the active muscles cause some change to occur in the blood and that it is this change which excites the liver cells. Such a control of the metabolic activities of one tissue by products of the activity of another, transmitted between them by way of the blood, is known as *hormone control*. We have already become acquainted with it in connection with the control of certain of the digestive glands, particularly the pancreas (see p. 72), and it is no doubt very largely by such a mechanism that a given metabolic process becomes active or suppressed, as occasion demands.

The hormones in such cases are in part the intermediary products of metabolism, but besides these hormones others must exist

to call forth or regulate the activities of tissues which are not immediately concerned in general metabolism but rather with special processes, such as the excitability of the nervous system (e. g., adrenalin), the behavior of the reproductive glands (e. g., in the secretion of milk), the growth of certain tissues (e. g., of subcutaneous tissues, of hairs) or the atrophy of others, (e. g., of the uterus after pregnancy is terminated). For such hormones, special manufacturing centres are provided in the *ductless glands*. The thyroid and thymus glands in the neck, the pituitary in the brain, the spleen and adrenal glands in the abdomen are good examples. None of these has any duct, but they discharge the products of their activity—*internal secretion*—into the blood stream, by which it is carried to the tissue or organ on which it acts. Internal secretions may also be produced by certain cells of the digestive glands, as, for example, the so-called Isles of Langerhans of the pancreas (see p. 72), and likewise there are certain organs, such as the ovaries and testes, whose main functions are of a special nature, but which also possess the power of producing very powerful internal secretions.

We shall confine our attentions for the present, however, to the strictly ductless glands. Their function is ascertained experimentally either by removing the gland by operation or by injecting an extract of it and then observing the behavior of the animal. Much can also be learned by observing patients in whom the gland is diseased.

The Thyroid and Parathyroid Glands.—The thyroid gland consists of two oval lobes situated one on either side of the trachea just below the larynx or voice box, and connected together over the trachea by an isthmus of thyroid tissue. Embedded in the substance of each lobe of the gland on the posterior surface are the two very small *parathyroid glands*. Minute examination shows the thyroid glands to be composed of vesicles lined by low columnar epithelium and filled with a clear glossy substance called colloid. The parathyroids have an entirely different structure, being composed of elongated groups of polyhedral cells with no colloid material.

The functions of the two glands are probably essentially dif-

ferent, the thyroid having to do with the general nutrition of the animal, and the parathyroid with the condition of the nervous system. They lie so close together, however, that it is very difficult to study their separate functions. The importance of the glands is indicated by the relatively large blood supply.



Fig. 10.—Cretin, 19 years old. The treatment with thyroid extract was started too late to be of benefit. (Patient of Dr. S. J. Webster.)

When the thyroid is not properly developed in children, the condition is known as *cretinism* (Fig. 10). The child fails to grow in height, although its bones may thicken. The cranial bones soon fuse together, so that the growth of the brain is hin-

dered and the mental powers fail to develop. The child becomes idiotic, and although it may live for years, it will remain, even at thirty years of age, a stunted, pot-bellied, ugly creature with the intelligence of an infant. The cause of this failure to develop is undoubtedly bound up in some way with the deficiency of the thyroid, for if the cretin be given the extract of this gland, its condition will immediately improve, and indeed, if taken early enough, it may quickly make up for lost time and grow both physically and mentally as it ought to.

Atrophy of the thyroid gland in older persons causes *myxædema*. (Fig. 11). The symptoms of this are very characteris-



A.

B.

Fig. 11.—A, Case of myxædema; B, Same after seven months' treatment. (Tigerstedt.)

tic, being most commonly seen in women. The skin is dry and often of a yellowish color, the hair falls out, the subcutaneous tissues grow excessively, so that the hands, the feet and the face become large and puffy, and the speech indistinct, because of the thickening of the lips. The metabolism also becomes very sluggish, so that the intake of food and the excretion of nitrogen in the urine become diminished, and the temperature subnormal. If

unchecked, mental symptoms become apparent, first of all, a dulling of the intellect with sleepiness and lethargy, and later, muscular twitchings and tremors. Just as in cretinism, so in myxœdema, administration of thyroid extract causes these symptoms to disappear, so that in a month or so the patient may have returned to his or her normal condition, to maintain which, however, the thyroid extract must continue to be given.

When the gland is removed surgically, either in lower animals or in man, very acute symptoms ending in death usually supervene. These include a peculiar form of muscular tremor called *tetany*, passing into actual convulsions, which, by involving the respiratory muscles, ultimately cause dyspnoea and death. It is, however, probable that these nervous symptoms are due to the unavoidable removal of the parathyroid glands. The tetany is removed by giving calcium salts. These conditions associated with deficiency of the thyroid are grouped together as *hypothyroidism*.

Even in healthy individuals thyroid extract taken by mouth excites a more active metabolism, and may cause increased heart activity. One result of this increased metabolism is disappearance of subcutaneous fat and increased appetite, thus rendering the administration of moderate doses of thyroid extract a not uncommon method of treatment for obesity. Such treatment should never be attempted except under the control of a physician, for it is very easy to take too much of the extract and cause palpitation and nervous excitement.

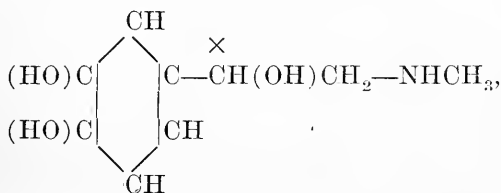
When the thyroid (and parathyroid) glands become excessively active in man, the condition is called *hyperthyroidism*, and the symptoms are very like those above described as produced by taking thyroid extract. To be exact, they are palpitation, wasting of the muscles and consequent weakness, extreme nervousness and protrusion of the eyeballs. On account of this last mentioned symptom the condition is usually called *exophthalmic goitre*. This acute and often fatal disease is to be distinguished from *chronic goitre*, in which there are very few general symptoms, but great enlargement of the thyroid gland, indeed an enlargement which may be so pronounced as practically to obliterate

ate the neck and sometimes so compress the trachea as to interfere with breathing. The cases of chronic goitre occur in the same districts in which the exophthalmic variety is common, these being, in this country, the shores of the great inland lakes and the river valleys, but not in districts bordering on the sea. They are also common in certain districts in Switzerland and England. It is of interest that in the lake and river districts in this country the thyroids of over ninety per cent of all dogs are more or less hypertrophied.

The above remarkable influence of the thyroids on metabolism is in some way dependent upon the colloid material which fills the vesicles of the gland. This colloid contains a peculiar substance called iodothyryn, because it contains iodine, an element which is not found present in any other part of the animal body.

The Adrenal Glands.—As their name signifies, these are situated one on either side just above the kidneys. Each gland is yellowish in color, and is seen on microscopic examination to be composed of a medullary and a cortical portion. The medulla consists of irregular collections of cells containing granules which stain deeply brown with chromic acid and are therefore called chromophile granules. Similar chromophile granules may exist in other parts of the body. The great splanchnic nerve, which it will be remembered arises from the sympathetic chain in the thorax (see p. 278), makes very intimate connection with the adrenal medulla, for which reason and because of the fact that it is developed from the same embryonic tissue as the sympathetic system of nerves, the medulla of the adrenal gland is believed to be closely bound up with the functions of the sympathetic nervous system. The cortex is composed of rows of columnar cells which do not contain chromophile granules. Small though they be, the adrenal glands are essential to life, for their removal causes extreme muscular weakness and a fall in blood pressure followed by death within twenty-four hours. When they are the seat of disease (tuberculous), symptoms of extreme muscular prostration, accompanied by vomiting and a peculiar bronzing of the skin, set in and grow steadily worse until at last the patient succumbs. This is called *Addison's disease*.

The most striking proof of their importance is obtained by injecting an extract of the medulla of the adrenal gland into a vein. It causes an immediate rise in blood pressure, which is more or less proportional to the strength of the extract. The rise is accompanied by a slowing of the heart, due to the reflex stimulation of the vagus centre excited by the rising blood pressure. When this reflex slowing is rendered impossible by cutting the vagi, the rise in blood pressure following the injection may be enormous. The active substance in the extract is called *adrenalin*, *suprarenin*, *adrenin* or *epinephrin*. It is a comparatively simple chemical body, having the formula:



and existing in two varieties which differ from one another according to the direction toward which the plane of polarized light is rotated. The variety rotating to the left is, by many times, stronger in its physiological actions than that which rotates to the right. The discovery of its chemical structure has made it possible for chemists to prepare suprarenin synthetically, and also to prepare a series of related substances having less marked though similar properties. These are closely related to certain of the bodies which appear during the putrefaction of meat.

By careful studies of the action of the suprarenin, or related substances, it has been found that the rise in blood pressure, above referred to, is due to stimulation of the muscle fibers in the walls of the blood vessels. It is on this account that a weak solution of suprarenin is used to stop hæmorrhage, as after removing polypi from the nose, or in bleeding from the gums, as after tooth extraction. The muscle of arteries is by no means the only structure on which adrenalin acts; indeed it stimulates every structure which is capable of being stimulated by the sympathetic nervous system (see p. 277). Thus, it causes the pupil to dilate, saliva

to be secreted (p. 41), the movements of the intestine to be inhibited (p. 79), whereas it has no action on the blood vessels of the lungs or brain, which do not possess vasomotor nerves. This similarity between the results which follow suprarenin injection and stimulation of the sympathetic system is particularly significant when we call to mind the fact that the medulla of the adrenal gland is developed from the same embryonic tissue as the sympathetic system. The clotting power of the blood is diminished after injections of suprarenin.

The Pituitary Gland.—This occupies the Sella Turcica of the base of the cranium and is composed of three portions or lobes. The anterior lobe consists of large epithelial cells and is really an isolated outgrowth from the epiblast of the upper end of the alimentary canal. Its complete excision causes death in a few days, but if only a part is removed, a condition called *hypopituitarism* develops, of which adiposity and sexual impotence are the main symptoms. When this lobe becomes excessively active in man (because of hypertrophy), it causes a peculiar growth of the bones, particularly of the lower jaw, thus making the person look as if he were very powerful. This disease is called *acromegaly* (Fig. 12), and besides the changes in the bones, there is frequently considerable metabolic disturbance, causing a mild form of diabetes. When the hypertrophy of the anterior lobe occurs in youth, most of the bones of the body may be affected, thus causing the condition known as *giantism*.

The intermediary lobe is also composed of columns of epithelial cells, but there is often some colloidal material between the columns. This colloid differs from that of the thyroid in containing no iodine.

The posterior lobe is really a downgrowth from the brain, and is composed of neuroglia mixed with some of the epithelial cells of the intermediary lobe. This lobe can be excised without causing any evident change in the animal, but nevertheless it must have some important functions to perform, because extracts of it, when injected intravenously, have very pronounced effects, viz.: (1) a rise in blood pressure; (2) a very striking diuretic action (i. e., causes urine to be excreted); (3) secretion of milk. The

active principle of these extracts has not as yet been isolated, although the extracts can be considerably concentrated, thus yielding the trade preparation called *pituitrin*.

It is particularly interesting to note that although the anterior lobe does not yield any active extract, yet its excision is fatal. On the other hand, the posterior lobe can be removed with impunity, although extracts of it have profound physiological effects when they are injected into normal animals.

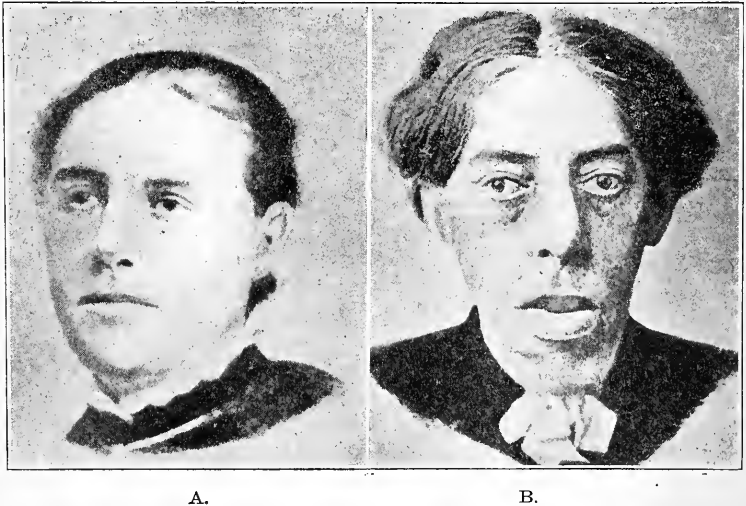


Fig. 12.—A, To show the appearance before the onset of acromegalic symptoms; B, The appearance after seventeen years of the disease. (After Campbell Geddes.)

The Spleen.—Notwithstanding the fact that this is the largest of the ductless glands, it is the one whose functions are the least well understood. It can be excised without causing any evident disturbance, and extracts of it when injected intravenously do not have any characteristic effects. It becomes very much enlarged in certain diseases, namely: (1) in leucocythemia, a form of anæmia, which is characterized by a great increase in the leucocytes of the blood (see p. 145); (2) in typhoid fever (enteric fever); (3) in malaria. It becomes contracted after

taking quinine. Under the microscope it is seen to be composed of a sponge of fibrous tissue, the spaces being filled with blood, which flows freely into them from arterioles in whose walls lymphoid tissue is abundant. Here and there, this lymphoid tissue becomes collected in nodules, which are large enough to be seen by the naked eye and are called Malpighian corpuscles.

In the blood of the spleen, partly broken down erythrocytes are often visible. Sometimes, also, cells like those found in red bone marrow and having to do with the manufacture of new red corpuscles make their appearance.

Taking all these facts together, it is believed that the spleen has the following functions: (1) manufacture of leucocytes; (2) manufacture of erythrocytes; (3) destruction of erythrocytes; (4) removal from the blood of certain poisons.

The Thymus Gland.—The thymus gland, situated at the root of the neck, is quite large at birth, but its size gradually diminishes as the animal grows. By the time that puberty is reached, it has almost disappeared. It is composed of peculiarly arranged lymphoid tissue, having nests of epithelial cells embedded in it. It seems to bear some relationship to the generative glands, for its removal in young male animals hastens the growth of the testes.

CHAPTER XIV.

ANIMAL HEAT AND FEVER.

In considering the problem of animal heat, it is essential to bear clearly in mind the distinction between amount and intensity of heat. The former is measured in calories (see p. 84), and the latter in degrees of temperature. To measure the temperature of a man a maximal thermometer with the Fahrenheit or Centigrade scale is placed in some protected part of the body, as the mouth, the axilla or the rectum. It is found by such measurement that the temperature varies according to the site of observation and the time of day. It varies between 36.0° C. (96.8° F.) and 37.8° C. (100.0° F.) in the rectum; between 36.3° C. (97.3° F.) and 37.5° C. (99.5° F.) in the axilla; and between 36.0° C. (96.8° F.) and 37.25° C. (99.3° F.) in the mouth. These variations indicate that the temperature is higher in the deeper than in the superficial parts of the body; in other words, that the visceral blood is warmer than that of the surface of the body. The variations of temperature due to the time of day are most evident when it is taken in the rectum, and they amount in health to a little over 1° C. or a little below 2° F., the highest temperature occurring about 3 p. m., and the lowest about 3 a. m. This is called the *diurnal variation* and it may become much greater in febrile diseases.

Animals whose temperature behaves as above described are called *warm-blooded* in contrast to those animals, called *cold-blooded*, in whom it is only a degree or two above that of the air, with which it runs parallel. Such animals include fishes, amphibians, snakes, etc. Between the cold and the warm-blooded animals is a group in which the animal is warm-blooded in summer and cold-blooded in winter. These are the *hibernating animals*, such as the hedgehog, the marmot, the bat, etc. In this connection it is interesting to note that the human infant be-

has more or less like a cold-blooded animal for some time immediately following birth, during which period it must therefore be carefully protected from cooling, for, if its temperature be allowed to fall to any considerable extent, it is not likely to survive. It takes several months before the heat regulating mechanism becomes so developed that the infant can withstand any considerable degree of cold.

Factors Concerned in Maintaining the Body Temperature.—

The body temperature is a balance between heat production and heat loss. Heat is *produced* by combustion of the organic food-stuffs in the muscles, the amount which each foodstuff thus produces being the same as when it is burned outside the body, except in the case of protein, when allowance must be made for the incomplete combustion of this substance in the animal body (see p. 85). The muscles are therefore the furnaces of the animal body, the fuel being the organic foodstuffs. Heat is *lost* from the body mainly from the skin, but partly also from the lungs and in excreta. Heat loss from the skin is brought about by the utilization of several physical processes, namely: (1) by conduction along objects which are in contact with the skin or through the air; (2) by convection, that is, by being carried away in currents of air which move about the body; (3) by radiation; (4) by evaporation of sweat. This last is the means by which most heat can be lost, because it takes a large amount of latent heat to vaporize the sweat (see p. 20).

Heat loss from the lungs is mainly due to vaporization of water, with which the expired air is saturated. A small amount is also absorbed in warming the air itself. The heat lost in the urine and faeces is almost negligible.

The Regulation of the Body Temperature.—It is plain that a very sensitive regulatory mechanism must exist in order that the production and loss of heat may be so adjusted as to keep the body temperature practically constant. When heat loss becomes excessive, then must heat production be increased to maintain the balance, and *vice versa* when heat loss is slight. The conditions are to a certain extent comparable with those obtaining in a house heated by a furnace and radiators and provided with a

thermo-regulator, which, being activated by the temperature of the rooms, acts on the furnace so as to raise or lower its rate of combustion.

In the animal body the thermo-regulator is the nervous system. Whenever the temperature of the blood changes from the normal, a nerve center called the *thermogenic* becomes acted on with the result that it transmits impulses to the muscles, which, by increasing or diminishing their tone (see p. 253), cause a greater or a less heat-production. But the center does more than the thermo-regulator of a house, for it controls the agencies of heat-loss. Thus, when the blood temperature tends to rise, the thermogenic center causes more heat to be lost from the skin and lungs in the following ways: (1) It acts on the blood vessels of the skin, causing them to dilate so that more blood is brought to the surface of the body to be cooled off. (2) It excites the sweat glands, so that more heat has to be utilized to evaporate the sweat. (3) It quickens the respirations, so that more air has to be warmed and saturated with moisture. The degree to which these cooling processes are used varies in different animals. Thus in the dog, since there are no sweat glands over the surface of the body (they are confined to the pads of the paws), increase in the respiration is the chief method of cooling, hence the panting on warm days.

In the case of man, civilization has stepped in to assist the reflex control of heat loss, as by the choice of clothing and the artificial heating of rooms. Desirable though this voluntary control of heat-loss from the body may be, there can be little doubt that it is often overdone to the detriment of good health. Living in overheated rooms during the cooler months of the year suppresses to a very low degree the heat loss from the body and thereby lowers the tone and heat production of the muscular system. The food is thereby incompletely metabolized and is stored away as fat; the superficial capillaries are constricted and the skin becomes bloodless. But it is not looks alone that suffer, but health as well, for, by having so little to do, the heat-regulating mechanism gets out of gear so that when it is required to act, as when the person goes outside, it may not do so promptly

enough, with the result that the body temperature falls somewhat, and catarrhs, etc., are the result. There can be little doubt that much of the benefit of open-air sleeping is due to the constant stimulation of the metabolic processes which it causes.

The importance of the evaporation of sweat in bringing about loss of heat in man partly explains why *climate* should have so important an influence on his well-being. It is not so much the temperature of the air, as its relative humidity, that is of importance; that is, the degree, expressed in percentage, to which the air is saturated with moisture at the temperature of observation. Thus, a relative humidity of 75 per cent at 15° C. means that the air contains 75 per cent of the total amount of moisture which it would contain if it were saturated with moisture at a temperature of 15° C. A high relative humidity at a high temperature makes it impossible for much sweat to be evaporated, with the result that the body cannot cool properly, and the body temperature is likely to rise unless muscular activity be reduced to a minimum. This explains why it is impossible to do much muscular work in hot humid atmospheres. On the other hand, if the relative humidity is low, the temperature may rise to an extraordinary degree (even above that of the body itself) without causing fever, provided always that the body is not so covered with clothing that evaporation of sweat is impossible.

At low temperatures of the air, relative humidity has an effect which is exactly opposite to that which it has at high temperatures, for now it affects, not the evaporation of sweat, but the heat conductivity of the air itself. Cold moist air conducts away heat much more rapidly than cold dry air. Hence, a temperature many degrees below zero on the dry plains of the West may be much more tolerable to man than a much higher temperature along the shores of the Great Lakes.

Fever.—Any rise of temperature above the normal limits constitutes fever. When of slight degree, as it is in many semi-acute diseases, its detection demands frequent observation, so as to allow for the normal diurnal variation of the body temperature. For example, if the temperature were recorded in the morning in such a patient, a slight degree of fever might quite

easily be missed, because at this time the normal temperature is low. In acute infectious diseases, the afternoon temperature may rise to 106° F. or 41° C., or even above this, without proving fatal. A temperature of 113° F. or 45° C. has been observed, but lasting for only a short time. Fever is always higher in infants and young children than in adults.

As to *the causes of fever*, two possibilities exist: either (1) that heat production has been increased, or (2) that heat loss has been diminished, or, of course, both factors may operate simultaneously. To go into this unsolved problem is unnecessary here; suffice it to say that there can be no doubt that disturbance in the thermogenic center is the underlying cause of fever, and that it is the avenues of heat loss by the skin rather than the sources of heat supply in the muscles that are first of all acted on. The cold sensation down the back, the shivering, the goose skin, are the familiar initial symptoms of fever, and when the fever comes to an end, excessive sweating sets in and this, in part at least, explains the fall in temperature. Increased combustion in the muscles no doubt occurs during the height of the fever and accounts for the great wasting, but that this is not the only cause of the rise in temperature is evidenced by the fact that severe muscular exercise does not in itself cause fever, even although there may be much more combustion going on in the body (see p. 88).

Certain drugs called antipyretics lower the temperature in fever. The most important of these are acetanilide, salicylates (aspirin), phenacetin, and quinine. The first three mentioned act on the thermogenic center, whereas quinine seems to act directly on the combustion processes in the muscles. The body temperature is raised by cocaine and by the toxic products of bacterial growth. Even cultures which have been attenuated by keeping them for some time at high temperatures have this effect, and it is believed by many that fever is of the nature of a protective mechanism to destroy or attenuate the invading bacteria. There is bacteriological as well as clinical support for this view, thus, certain pathogenic organisms (such as the streptococcus of erysipelas) cannot live at a temperature above 41° C.,

and cholera patients are much more likely to survive if the disease be accompanied by a moderate degree of fever.

Heat stroke, or *sun stroke*, is due to an increase in body temperature that is above the limits of safety. When sweating and the other processes by which heat is lost from the body are acting properly it is remarkable how high an air temperature may be borne without danger; for example, in dry air a man can sit for some minutes in an oven at 100°C. while his dinner cooks beside him (Leonard Hill). But if anything should interfere with heat loss, or if heat production be excessive, as during muscular exercise, there is always danger of heat stroke. Free movement of the air is probably the most important way for safeguarding against deficient heat loss. It is almost certainly on account of the absence of such air movement, coupled with a high relative humidity, that discomfort is experienced in hot, stuffy atmospheres, for the faulty heat loss causes a slight rise in body temperature. This slight degree of hyperpyrexia lowers the resistance of the organism to infection.

CHAPTER XV.

THE BLOOD.

Introduction.—The individual cells forming the most simple types of life are nourished by substances which they obtain directly from the water in which the animal lives. In exchange for this food, they excrete into the water the waste materials of their metabolism. As the organism becomes more and more complex this direct interchange of materials becomes impossible, and the blood and lymph assume the task of delivering food to the tissues and of removing the waste materials. To accomplish this, these fluids come into close relation with the absorbing, eliminating, and general tissue elements of the body, the lymph being in immediate contact with the cells and the blood moving quickly from place to place. Therefore all the elements found in the tissues and all the waste materials produced by the body are present at some time in the blood. The blood may indeed be compared to the wholesaler of commerce, who handles all the materials for the support of life, and the lymph to the retailer, who distributes to the tissue cells the materials which they need. In short, it may be said that the blood replenishes the lymph for the losses which it incurs in supplying the tissues.

Physical Properties.—Ordinary mammalian blood is an opaque, somewhat viscid fluid, varying in color from a bright red in arterial blood to a dark red in venous blood. Contact with air changes venous blood to arterial blood. Microscopical examination shows that the blood is not perfectly homogenous, but consists of a clear fluid in which cells called corpuscles are suspended.

The Corpuscles.

There are three varieties of these: the *red corpuscles* (to which the color of blood is due), the *white corpuscles* and the *blood platelets*.

Erythrocytes.—The *red corpuscles*, or *erythrocytes*, as they are called, are by far the most numerous, there being five million of them in a cubic millimeter of normal blood. Examined under the microscope, they are seen in man to be flattened, biconcave, non-nucleated discs; but in the embryo, as well as in birds and reptiles, they have a nucleus. Each corpuscle consists of an envelope and a framework of protein and lipid material containing a substance known as hæmoglobin.

HÆMOGLOBIN is a very complex body, belonging to the general class of compound proteins (see p. 21). Hæmoglobin has the ability to unite with large amounts of oxygen, thus enabling the blood to carry the oxygen gathered in the lungs, to the distant tissues. It consists of a combination of a simple protein, globin, and a pigment, hæmatin. *Hæmatin* contains iron, which is responsible for the ability of oxygen to unite with the hæmoglobin molecule. The combination of hæmoglobin with oxygen is not very stable, and can be readily broken with the liberation of oxygen. It is for this reason that this molecule is adapted to carry oxygen to the tissues. The quantity of hæmoglobin held by the corpuscle may vary and in some diseases, as in chloroanæmia, for instance, it may be greatly diminished, so much so that the tissues may be unable to obtain the proper amount of oxygen. The amount of hæmoglobin actually present in a sample of blood may be estimated by the intensity of the red color it gives to the blood. To estimate this intensity a drop of blood is received on blotting paper, the stain being then compared either with that produced by normal blood in various dilutions on the same paper, or with a standardized chart. From the concentration of normal blood whose stain most nearly matches that of the unknown sample, we can determine the percentage of hæmoglobin in the latter, or we can read this directly from the chart.

ENUMERATION OF THE BLOOD CORPUSCLES.—The number of red or white cells present in a cubic millimeter of blood may be estimated by the use of a hæmocytometer or blood-counter. This consists of two mixing capillary tubes, in one of which the blood is diluted one hundred times with saline solution, and in the

other, ten times with 0.337% acetic acid. The former dilution is for counting red, and the latter, for counting white corpuscles. A drop of the diluted blood is then placed on a special glass slide which contains a counting chamber of such a depth that when a cover slip is put over a drop of fluid in the chamber, a column of fluid one-tenth of a millimeter deep is obtained (Fig. 13). The chamber is graduated with cross lines, so that each square represents a known fraction of a millimeter. The average number of corpuscles found in a number of squares, by actual count with a microscope, is multiplied by the factors of dilution employed, the product being the number of cells in a cubic milli-

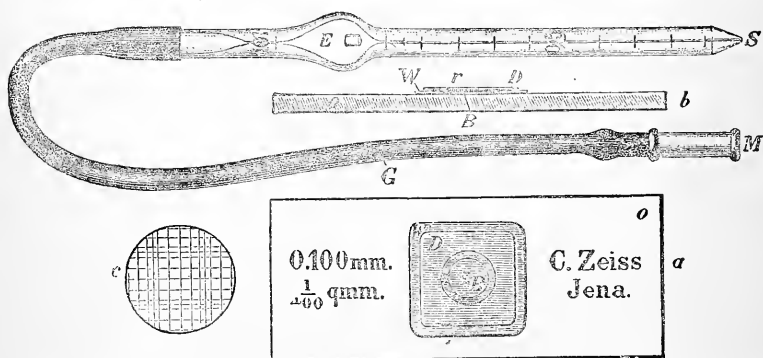


Fig. 13.—Thoma-Zeiss Haemocytometer, *M*, mouthpiece of tube (*G*), by which blood is sucked into *S*; *B*, bead for mixing; *a*, view of slide from above; *b*, in section; *c*, squares in middle of *B*, as seen under microscope.

meter of blood. The erythrocytes, which in health number about five million in a cubic millimeter, may decrease to less than a million in disease, such as pernicious anæmia, or after hæmorrhage. On the other hand, they may number six or seven million in people who live at high altitudes. The oxygen-carrying power of the blood is proportional to the percentage of hæmoglobin, so that by estimating this and the number of corpuscles, a fair idea of the condition of the blood is obtained.

THE ORIGIN OF ERYTHROCYTES.—It is interesting to inquire into the source of the blood cells, but although this has been the subject of many researches, it is by no means definitely settled

just what the process is or in what part of the body the cells originate. Nor is it definitely known just where the worn out cells are dealt with. In the embryo certain cells are set apart to develop the vascular system. Some of these form the blood vessels and some the red corpuscles, but later in foetal life, the latter come from cells in the spleen, liver and red bone-marrow. At first the red corpuscles are nucleated, but towards the end of foetal life they begin to lose their nuclei, so that at birth there are very few nucleated red corpuscles remaining in the blood. After birth, the red corpuscles are formed in the red bone-marrow of the flat bones. In these places special nucleated cells are found, which are called erythroblasts, and from these the erythrocytes develop. After severe hæmorrhage nucleated red cells may appear in the blood for a short time; the same is true in some forms of anæmia in which there occurs a very rapid destruction accompanied with a very rapid formation of red cells.

Since the life of an *erythrocyte* is necessarily limited, provision must be made for the destruction and elimination of the substances of which they are composed. In the pigments of the bile we find the remains of part of the hæmoglobin. The bile is secreted by the liver into the intestine (see p. 71), and in case the free outflow of bile is interfered with, the blood absorbs the pigment and the individual becomes yellow or is said to be jaundiced. The bile pigments do not, however, contain all the elements of the hæmoglobin, for the iron is not excreted by the bile. It is, on the contrary, stored up by the liver to be used again in the formation of fresh hæmoglobin. Some have thought that the function of the spleen is to destroy the *red blood cells*, the waste products of which are sent to the liver through the splenic vein. The evidence for this is the presence of pigment and iron-containing substances in the blood of this vein.

Iron is an essential constituent in the hæmoglobin molecule, and it is necessary that some be constantly supplied to the body in the food. But this amount need not be large, since the iron-containing substance can be used time and again in the manufacture of new hæmoglobin, and once the body has the requisite amount, little more need be added (see p. 120). Indeed, it is

questionable if the inorganic forms of iron can be utilized by the body, the iron in our blood being probably derived from a conjugated protein known as hæmatogen, found in small quantities in the food.

The White Blood Cells.—In normal human blood there are about ten thousand cells in a cubic millimeter of blood, or about one to every five hundred red cells. In many ways they resemble the unicellular amœba, for like it they have the power of making independent movement by extending tiny processes called pseudopodia in one direction and by retracting them in another. By virtue of this peculiar movement they are able to flow, as it were, between the endothelial cells of the capillaries and find their way into the tissue spaces. There are a number of forms of white cells differing from each other in size, in the character of their nucleus, and in the granules they contain. In general, they are classified in two main groups on morphological grounds, viz., *leucocytes* and *lymphocytes*.

The leucocytes are the most numerous and compose about 65 per cent of the total white cells. They are characterized by a lobed nucleus, the parts of which are connected by strands of chromatin material. To this class belong several sub-groups. The most important of these are the cells known as polymorphonuclear leucocytes. They comprise about 96 per cent of the leucocytes. Others are known as eosinophiles, since they have granules which have a marked affinity for acid stains.

The Lymphocytes, the second variety, are so-called, since they are supposed to be formed in the lymph glands of the body. They possess a single large round nucleus surrounded by a clear layer of protoplasm. There are two sub-groups in this class: the *large mononuclear lymphocytes*, which contain a rather abundant cytoplasm about the nucleus, and the *small mononuclear lymphocytes*, in which the amount of cytoplasm is very small. The former comprise about 4 per cent, and the latter about 30 per cent, of the white cells.

ESTIMATION OF THE WHITE CELLS.—The number of white cells found in the blood is estimated by the same principle that is employed in the counting of the red cells (see p. 142). In certain

diseases their number may vary greatly. The number is also increased after meals. A marked increase over normal is known as a leucocytosis.

THE FUNCTION OF THE LEUCOCYTES.—In acute infections, as in appendicitis, pneumonia, and localized or general septic conditions in which pus is formed, there is usually a great increase in the number of the polymorphonuclear leucocytes. In more chronic infections, as in tuberculosis, the lymphocytes are found in greater number. In the parasitic diseases of animal origin, as tapeworm and hookworm, in some skin diseases, and in scarlet fever, the eosinophile leucocytes are more abundant. In the disease leucocythæmia the lymphocytes may be present in such great numbers that they impede the movement of blood by increasing its viscosity or thickness. The above observations suggest that leucocytes play an important rôle in the protection of the body from infective processes. This function will be discussed later. Another important function they may have is the preparation of the peculiar proteins which are found in the blood plasma.

THE BLOOD PLATELETS.—These bodies are smaller than the erythrocytes, and number about 300,000 in a cubic millimeter of blood. When blood is shed they disintegrate very rapidly, and set free a substance which plays a part in the coagulation of the blood. Little is known concerning their chemical constitution or their physiological function.

The Blood Plasma.

The blood plasma is a very complex fluid containing all the varied substances associated with the function of the blood. Water composes 90 per cent of the plasma. The plasma proteins constitute the largest solid constituent (7 per cent), and include serum globulin, serum albumin, and fibrinogen. There are a number of bodies which contain nitrogen which are not proteins. These may be grouped into two classes, the first, represented by the amino acids and other nitrogenous bodies derived from the protein of the food and from which the tissue cells are built, and the second group, represented by waste materials given off by the

tissue cells. These include substances such as urea, uric acid, creatinin, and ammonia. The non-nitrogenous organic bodies are dextrose, of which 0.1 per cent is present in normal plasma, and a small quantity of fat. About 1 per cent of inorganic salts are found, the chief of which is sodium chloride, which constitutes 60 per cent of the ash. Sodium carbonate is found in a little less degree. Besides these two we find small amounts of potassium, sodium and calcium chlorides and phosphates. An important group of substances known as hormones are excreted into the plasma by some of the glands of the body, and affect the metabolism of the tissues in a specific manner. Another group of bodies, the antitoxins, complements, and opsonins (see p. 154), are found in the blood. These are concerned in the protection of the body against infective organisms.

CHAPTER XVI.

THE BLOOD (Cont'd).

The Defensive Mechanisms of the Blood.

The Coagulation of the Blood.—Whenever a blood vessel is slightly cut, the blood, which at first comes very freely, soon ceases to flow because of the formation of a plug or clot of blood at the site of the injury. The process by which the blood spontaneously forms the plug in the injured vessel is known as coagulation, or clot formation. It protects the body from fatal hemorrhage in case of an ordinary wound. A clot is a semi-solid mass, which on microscopical examination is seen to consist of a meshwork of fibrils holding the blood corpuscles in their interspaces. If blood is collected in a basin and whipped with some twigs while it is clotting, the fibrils will collect on the twigs in stringy masses, and the blood will remain fluid. The stringy material is called fibrin. Obviously, fibrin cannot exist in the blood stream, else the blood would form a clot within the blood vessels; it is formed only when occasion demands, such as an injury to the blood vessel. There are a number of experiments which explain the process of coagulation.

Thus, if blood is prevented from clotting by cooling it to 0.° Centigrade, and is then mixed with a saturated solution of salt, a white precipitate forms, which may be filtered off and dissolved in 0.1 per cent salt water. This solution may be made to clot by the addition of a very little blood from which the fibrin has been removed. In other words, we have prepared a substance which under proper conditions forms the fibrin of the clot. This substance is called *fibrinogen*, since it is the precursor of *fibrin*.

Again, if blood be treated with sodium oxalate, it will not clot unless *calcium salts* be added in amount sufficient to precipitate

completely all the oxalate and leave some in excess. In other words, the presence of a soluble calcium salt is necessary in order to have the blood clot. Defibrinated blood will, however, cause the clotting of pure fibrinogen solutions even though all the calcium be removed from both solutions.

In order to explain the above facts, we must assume that three substances are present in solution in the blood: *fibrinogen*, *calcium salts*, and another substance, which has been called *thrombogen*. Under the proper conditions, thrombogen will combine with calcium salts to form thrombin, which in turn unites with fibrinogen to form fibrin, which is the substance forming the framework of the clot.

The reason why the blood does not clot within the blood vessels is not definitely known. It is probable that the blood contains a substance which prevents the combination of thrombogen with calcium salts, and which we call *anti-thrombin*. Whenever a blood vessel is injured, the tissues and the blood platelets liberate a lipid body called *kephalin*, which unites with the anti thrombin and thus allows the formation of thrombin to take place at the site of the wound. The whole process may be graphically shown in the following schema :

Anti-thrombin + kephalin = inactive anti-thrombin.

Thrombogen + calcium salts = thrombin.

Thrombin + fibrinogen = fibrin.

Fibrin + corpuscles = clot.

Antibodies in the Blood.—The coagulation of the blood is only one of the measures which are developed in the blood for the protection of the animal. No less important in this regard are the destruction and removal of toxic and injurious substances from the body.

All the infectious diseases are caused by the agency of microorganisms. The greater number of these are microscopic plants known as bacteria and fungi; some, however, are unicellular animals known as protozoa. It is especially against the bacteria that a method of defense exists in the body; the protozoal diseases, on

the other hand—such as syphilis, malaria, sleeping sickness and those caused by amœba in the mouth and alimentary tract—find relatively little resistance offered to their growth in the body, and their destruction therefore must be for the most part brought about by drugs.

The Process of Inflammation, which in a general way is known by the common symptoms of fever, pain, swelling and redness, is a sign of an increased activity on the part of the tissues in an effort to destroy some foreign body which is poisonous to the cells. Microscopical examination of a section of inflamed tissue will show that the blood vessels are dilated, and that the tissue spaces are infiltrated with leucocytes. It suggests that the blood elements must have a very important part in the process. The study of this function of the body is one of the most interesting chapters of physiological science, and includes the questions of immunity from disease and the cure of infectious processes.

Many pathogenic organisms can be cultivated on artificial media and the products of their metabolism can then be studied. It has been found that they may be divided into two groups: the one group producing the soluble poisons, or true toxins, which are excreted from the cell; and the other producing toxic substances, the endo-toxins, which are not excreted from the cell. We will first take up the manner in which the body deals with the *toxins*.

Toxins.—If a culture of diphtheria or tetanus bacilli be filtered through a porcelain filter, the bodies of the bacilli are removed and the filtrate contains the soluble toxic principles which the bacilli have produced and excreted into the nutrient fluid. Injections of a small amount of this filtrate into an animal will produce the same symptoms as are produced when a pure culture of the bacilli is injected. Each bacillus produces a specific kind of toxin. Diphtheria toxin acts primarily on the vascular system; tetanus toxin, on the central nervous system. The chemical nature of the toxin molecule is unknown, since it has been impossible to separate it in pure form. It is probably closely related to the protein molecule, and on the other hand resembles the

ferments in many of its actions (see p. 34). A peculiarity in the action of the toxins is that a relatively long period elapses between the injection of the toxin and the reaction of the body, whereas in the case of the alkaloids or vegetable poisons, the reaction appears very quickly.

Antitoxin.—In spite of the very poisonous character of the toxin molecule, the body is provided with a means of defense against it, and is able to make itself still further immune to the action of the toxin. Thus, if somewhat less than the fatal dose of diphtheria or tetanus toxin be injected into the body, certain symptoms will follow, and the animal will react to the toxin in such a way that a subsequent injection can be made larger without proving fatal. If successively increasing doses are given, the animal after some weeks will be able to withstand very large doses of the toxin. In other words, the body develops an immunity towards the toxic agent; it produces an antibody which neutralizes the poison of the toxin. To this body we give the name of antitoxin. Since these antibodies are found in solution in the blood, it is possible to withdraw the blood from such an immune animal, and inject it into a non-immune animal, thus rendering the latter immune to the toxin. It is this principle that is used in the preparation of diphtheria and tetanus antitoxins. The exact nature of the combination of the toxin and the antitoxin cannot be learned from chemical studies, but Ehrlich has given to the phenomenon a biological explanation based on the various known reactions of the bodies.

Ehrlich's Side Chain Theory of Immunity.—Briefly summarized Ehrlich's theory is as follows: Each toxin molecule is made up of a central nucleus of chemical radicles similar to those found in organic compounds. To the main body of this molecule are attached at least two other radicles, or side chains. One of these has a great affinity for certain chemical constituents of the tissues of susceptible animals, and unites the toxin molecule to the tissue cell. This chain is known as the *haptophore group*. The other side chain, the *toxophore group*, exerts the injurious effect upon the tissue after the haptophore group has joined the toxin to the cell. For example, tetanus toxin owes its effect to

the fact that nervous tissue contains a chemical substance which unites readily with the haptophore group of the tetanus toxin, and also substances that are readily attacked by the toxophore group of the toxin. The antitoxins are supposed to act by combining with the haptophore group, thus preventing the toxin from uniting with the cell.

According to this theory the formation of antitoxins may be accounted for as follows: When a *receptor*, as we may term the portion of the cell which unites with the haptophore groups, is united to the toxin, the cell endeavors to adapt itself to the loss of this radicle by the production of another similar one. Since the general rule of nature is to respond to an action with an over-reaction, many more receptors are made than are actually needed to unite with the haptophore groups of the toxin present. The receptors produced in such great number break away from the parent cell. These accordingly are stored up in the blood, and whenever any of the particular toxin for which they are adapted is present in the circulation, they unite with it and thus prevent the toxin from uniting with the tissue cells. A body which possesses a store of such antibodies is said therefore to be immune.

Toxins are not the only substances which will produce specific antibodies. This property is a general characteristic of proteins. Any substance producing an antibody is known as an antigen. For example, if human blood be injected into a rabbit, and after several days some of the rabbit's blood serum is mixed with human blood serum, a precipitate will form, whereas the blood of a normal rabbit will produce no such precipitate. The first injection of human blood serves to stimulate the rabbit cells to form some substance which precipitates any human blood subsequently added. The reaction is specific, for the blood of any other species of animal will not be precipitated by blood from a rabbit sensitized with human blood, and the reaction offers a very accurate method of differentiating between human blood and other blood in medico-legal cases. The body thus formed is known as a *precipitin*.

Anaphylaxis.—Again, if a rabbit be injected with some hu-

man serum two or three weeks after a previous injection, the animal will go into a very profound state of shock. The blood pressure will be lowered, the heart's action weakened, and breathing interfered with. This condition is known as *anaphylactic shock*. The reaction is a general one for proteins and is specific for each protein used. The phenomenon is explained by assuming that the first injection, while producing the bodies which we referred to above as precipitins, also produces an excess of a ferment which is able to break down the foreign protein very quickly when the second injection takes place. The products of the broken protein molecule, as they are produced in the blood, are poisonous to the body and produce the phenomenon above described.

Phagocytosis.—By far the greater number of pathogenic organisms do not excrete a poisonous toxin into the surrounding medium, but they cause disease by directly attacking the tissues. The diphtheria bacillus does not enter the body, but only excretes a soluble toxin which the body absorbs. When a disease involves the infection of the tissues themselves by a micro-organism, other types of defense than those described above are used. This defense depends on the fact that some of the leucocytes of the blood and lymph have the ability to ingest and destroy foreign bodies which are present in the blood and tissues, in much the same way as the amœba takes its food. This function of the leucocytes to destroy foreign bodies is known as *phagocytosis*. In the changes which accompany the metamorphosis of certain forms of larva, the leucocytes are the agents which remove those parts of the body which are no longer of service to the animal. Likewise the leucocytes of the blood can be shown to ingest pathogenic bacteria and to destroy them. The exact function of the different varieties of white cells in the blood is not definitely known. In active inflammatory processes the polymorphonuclear leucocytes are by far the most numerous. On the other hand, in cases of chronic infection, as in tuberculosis the number of lymphocytes is increased. Some of the forms of white cells do not take an active part in the ingestion of bacteria, and therefore cannot directly destroy them. Yet, in the defense

of the organism, they take a part which is no less important than that of the phagocyte.

In very simple forms of life the cells of the alimentary tract both ingest and digest the food material. In higher forms the cells of the alimentary tract secrete the fluids which digest the food. In the one case the digestion is intra-cellular, and in the latter, extra-cellular. In the same way we find the blood leucocytes able both to destroy and to digest substances by intra-cellular action, and also sharing with other cells of the body the power to secrete substances into the blood plasma which have the power of destroying the organisms or toxic material.

Opsonins.—Normal blood serum has a very strong destructive influence on most species of bacteria, whether they are pathogenic or not. This ability is not possessed to the same extent by the blood plasma. The difference is explained by the fact that in the process of coagulation the white blood cells are broken down and liberate their bactericidal bodies. Extracts made of leucocytes have this same effect, but the reaction is much more rapid in the presence of blood plasma or serum. The co-operation on the part of the plasma or serum is explained by the presence of some substance in solution which enables the leucocytes to attack the bacteria more readily.

That some such substances also aid in the phagocytic action of the leucocytes is indicated by the fact that the white cells ingest bacteria much more quickly in blood serum than in normal saline solution. These substances are known as *opsonins*, and are characteristic for each individual organism which stimulates their production. At the beginning of an infective process, in which the phagocytosis is very active, each leucocyte may be able to attack only one or two bacteria; later in the disease, however, when the opsonic power has been increased for the infective agent, the leucocytes may be able to ingest a much larger number without injury to themselves. The opsonic index is a figure expressing the ratio of the number of pathogenic organisms of a certain kind that a normal leucocyte can ingest in serum, to that which the same leucocyte can ingest in the presence of the serum of a

patient who is suffering from the infective agent. A high opsonic index therefore indicates a relative immunity or high resistance to the disease in question. The bactericidal power of the leucocytes for many bacteria can be greatly increased by the injection of dead bacteria into the body. This fact is made use of in the manufacture of bacterial vaccines, which consist of suspensions of dead bacteria in a saline solution.

CHAPTER XVII.

THE LYMPH.

The blood circulates in closed tubules, so that the nourishment which is supplied the tissues and the effete products which result from their activity must pass through the walls of the vessels. The fluid which is transuded from the capillaries and which surrounds the cells of the tissues is known as the lymph, and serves as the medium of exchange between the cells and the blood plasma. It is the middleman of exchange between the blood and the tissues. Lymph is a slightly yellow transparent fluid, closely resembling the blood plasma from which it is derived. To aid in returning the lymph to the blood, there is provided a special system of vessels called the lymphatics, which are very thin-walled capillary tubules lined with endothelial cells. These tubules lead to larger ones which, after passing through a lymph gland along their course, finally empty into a large vein-like vessel, the thoracic duct, lying alongside of the œsophagus in the thorax, and emptying into the left subclavian vein. A smaller lymphatic vessel, the right thoracic duct, empties into the right subclavian vein.

The lymph obtained from the thoracic duct by means of a fine tube inserted into the vessel varies somewhat in nature. After a meal the fluid is like milk, because of the presence of droplets of fat which have been absorbed from the intestines. The lymphatics of the viscera appear as white lines in the mesentery and on this account are called lacteals. The lymph which is collected during a fast is very much like the blood plasma. Its specific gravity is less than that of blood, since it contains less protein material, but on the other hand its salt content is the same and it clots in much the same manner as blood. On microscopic examination there are found many colorless corpuscles, identical with those present in blood. Some of these corpuscles are formed within the lymph

glands through which the lymph vessels pass on their way to the subclavian vein.

Lymph Formation.—Many physiologists have attempted to discover the precise mechanism by which the plasma passes through the capillary walls into the lymph spaces, but the complete knowledge of the process is not yet at hand. The relatively high blood pressure within the capillaries provides filtration pressure by which a fluid might be filtered through the capillary walls, and there is no doubt that such a process does occur, as, for example, after the capillary pressure has been increased by constriction of the veins by a bandage, etc. Filtration, however, cannot explain all the known phenomena of lymph formation. Osmosis (p. 27) also plays a part as follows: The tissues use up the nutritional elements brought to them by the lymph. The diffusion pressure of the substances in the lymph is now reduced so that it becomes less than that present in the blood. Therefore substances within the blood must pass out through the capillary walls into the lymph, thus keeping the concentration of the fluid more or less constant. The waste products of the tissue pass into the lymph and, by increasing the molecular concentration of the lymph, draw water from the blood. Again, the breaking down of the large protein molecules into smaller ones, in the processes of tissue metabolism, will cause the molecular concentration of the tissues to rise, increasing the osmotic pressure. This causes water to be abstracted from the lymph, which in turn draws on the blood for water.

Lymphagogues.—There are certain substances which affect the rate of lymph formation in a very peculiar way. These are called lymphagogues, and include extracts from many shell fish, leech extract, peptones, etc. When such substances are injected into the blood of an animal, there follows a great increase in the rate of lymph formation and lymph flow. Indeed some people are very susceptible to this action, and eating shell fish, oysters, and some fruits will cause their tissues to become swollen because of an increased lymph formation. How these substances can effect the change by altering the physico-chemical constitution of the blood plasma is not clear. Some investigators believe

that they have a stimulating action on the endothelial cells lining the capillaries and thus produce an actual secretion of lymph. It is more probable, however, that they poison these cells in a way which increases their permeability and thus permits a freer filtration of lymph from the blood plasma. There are other facts nevertheless which support the theory of an actual secreting mechanism within the cells of the capillary walls, but they are too technical to consider here. They suggest that although the physico-chemical laws of diffusion, osmosis, filtration, etc., play the most important role in lymph formation, the cells of the capillary walls may themselves have an active part in the process.

Lymph Reabsorption.—Within the tissue spaces, and within the cells of the tissues, changes are continually taking place which alter the character of the lymph. Oxygen and food substances are removed from the lymph by the tissue cells, and waste substances, the result of the tissue metabolism, are added to it. In the case of oxygen and carbon dioxide, the exchange is so regulated as to keep constant the supply of these bodies in the lymph. The loss of any substance is quickly compensated for by the addition of new material from the blood. The solid waste matter excreted by the cell can also find its way directly from the cell through the lymph and into the blood plasma. It is probable that during periods of rest or of slight activity the lymphatics are of little importance in the exchange of the lymph. However, when the exudation of lymph becomes increased, as during exercise or following the use of some lymphagogue, or when there are substances in the lymph which the capillaries cannot absorb into the blood, the lymphatics become very important in helping to remove the excess of lymph formed.

The Movement of the Lymph.—The mechanism by which the lymph of the tissues is collected by the capillaries of the lymphatic system is not understood any better than the mechanism of lymph formation, but no doubt the same laws apply to both processes. The movement of the lymph along the lymphatic vessels is possible because of the presence of valves along the course of the vessels.

The process of lymph absorption is rather slow except when it is aided by the massage produced by the movements of the surrounding parts. The rapid action of poisons, or drugs introduced by a hypodermic syringe, is due to their absorption from the intra-cellular or lymph spaces directly into the blood. Colored solutions as india ink are absorbed by the lymphatics, and by using a substance like this it is possible to trace the lymphatics of a portion of the body. Micro-organisms, such as the streptococcus, which causes one of the familiar forms of what is known as blood poisoning, are taken up by the lymphatics, and it is easy to trace the channels traversed by the organism by the inflamed lymphatic walls which appear as red lines under the skin. Since all these vessels pass through a lymphatic gland on their way to the subclavian vein, these glands are often very much swollen, and may even be destroyed as the result of the infection. It is probable that one of the functions of the lymph gland is to catch and render non-toxic, poisons which are being carried into the circulation by way of the lymphatics. One of the most dreaded diseases, carcinoma, is carried by the lymphatic system to other parts of the body. For this reason we most often see the metastatic growths of cancer in the region of the lymph glands which have caught the straying cancer cell and have been infected by it.

The increased exudation of lymph in the tissues which occurs in inflammatory conditions is no doubt of great advantage to the tissues, since, by this means, a greater supply of nourishment is provided for the repair of the damaged cells, and the defensive substances (antibodies, etc.) are brought into play.

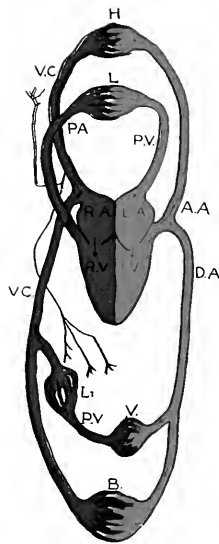


Fig. 14.—Diagram of Circulation. The blood circulates as follows: *V.C.* (venæ cavæ), *R.A.* (right auricle), *R.V.* (right ventricle), *P.A.* (pulmonary artery), *P.V.* (pulmonary vein, red), *L.A.* (left auricle), *L.V.* (left ventricle), *A.A.* and *D.A.* (ascending and descending aorta), *H.V.* and *B.* (capillaries of head, viscera and body generally), *P.V.* (portal vein, blue), *Li.* (liver). The small black vessels are the azygos veins.

CHAPTER XVIII.

THE CIRCULATORY SYSTEM.

Introduction.—The circulatory system provides for the transportation of blood through the tissues, thus enabling each individual cell to obtain nourishment and to rid itself of the waste products of its activity. The system includes the heart, the blood vessels, and the lymphatics.

From a mechanical standpoint, we may say that the heart consists of a pair of pumps; each pump consisting of two parts, an upper chamber, the *auricle*, and the lower one, the *ventricle*. Thin, membranous valves, called auriculo-ventricular, separate the upper and lower chambers and prevent the blood from flowing back into the auricle when the ventricle contracts. Connected with the ventricles are the *arteries*, which conduct the blood away from the heart, to which it is returned by the great veins leading into the auricles. At the point where the arteries emerge from the heart are cup-shaped valves, called semilunar, which prevent the passage of blood from the arteries into the ventricles while the latter are relaxing.

As will be seen from the accompanying diagram (Fig. 14) the blood pumped from the two sides of the heart circulates through two distinct and separate systems of blood vessels. From the right ventricle the blood goes through the pulmonary artery to the lungs and is returned to the left auricle by the pulmonary veins, then to the left ventricle, whence it is sent over the body through the aorta and its branches, to the capillaries imbedded in the tissues. - From these it is returned through the veins to the *venæ cavæ*, which discharge it into the right auricle. . We may say, therefore, that the circulatory system consists of two circles of tubing interposed in which are two force pumps, the valves of which are so disposed as to allow the blood to flow in one direction only.

I. The Heart.

Anatomical Considerations.—The heart is suspended at its base by the large arteries, and lies practically free in a sac of tough fibrous tissue called the *pericardium*. On each side are the lungs, with the diaphragm below, the chest wall in front, and the œsophagus behind (Fig. 15). The surface of the heart and the interior of the pericardial sac are bathed with a serous fluid, the pericardial fluid. The muscular fibers forming the walls of the four chambers of the heart are arranged so that their contrac-

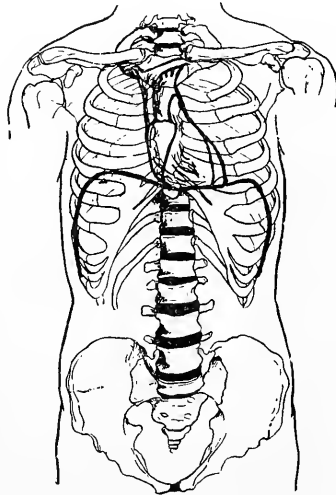


Fig. 15.—The position of the heart in the thorax. (T. Wingate Todd.)

tion diminishes, the size of the cavities and empties the heart of blood.

From the study of the embryonic heart, and from comparative studies in the lower animals (Fig. 16), we know that the heart has developed from a single tube, the division of the auricles and the ventricles being a rather late stage in the development of the mammalian heart. The fact that the two auricles beat synchronously, followed by the contraction of the two ventricles, is significant of the development of the auricles from the proximal, and

of the ventricles from the distal end of the primitive cardiac tube.

The fibers of the auricles run transversely, beginning and ending in the fibrous tissue which separates the auricles from the ventricles. The musculature of the ventricles is somewhat harder to trace. There are layers that run transversely around the ventricles, and also layers which describe more or less of a spiral course from the base of the ventricles to the apex and then are reflected back in transverse layers, until they finally end in the papillary muscles, which are connected with fibrinous threads,

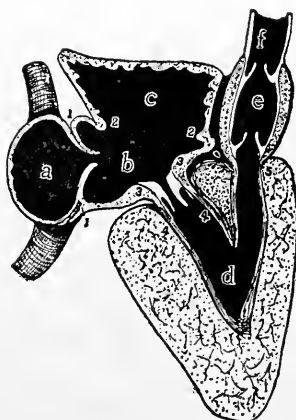


Fig. 16.—A generalized view of the vertebrate heart (Keith) showing: *a*, the sinus venosus; *b.c.*, the auricle; *33*, the auriculo-ventricular orifice and valves; *d*, the ventricle; *e*, the beginning of the aorta with the semilunar valves at *5*. The valves between *e* and *f* do not exist in the heart of man. (From Howell's Physiology.)

the chordæ tendineæ, to the edge of the auriculo-ventricular valves.

When the ventricles contract, this arrangement of muscular fibers causes the apex and the base of the heart to approach one another, and the transverse section is changed from an ellipse to a circle. The base of the heart, hung as it is to the large vessels in the thorax, appears to be fixed, and one would expect that the apex is the part which moves up and down. This is not the case,

however, as is shown by experiment, and is explained by the fact that the blood, when it is forced from the ventricle during the cardiac contraction, exerts its force on the apex as well as on the blood in the arteries. This serves to fix the apex in the vertical position and to bring the base of the ventricles downwards during their contraction. In some individuals there is a visible pulsation at about the level of the fifth rib on the left side. This is called the *apex beat*, and is caused by the rotation of the apex in the transverse diameter and by the sudden change of the ventricle from a soft flabby condition into a firm one.

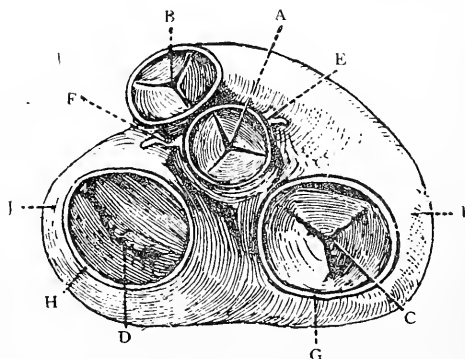


Fig. 17.—Diagram of Valves of the Heart. The valves are supposed to be viewed from above, the auricles having been partially removed. *A*, aorta with semilunar valve; *B*, pulmonary artery and valve; *C*, tricuspid, and *D*, mitral valve; *E*, right, and *F*, left coronary artery; *G*, wall of right, and *H*, of left auricle; *I*, wall of right, and *J*, of left ventricle. (From Stewart's Physiology.)

The walls of the auricles are relatively thin, as they are not required to do heavy work. The ventricular muscles, on the other hand, are well developed, that of the left ventricle being very strong and adapted to the heavy work it must perform.

The valves guarding the opening between the auricles and ventricles are composed of thin membranes of fibrous tissue, covered with endothelial cells similar to the lining of the heart and the blood vessels (Fig. 17). In acute rheumatism and tonsillitis, the endothelial covering of the interior of the heart and of the valves is often inflamed, and permanent changes may take

place which injure the valves and produce what is known as valvular disease of the heart. The chordæ tendineæ connect the free margins of the valves with the papillary muscles, which arise from the musculature of the ventricle like little knobs of tissue. This arrangement prevents the valves from being everted into the auricle during the contraction of the ventricle. The valves on the left side consist of two flaps and are called the *mitral valves*; those on the right side have three flaps and hence are called *tricuspid valves*. The valves guarding the arterial orifices consist of three cup-shaped membranes and are known as the *semilunar valves*, because of their crescent-shape when they are closed. Whenever the pressure in the arteries is greater than that in the ventricles, these valves are tightly closed, and prevent any blood entering the ventricle from the arteries.

The Physiologic Properties of Heart Muscle.

The Character of Cardiac Contraction.—The contraction of our voluntary muscles is not due to a single stimulus sent from the brain through the nerves, but rather to a series of such stimuli, which produce a more or less continued or tonic contraction of the muscle. If this were not the case, our movements would be very quick and jerky, similar to those made by a person suffering with St. Vitus dance. In the case of the heart muscle, however, each beat consists of a single complete muscular contraction, and it is impossible to produce a tonic or continued contraction in the heart such as can be produced in voluntary muscle by rapid successive stimuli. Another peculiarity of heart muscle is that each time it contracts it does so with all the force that it has at the moment. Skeletal muscle contracts with greater or less intensity according to the strength of the stimulus it receives.

Heart muscle, and in a lesser degree some other muscles, such as those of the intestinal tract and spleen, have the power of making automatic rhythmic contractions which follow each other in a definite sequence. This phenomenon in the case of cardiac muscle is not dependent on the influence of the nerves, as can be shown by the fact that the heart removed from the body will con-

tinue to beat for some time if it is properly nourished by perfusing blood through it under pressure. The cause of this property of automaticity is still unsettled, and there have been some very interesting discussions and arguments among physiologists concerning it. Some believe that the heart muscle has this property inherent in itself, and that it originates the impulse which causes the contraction of the heart; while others think that there are present in the heart-muscle cells of a nervous character whose special function it is to originate the beat. Experimental facts can be found in support of either theory, but the question is still in dispute. Heart muscle differs from other muscle in that each fiber consists of a single cell containing striated protoplasm. It may quite well be that this kind of muscle possesses some characteristics usually ascribed to nervous tissue, and that it does originate the stimuli which produce automatic movements.

The Sequence of the Heart Beat.—Inspection of the beating heart of a recently killed turtle or frog shows that the heart beat begins by a contraction in the large veins where they join the auricles. From these vessels the beat spreads, as it were, to the auricles and then to the ventricles, beginning at the base and ending at the apex. It is possible to stop the contraction of the ventricles by drawing a thread tightly around the heart between the auricles and the ventricles. The auricles will continue to beat as before, and the ventricles can be made to beat rhythmically again by artificially stimulating them. In this case, however, they will contract without any reference to the auricular beat. Likewise the base of the large veins, or the sinus venosus as this is known in the amphibian heart, may be separated from the auricles by a tight thread. The auricles now continue to beat, but at a much slower rate, whereas the beat of the sinus is not changed. The tissues of the sinus must possess to a marked degree the power of making individual or automatic movements; they are thus able to control the rate of the heart. For this reason the sinus has been called the *cardiac pacemaker*.

The great muscular development of the human heart has caused it to lose some of its primitive characteristics. Nevertheless, there still exist in the musculature of the heart some strands

of tissue which resemble the tissue of the less developed or more primitive heart. We find in the walls of the auricles small nodes and islets of tissue, which no doubt represent the sinus tissues found in the frog's heart. These nodes of tissue are really the pacemakers of the heart, for it is in them that the impulse or stimulus arises which sets agoing the contraction of the auricles and the ventricles. These nodes are connected by fibers with the musculature of the auricles and ventricles, those running from

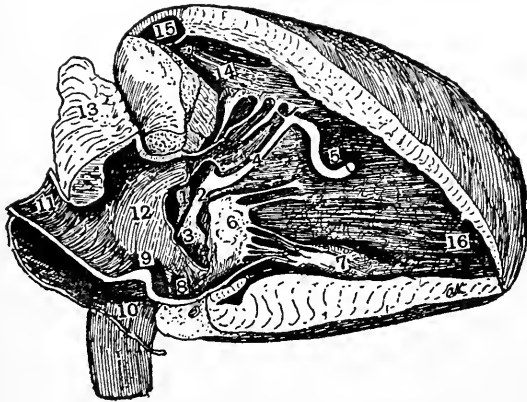


Fig. 18.—Dissection of heart to show auriculo-ventricular bundle (Keith); 3, the beginning of the bundle, known as the A-V node; 2, the bundle dividing into two branches; 4, the branch running on the right side of the interventricular septum. (From Howell's Physiology.)

the auricles to the ventricles being gathered into a bundle of tissue which has been named the *bundle of His* (Fig. 18).

Numerous cases have been recorded of individuals having a very irregular or a very slow heart beat in whom post-mortem examination of the heart showed a diseased condition of the bundle of His. The conditions observed in man have been reproduced in the case of animals by cutting or clamping the tissue about this bundle. The result is much the same as that observed in the turtle's heart when the string is tied between the auricle and the ventricle. The ventricle may continue to beat, but it does so without reference to the auricles. Such a condition is known as *heart block*.

It is of interest to know that there has been quite an advance recently in the knowledge of the conduction of the cardiac impulse from the auricles on to the ventricles. It has been known for a long time that when a muscle contracts, a small but definite electric current is set up between the relaxed and the contracting portions of the muscles. New methods of detecting and recording the direction of the flow of such currents produced in the heart in man have shown that cases of heart block are by no means rare. The instrument used for this purpose is a highly sensitized galvanometer, and the tracings are known as *electrocardiograms*. By this method it can be shown that in certain cases of heart disease the auricles beat twice to the ventricles once, or again that the auricles may beat very fast while the ventricles are beating very irregularly and slowly.

The Action of Inorganic Salts on the Heart Beat.—A very interesting theory has recently been advanced concerning the cause of the heart beat. It will be remembered that the blood contains salts of sodium, potassium and calcium in solution. If these salts are replaced by other non-poisonous salts in the same concentration as the salts removed, the heart will not beat. If the heart is perfused with a solution of sodium chloride alone, the beat becomes very weak and finally stops. If, however, a small amount of calcium and potassium salts is added to the sodium chloride solution, the heart will again begin to beat, but it stops after a while in a state of relaxation, or diastole, if calcium chloride is removed from the solution, or in systole, or contraction, if the potassium salts are removed. These experiments suggest that the salts of the blood offer a solution to the problem of the cause of the heart beat, the potassium favoring relaxation, and the calcium contraction. If the proper balance of these salts is present in the blood, it is conceivable that a regular sequence of contraction and relaxation of cardiac muscle will take place because of the action of the salts.

The Vascular Mechanism of the Heart.

Definition of Terms.—A definition of the terms applied to the different phases of the heart's activity will help in the de-

scription of the events which occur during one complete heart beat. The period of actual contraction of the heart is termed *systole*. This is divided into *auricular* and *ventricular systole*. The term *sphygmic period* is applied to that part of ventricular systole during which the blood is actually leaving the ventricles. The period of relaxation and rest of the cardiac muscles is called *diastole*. The *cardiac cycle* includes the time of systole and diastole of the heart.

The Events of the Cardiac Cycle.—During diastole the blood flows in a steady stream from the great veins through the two auricles into the ventricles, the auriculo-ventricular valves being open. When the ventricles are as full as the weight and the pressure of the blood can make them, auricular systole begins. The auriculo-ventricular valves at this instant are floating in the blood which has collected in the ventricles, and are almost in the position of closure, but a narrow chink still remains between them, and through this, auricular systole forces blood under pressure into the ventricle, thus filling the ventricles completely. At the dead stop of auricular systole there are currents of blood reflected back along the sides of the ventricles which strike the under surface of the valves and completely close them. Ventricular systole now begins. The closed valves prevent the passage of blood back into the auricles, and the entire force of the ventricles is expended in forcing the blood out through the arterial openings. Whenever the pressure in the ventricles exceeds that in the arteries, the semilunar valves open and remain open till the force of the ventricle falls below the pressure of blood in the arteries. The time between the closing of the auriculo-ventricular valves and the opening of the semilunar valves is called the period of getting up power, or the *pre-sphygmic period* (Fig. 19).

It is obvious that when the blood is leaving the ventricles the pressure must be less in the arteries than in the heart. Each ventricle pours out more blood into its artery than can pass through the capillaries in the same unit of time, and hence the arterial walls are stretched and the blood is put under their elastic tension. At the moment the ventricles exert less pressure than does

the elastic recoil of the arteries on the blood, the semilunar valves are closed tightly by backward eddying currents in the arteries. Their closure prevents any return of blood into the ventricles.

The blood, having attained a certain momentum during the sphygmic period, is carried on by its inertia for a fraction of a second after the ventricle ceases to exert pressure on it, thus producing a partially relaxed artery just beyond the semilunar valves. This momentum being lost, the blood, by the pressure which the stretched elastic wall of the arteries exerts on the

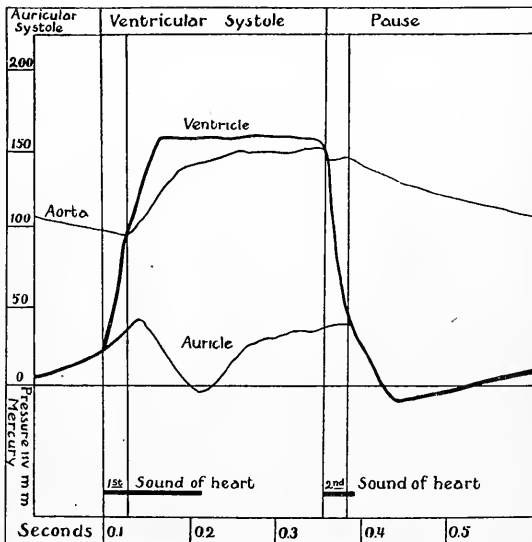


Fig. 19.—Diagram showing relative pressure in auricle, ventricle and aorta.

blood, is forced back on to the semilunar valves and into the partially relaxed base of the aorta. The blood, being thus prevented from returning to the heart, must continue to flow on into the capillaries, and this onward flow never ceases, because the next cardiac systole occurs before the arteries have ceased to exert all of their recoil pressure on the blood (see also p. 173).

After the arterial valves close, the ventricles continue to relax, and the pressure within quickly falls below that which obtains

in the partially filled auricles. At this moment the weight of the blood which has accumulated in the auricles during the systole, forces the valves of the auriculo-ventricular orifice open, and the ventricle again begins to fill. The period between the closure of the semilunar valves and the opening of the auriculo-ventricular valves is known as the *post-sphygmie period*, and is the beginning of the diastole of the ventricles. The above events comprise those taking place in a complete cardiac cycle.

The Heart Sounds.—If one applies his ear to the front of the chest, or better still uses a stethoscope, which physicians use to examine the sounds of the lungs and heart, two sounds will be heard during each cardiac cycle. The first sound is dull, low pitched, and long; the second sharp, high and short. Following the second sound is a short pause. It has been determined experimentally that the first sound is caused partly by the closure and sudden tension of the auriculo-ventricular valves at the moment of cardiac systole, and partly by the muscular contraction of the ventricle. Anything which interferes with the closure of the valves causes an alteration in the sound; for instance, if the valves are diseased there will be a leaking of blood back into the auricles during systole, and this will cause a distinct murmur to take the place of the sound. If the musculature of the heart is weakened, the sound is also modified. Hence the first sound of the heart is an important diagnostic sign in heart disease. The second sound of the heart is due to the sudden tension exerted on the semilunar valves at the moment the blood is forced back on them, following ventricular systole. This sound is also subject to variations in heart disease, especially in disease of the valves themselves, in which case because of roughening they may offer resistance to the outrush of blood from the ventricles, or by not closing tightly, allow the passage of blood in the wrong direction. In either case the sound is changed in character and is a useful diagnostic sign.

By using these heart sounds as signals of the events occurring within the heart, it is possible to calculate the time relations of the various phases of the cardiac cycle. The heart in the ordinary individual beats about seventy times a minute, so that we may

say that the cardiac cycle is completed in about eight-tenths of a second. Systole of the auricles takes about one-tenth of a second, systole of the ventricle three-tenths of a second, and diastole about five-tenths of a second.

Diseases of Cardiac Valves.—If the mitral valve is diseased, the blood may be retarded from flowing from the auricle into the ventricle. This condition is called *mitral stenosis*. If the valves cannot close tightly and thereby permit the blood to regurgitate into the auricle during ventricular systole, the condition is called *mitral insufficiency*. Disease of the semilunar valves is likewise divided into *aortic stenosis* and *insufficiency*, depending on the character of the functional change in the valves.

CHAPTER XIX.

THE CIRCULATION (Cont'd).

The Blood Flow Through the Vessels.

Introduction.—A clearer idea of the principles governing the circulation of blood through the vessels can be had if the laws governing the flow of water in a city water system are called to mind. For example, a water-works system is arranged by means of either special pumps or a standpipe, to furnish a stream of water at a constant rate and pressure into the city water mains. The water is first forced into one large pipe and from this delivered to the consumer by means of much smaller pipes. By simple mathematical calculation it can be shown that the total cross-section area of the smaller pipes is many times that of the main pipe; for the sake of argument, let us say 800 times greater. Therefore the average rate of flow of water in the smaller pipes must be 800 times less than in the main pipe, providing all the outlets are open. However, if only one-half of the distributing pipes are in use, the flow of water would be only 400 times less than in the main pipe, and the resistance offered by the walls of the pipes to the flowing water is also halved. Thus the same amount of water is delivered in the same unit of time but under twice the pressure, since only one-half of the force used to deliver the water through all the pipes is used in delivering it through one half of them. In other words, it takes X force to overcome the resistance offered by Y , therefore X equals Y . When X remains constant and Y is halved, then $X - Y/2$ equals $X/2$, leaving $X/2$ as a remainder. To bring it home, there is less water delivered from the garden hose and it has far less pressure behind it when all the neighbors are also using the water, than there is when only a few outlets are in use. Likewise, if the amount and the pressure of water in the main pipe are varied by changing the force of the pumps or the level of water in the stand pipe, the amount and pressure of water delivered are also varied in the same direction.

The pumps or the standpipe correspond to the heart and the large arteries, the distributing pipes to the smaller arteries and capillaries. With these ideas in mind let us consider the part the heart and blood vessels play in maintaining the circulation.

The Part the Heart Plays.—At each systole 60 to 90 c. c. of blood are forced into the aorta. Cardiac systole lasts about 0.3 of a second, the diastole 0.5 second. Therefore the heart is resting about 60 per cent of the time. By experiment it has been demonstrated that the left ventricle forces the blood out into the aorta with a pressure equivalent to the weight of a column of mercury from 160 to 190 mm. in height. The heart alone, however, actually propels the blood through the arteries for only the time of its systole; during the diastole, as already explained, the blood would cease to flow entirely if it were not for the part which the large arteries play in maintaining the circulation.

The Part the Arteries Play.—If 100 c. c. of water are forced in 0.3 second into an ordinary metal pipe at intervals of 0.8 of a second, 100 c. c. must flow out from the opposite end in 0.3 second; during 0.5 second no water will be flowing in the tube. Let us now replace the metal tube with an elastic rubber tube, the end of which is fitted with a nozzle filled with glass beads. Now if 100 c. c. of water are forced into the tube in 0.3 second, the rubber tube expands because the beads retard the free outflow of water and thus make it impossible for 100 c. c. of water to pass through them in the time allotted. After the water ceases to flow into the tube, the water stored up in the expanded portion continues to flow out through the beads because of the elastic recoil of the rubber. If the resistance offered to the water and the expansile force of the tube be properly adjusted, a constant stream of water may be obtained from the outlet, in spite of the fact that an intermittent force is supplying the water (Fig. 20).

The intermittent stream of the arteries is changed into the constant stream in the veins by a somewhat similar process. The walls of the arteries are composed in part of a layer of strong elastic tissue, and this expands to a greater or less degree at each heart beat. The resistance which the arteries and the capillaries

offer to the flow of blood prevents the passage of the entire systolic output of the heart into the veins during the actual ventricular contraction. It is, therefore, necessary that the large arteries expand in order to make room for the blood. A part of the energy of the heart beat is stored up in the elastic coats of the arteries, and after closure of the semilunar valves, which guard the ventricular orifice, the blood in the distended arteries is forced on through the capillaries by the pressure of the arterial walls.

Arterial Blood Pressure.—From the foregoing description we see that there are several factors which contribute to the main-

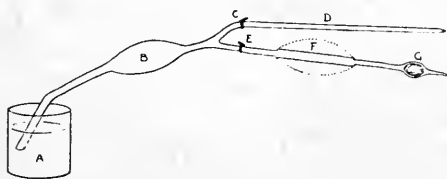


Fig. 20.—Diagram of experiment to show how a pulse (produced by compressing the bulb *B*) comes to disappear when fluid flows through an elastic tube (*F*) when there is resistance (*a*) to the outflow. *A*, basin of water; *B*, bulb syringe; *C* and *E*, stop cocks; *D*, rigid tube; *F*, elastic tube; *G*, bulb filled with sponge.

tenance of a constant stream of blood through the capillaries: viz., the pumping action of the heart, the resistance of the arterioles and capillaries, the elastic recoil of the blood vessels, and the amount of blood itself. That the velocity and the pressure of the blood depend on these factors was first of all demonstrated in 1732 by Rev. Stephen Hales, who in a book published in that year reports having experimentally determined the blood pressure in the femoral artery of a horse. He found that the pressure was sufficient to raise the blood in a tube seven feet above the level of the heart, and he also observed that each beat of the heart and each respiratory movement affected the pressure of the blood. The pressure exerted by the blood on the vessel wall at the height of the systole of the ventricle is known as the *systolic blood pressure*, and that exerted by the elastic recoil of the arteries on the blood during the diastole of the heart is known

as the *diastolic blood pressure*. The average between these two pressures is called the average or mean arterial blood pressure.

Since Hales' experiment better apparatus has been devised to

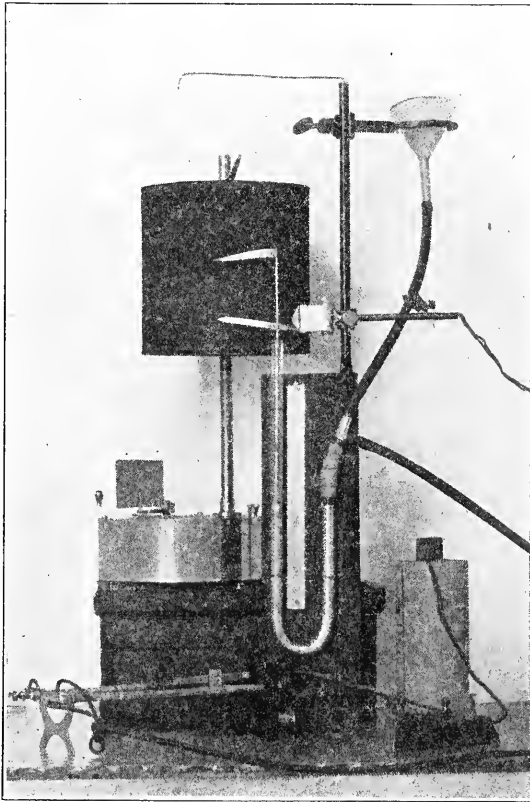


Fig. 21.—Apparatus for taking a tracing of the blood pressure.

measure the blood pressure in animals under different conditions. The standard method consists in placing a tube, called a cannula, directly into a blood vessel. This is connected with a rubber tube filled with an anti-clotting mixture (see Fig. 21) with one arm of a U tube partly filled with mercury. When the blood vessel is opened, the pressure of the blood will force the mercury

down in one arm and up in the other arm of the U tube. The difference between the levels of the mercury in the two arms multiplied by 13.5, the specific gravity of mercury, gives the pressure of the blood in terms of water, or, as is usually done, the blood pressure is expressed as the number of millimeters through which the mercury has been raised.

Determinations of the pressure existing in different portions of the vascular system show that there is a steady decrease of pressure of the blood from the aorta to the entrance of the vena cava into the right auricle. It thus happens that the blood is always flowing from a place of higher pressure to one of lower pressure.

Methods which are of much practical importance in the diagnosis of vascular diseases have been devised to determine the blood pressure in man. The principle of these methods consists in measuring the pressure required to shut off completely the blood supply in an artery. This is accomplished by placing a rubber sac encased in a leather band about the arm (Fig. 22). By means of tubing this sac is connected with a mercury gauge and an air pump. When the sac is pumped up with air, the vessels in the arm are compressed, and when the blood can no longer force its way under the obstruction, the pulse at the wrist disappears and at this moment the height of the mercury in the gauge is measured. This represents the systolic blood pressure. If desired, a similar measurement may be made in the arteries of the leg.

To measure the diastolic pressure is more difficult. The method depends on the experimentally determined fact that when the pulse wave produced in the arteries by each systole of the heart, is of greatest amplitude, the pressure in the air sac or compressing band equals the lowest pressure present in the vessel between the pulses.

Recently improvements have been made in the method of judging the point of obliteration of the artery, and also the point of maximum pulsation, by listening to the sounds produced at each pulse wave when the artery is being compressed.

The systolic blood pressure in the artery of the arm in healthy

young men varies from 110 to 130 mm. of mercury when it is determined in the sitting posture. When a person is lying down the pressure is a little less, and after hard exercise a little higher. The blood pressure under ordinary conditions is relatively constant, and is dependent on a delicate adjustment of the relationship existing between the force of the heart, the amount of blood

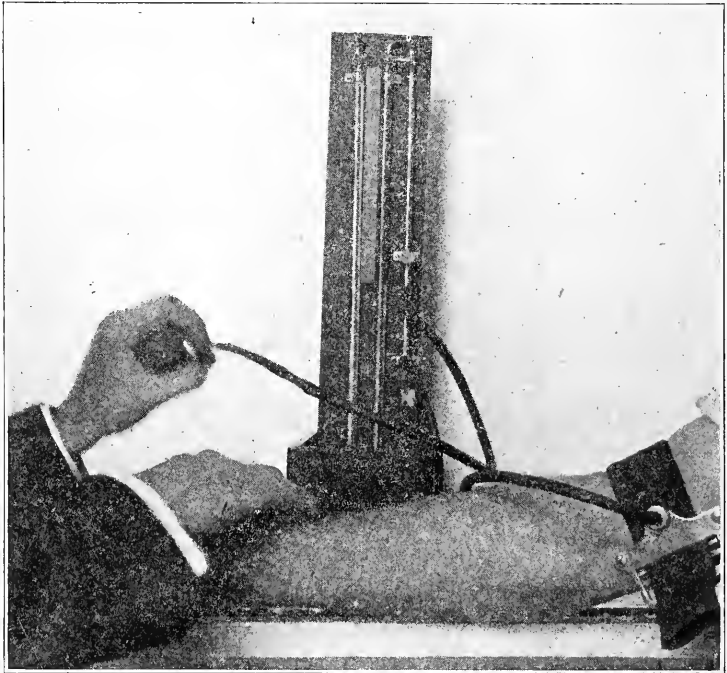


Fig. 22.—Apparatus for measuring the arterial blood pressure in man. The pressure in the cuff is raised by means of the syringe until the pulse can no longer be felt at the wrist. This pressure is read off on the mercury manometer (systolic pressure).

pumped at each beat, the resistance which the walls of the blood vessels offer to the flow of the blood, the size of the vascular system, and the amount of blood in the body. Since the amount of blood in the body is relatively constant, we may say that the factors which change are the heart and the blood vessels. How

these factors influence the blood pressure may be seen if we again compare the system to the city water supply.

Factors Which Maintain Blood Pressure.—When the most water is being pumped into the mains, then the water has the greatest velocity and pressure. Likewise, when the heart is pumping most blood into the aorta, the velocity and the pressure of blood in the vessels are the greatest. If the amount of water remains constant, a uniform outflow through all the outlet tubes will be maintained, but if the number of outlet tubes be diminished, then more water will have to flow, per minute of time, through the remaining tubes; hence the velocity and the pressure must be increased.

The same conditions are present in the body. A narrowing of the arterioles throughout the body or in some extensive vascular area, causes the pressure and the velocity of the blood to be increased in the remaining vessels, provided, of course, the heart beat is unchanged. A dilation of the arterioles, on the other hand, results in a fall of pressure and a decrease in the velocity of the blood. In the same way also an increase or decrease in the action of the heart will result in an increase or decrease in the pressure and velocity of the blood.

The dependence of these two factors, i. e., the heart and the vascular system, on the maintenance of the normal blood pressure, is seen in the fact that, with a fast heart and dilated blood vessels, the blood pressure may be exactly the same as when the heart is beating very slowly but the arterioles are all constricted. It is apparent, therefore, that the velocity of the blood in the vessels is dependent on the pressure of the blood and the extent of the vascular area at the time in question.

The Velocity of the Blood.—By the velocity of the flow of blood we mean the actual time it takes for a particle of blood to pass between two points. If the rate were uniform throughout the vascular area, we could compute the time which a particle of blood would take to pass through the circulatory system. This is not the case, however, for the flow of blood is much swifter in the aorta than in the smaller vessels, and here again our analogy between the circulatory system and the city water system applies.

Just as the combined cross area of the small pipes leading from the main pipe of the water system is greater by many times than the area of the main pipe, so it has been estimated that the total cross section of the capillaries of the body is 800 times larger than that of the aorta.

It has been estimated that the rate of blood flow in the aorta is about 320 mm. per second. The average rate of flow in the capillaries must then be 800 times less than that in the aorta, or 0.4 mm. per second. As the length of a capillary has been estimated to be about 0.5 mm., the blood takes about a second to pass through them into the veins. This has been verified by microscopic examination of the blood flow in the capillaries.

The velocity of the blood must be altered whenever the size of the vascular area is changed, and since during a cardiac cycle exactly the same amount of blood is delivered into the right auricle as the left ventricle forces out into the aorta, it follows that the same amount must pass through the vascular area of the body in the same time. In other words, the amount of blood which flows in a given series of blood vessels in a given time is independent of the size of the blood vessels.

The Return of the Blood to the Heart.—We must now consider the nature of the force which propels the blood, and study what changes take place in the movement of the blood during its passage through the vessels.

The blood is expelled from the left ventricle with considerable force and at a high velocity. On its way through the body much of the energy given out by the contraction of the heart is used to overcome the resistance offered by the walls of the vessels and the capillaries. In consequence of this, the velocity and the pressure of the blood on the sides of the vessels are much reduced.

The blood is collected from the capillaries by the veins, and since the volume of the veins is less than the volume of the capillaries its velocity is much increased. The relatively large caliber of the veins, however, offers little resistance to the flow of blood, and the energy remaining from that imparted to the blood by the heart has full power to make itself felt. Nevertheless, this is not

sufficient alone to force the blood onward and back to the heart, and we must seek *other accessory factors to explain the venous return.*

The veins are equipped with cup-shaped valves which permit the passage of blood only in one direction, i. e., towards the heart. Every movement of a muscle therefore squeezes some of the blood onward. This massaging influence of the muscles is very important. Its absence accounts for the fact that it is impossible to stand still for a long period of time without the limbs becoming very painful, especially in the case of varicose veins, where the valves of the veins are no longer functional, so that there is nothing to prevent the blood from returning to the more dependent positions. Another source of energy to the returning blood is the aspiratory effect of the thorax at each inspiration. This action will be considered in the study of the respiratory mechanism.

Circulation Time.—The actual time which is taken for the blood to traverse the circulatory system has been variously estimated. Obviously such figures can give only average results, since the distance through which blood to the arm must flow is less than that to the legs. In general, it may be said that the blood makes a complete circulation in from 25 to 30 beats of the heart. The circulation through the lungs requires about one-fourth of this time.

That the velocity of the blood flow through different vessels varies, is apparent from actual observations made on severing them and actually observing the rate of outflow. The following figures expressing the *blood supply per minute to each hundred grams of organ* have been determined experimentally:

Leg	5 c. c.	Liver (venous)	59 c. c.
Head	20 "	Liver (arterial) . . .	25 "
Stomach	21 "	Brain	136 "
Intestines	31 "	Kidney	150 "
Spleen	58 "	Thyroid	560 "

The Effect of the Circulation on the Blood.—If the circulation of the blood through the vessels of the lung or the web of a

frog's foot be examined by means of a microscope, several interesting facts will be noted. The red blood corpuscles will be seen flowing in the center of the blood vessels, while in the clear plasma which surrounds them are the much less numerous white cells. This arrangement is explained by the fact that the red corpuscles are heavier than the white cells or the plasma and are held in the center of the stream by a principle of hydraulics. The white cells flow more slowly along the sides of the vessels than the red corpuscles do in the center of the stream, which is suggestive of the function of the white cells as phagocytes (see p. 152); thus, any injury to the vessel wall will necessarily slow the flow of blood through the veins and allow a greater number of leucocytes to collect at the point of injury.

The Pulsatile Acceleration of Blood Flow.—The flow of blood in the arteries differs from that in the veins and the capillaries in that it is swifter and pulsatile in character. This pulsatile variation is due to the acceleration of the blood flow caused by each heart beat, and the reason that this is not seen in the capillaries and veins is that the resistance which the walls of the capillaries and arterioles offer to the blood is so great that the cardiac factor, acting only for a brief time, is lost. The energy represented in the increased rate of flow, is spent in stretching the walls of the arteries, which contract after the pulsatile wave has passed, and thus force the blood onward.

The Pulse.—The pulsatile expansion of the arteries at each heart beat has been mentioned in connection with the factors which help to maintain the normal blood pressure. It is this also which produces the phenomenon which is known as the pulse. From time immemorial the physician has been accustomed to come to an idea concerning the condition of the circulation by feeling the pulse, for it represents changes in the arterial tension occurring during each cardiac cycle. In order to study the pulse wave more carefully, instruments have been devised which graphically record its wave on a piece of paper. Such an instrument is known as a *sphygmograph* (*Fig. 23*), and some of these have been cleverly arranged so as to enable us to record simultaneously the pulse from different blood vessels.

Since the pulse is not due to an actual movement of blood along the arteries, but rather to changes in tension producing an expansion of the vessel wall, it follows that the transmission of the wave may be much more rapid than the movement of blood. This may be explained by reference to the motion imparted to a row of billiard balls when the one on the end is hit with the cue. The one hit actually moves very little, but imparts its energy of movement to the others, so that the ball at the end of the row moves away with some velocity, while the others move slowly. The wave of energy spreads in a fraction of a second

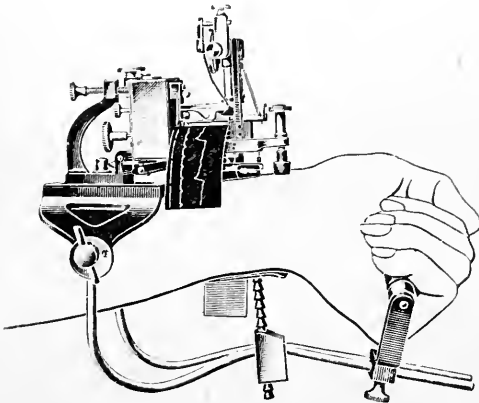


Fig. 23.—Jaquet Sphygmocardiograph.

from ball to ball. By simultaneously taking tracings of the carotid and the radial pulses, for example, it has been computed that the pulse wave is transmitted at the rate of ten meters a second, and that it may be six meters long. This means that the pulse wave reaches the peripheral vessels before the systole of the heart is completed. Any local change in the vessel may slow down the rate of transmission, and if there is a difference in the appearance of the pulse in the two arms or legs, it is indicative of some obstruction or change in one of the vessels.

When we analyze the pulse wave obtained by a sphygmograph taken, for example, from the radial artery, it is seen that the

first elevation is very rapid and abrupt (Fig. 24, a). This is caused by the sudden increase in pressure of the blood, due to cardiac systole, resulting in the sudden expansion of the artery. Following the abrupt rise, the curve gradually descends till the next heart beat occurs. During this period the arterial blood pressure is maintained by the elastic recoil of the stretched arteries. On the descending curve there are as a rule several small waves and depressions. Of these waves the large one (Fig. 24, b) is always present and is known as the dicrotic wave, and the dicrotic notch is the depression immediately preceding the wave. The presence of this wave is explained as follows: At the end of cardiac systole the blood, under the influence of the pressure exerted by the stretched walls of the arteries, is forced both towards the peripheral vessels and back towards the heart.



Fig. 24.—Pulse tracing made by sphygmograph. A, systolic wave; B, dicrotic wave.

The cardiac semilunar valves, being tightly closed at the end of systole, arrest the back flowing blood, and it rebounds, as it were, producing the depression with the wave which is reflected over the entire circulation. When the blood pressure is high, the secondary waves make very little depression, because of their relatively low pressure, but in conditions where the blood pressure is low, as in typhoid fever, surgical shock, a faint, and in deep anæsthesia, the dicrotic wave is easily felt by the finger.

Other qualities of the pulse which may assist the physician in judging of the condition of the circulatory system are its rate and its compressibility. Its rate tells us how fast the heart is beating, and its compressibility gives a rough idea of the blood pressure.

The Circulation Through the Lungs.—In general the same conditions are present in the circulation of the blood through

the lungs as are found in the systemic circulation. The right ventricle is far less powerful than the left, so that the pressure of the blood in the lung vessels is less than that in the systemic vessels. The respiratory movements also cause the size of the blood vessels in the lungs to vary in a marked degree. These changes in the capacity of the pulmonary blood vessels affect the systemic blood pressure. Thus, at the height of inspiration, the lungs may contain one-twelfth of the blood of the body, while during expiration this amount may be lessened to one-fifteenth to one-eighteenth of the total. This condition makes it possible for the heart to be filled more rapidly during the later part of inspiration and the beginning of expiration, than at other times, and accounts for the rise of blood pressure observed at this time.

CHAPTER XX.

THE CIRCULATION (Cont'd).

The Influence of the Nervous System on the Circulation.

Up to the present time we have considered the circulatory system as a purely automatic and mechanical apparatus for carrying blood to all parts of the body. It is necessary that this apparatus vary in its activity, not only according to the needs of the body as a whole, but also according to the needs of the various parts of the body. It would be poor economy for the heart to maintain through all parts of the body at all times a stream of blood which would be large enough for all emergencies. There must be some way of controlling the blood flow according to the needs of the body. This function is served primarily by the central nervous system, which is connected by means of nerves with the musculature of the heart and the blood vessels, and secondarily by secretions from the so-called ductless glands, the best known of which are the adrenal glands (see p. 129).

The Nervous Control of the Heart.

The Cardiac Nerves.—The heart is supplied with both sensory and motor nerves. Sensory nerves carry stimuli from the peripheral regions to the brain and are known as afferent nerves. Motor nerves, on the other hand, carry stimuli from the brain to the muscles or glands, and are known as efferent nerves. The efferent nerves of the heart are found in fibers coming from the spinal cord by way of the sympathetic system, and by the vagi or the tenth pair of cranial nerves (see p. 265). It must be clearly understood that the nerves merely regulate the heart beat, but have nothing to do with its occurrence. In other words, the heart continues to beat after all the nerves have been severed.

The Accelerator Nerves.—To understand how the fibers reach the heart, the reader is referred to the general description

of the sympathetic nervous system on page 277. The sympathetic fibers of the heart are found in the first and second spinal nerves of the thoracic region. After connecting with nerve cells situated in the stellate ganglion, they go to the heart, where they end about the cardiac muscular fibers.

Cutting the sympathetic fibers to the heart causes a slower beat and a prolonged diastole. On the other hand, stimulation of the nerves with an electric current increases the rate of the heart (Fig. 25). For the above reasons the sympathetic nerves to the heart are known as *accelerator* or *augmentory* nerves.

The Inhibitory Nerves.—The vagi are a pair of nerves arising on each side of the medulla, and running a course downwards through the neck into the thoracic and abdominal cavities. This pair of nerves supply fibers to the various organs of these regions

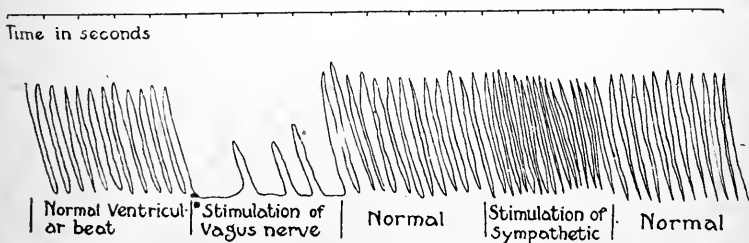


Fig. 25.—Effect of stimulating vagus and sympathetic nerves on the frog's heart.

including the heart, which receives branches from both vagi. It is possible by simple experiments to demonstrate the function of these fibers.

For example, if the vagus on one side be cut, the heart rate will increase a little; if both vagi be cut, the beat is still more markedly quickened, and the increased discharge of blood from the heart produces a rise in the arterial blood pressure (Fig. 26, No. III). By cutting these nerves we remove the influence which the central nervous system exerts through them on the heart rate. Since the heart beats faster after this operation, we must conclude that this organ constantly receives stimuli from the brain through the vagi, and that these stimuli cause

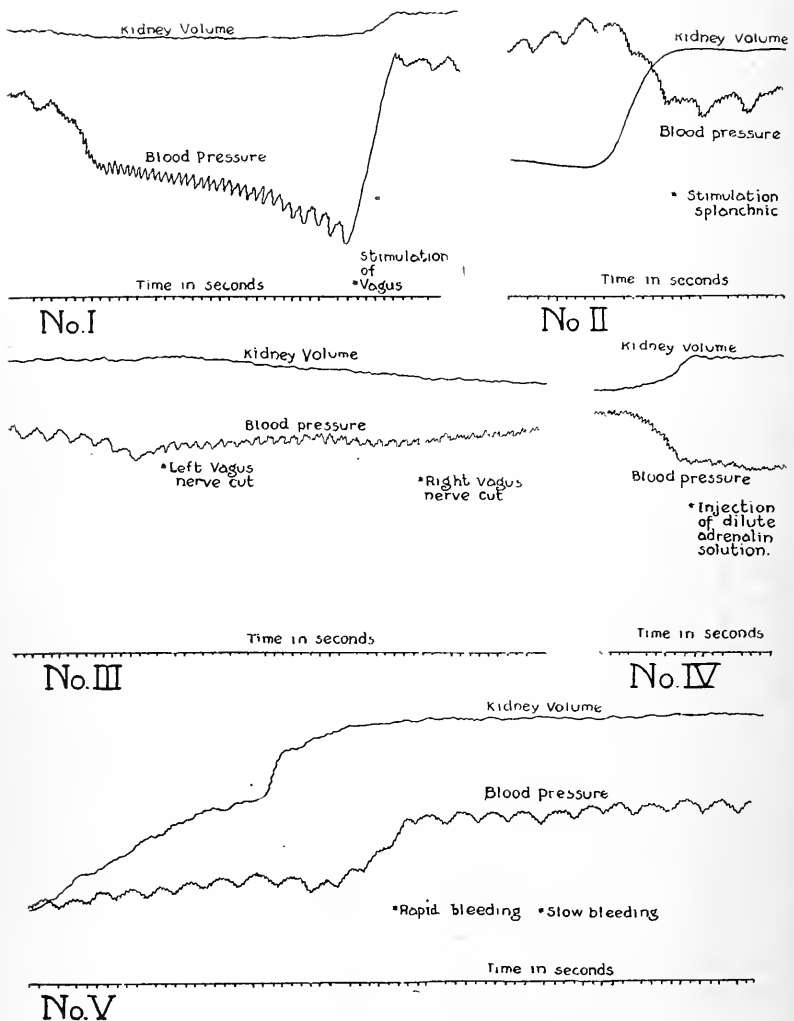


Fig. 26.—Tracings of arterial blood pressure (taken with apparatus in Fig. 21) and of kidney volume (taken with volume recorder) showing the effect of:

- I. Stimulation of the vagus nerve.
- II. Stimulation of the splanchnic nerve.
- III. Cutting one vagus nerve.
- IV. Injection of epinephrin (adrenalin).
- V. Hæmorrhage.

The tracings all read from right to left.

the heart to beat more slowly. Such a continued action of a nerve is known as a tonic influence.

That the vagi can slow the heart or even stop it altogether is shown by stimulation of these nerves with an electric current of suitable strength (Fig. 25). If weak shocks are employed, the heart is slowed, the blood pressure falls somewhat, and the diastolic pressure becomes markedly decreased, because the arteries have a greater period of time in which to empty between the beats. If somewhat stronger stimuli be used, the heart will stop beating entirely, and remain in the diastolic position for several seconds, during which the blood pressure will sink to zero (Fig. 26. No. I). It is scarcely possible to kill an animal by stimulation of the vagus, however, since the heart will begin to beat after a short time in spite of the continued vagus stimulation. This phenomenon is known as *escapement*. The time of its onset varies considerably in different animals. It has been suggested that the vagi have much more effect on the auricles than on the ventricles, which is suggestive of the auricles being the pacemakers of the heart.

Relation of the Sympathetic and Vagus Nerves to the Heart.

—The antagonistic action existing between the cardiac fibers of the sympathetic and vagus nerves allows the heart to respond quickly to any need that the body may demand of it. These demands are made through the brain, by various afferent or sensory nerves. This is brought about in the following way:

The Cardiac Center.—In the medulla, the hind part of the brain, there is a collection of nerve cells from which the cardiac branches of the vagus arise. Near by also are located the cells from which the sympathetic nerves of the heart arise. Both of these nerve centers, for by this term are known the important cell stations of the brain, are supplied by extensive connections with afferent or sensory fibers coming from all parts of the body, the brain and even the heart. The centers become more or less active in response to impulses reaching them along the sensory fibers.

The Cardiac Depressor Nerves.—One of the most important of the different cardiac nerves is that known as the *cardiac depressor*.

sor. It has its beginnings in filaments lying in the left ventricle and in the aorta, and runs to the medulla in the vagus trunk in most mammals, or as a separate nerve in the rabbit. Under ordinary conditions, cutting this nerve produces no effect on the heart beat, but stimulation of the upper end of the cut nerve, i. e., the end running to the head, results in a marked slowing of the heart and fall in the blood pressure. If the experiment is repeated after cutting the vagi, the heart is slowed, but the fall in blood pressure, though less evident, still occurs. The normal stimulus to the depressor nerve is a high blood pressure in the ventricles and aorta. The stimulus, thus set up, acts through the vagus center and the vagus nerve, and slows the heart. It also acts on the vasomotor center and causes the blood vessels to dilate. Both changes produce a fall in the blood pressure. The vagus nerve, besides the afferent vagus fibers, carries afferent or sensory nerves to the vagus center. This can be demonstrated by cutting one vagus and stimulating the central end, i. e., the end running to the brain. A marked slowing of the heart usually results. By acting through the vagus center and nerves, or through the sympathetic center and nerves, most of the sensory nerves of the body, if stimulated, can produce a reflex slowing or quickening of the heart beat. One cannot, however, always predict exactly what result will be obtained. The stimulation of the fifth nerve in the nasal cavity or in the mouth always causes a reflex slowing of the heart. Stimulation of the laryngeal nerve and the nerves of the peritoneum have a similar effect. It is also of interest to note that the act of swallowing will often cause a decrease in the rate of the heart through reflex vagus action.

The relation of the blood pressure to the rate of the heart has been noted in connection with the cardiac depressor nerve (p. 187). Anything which produces an increase in the pulse rate, other conditions being equal, will cause an increase in the blood pressure, and this acts reflexly to bring about a slowing of the heart. The reverse of this is likewise true. In this quickening or slowing of the heart, the vagi and the sympathetic nerves always act. In the adult the normal rate of the heart

varies between 68 and 76 per minute. In children the rate is a little faster, and in infants it may be normally 130 or more.

The Nervous Control of the Blood Vessels.

During muscular activity the metabolism of the body may be increased five or six times, as can be judged from the amount of carbon dioxide given off by the lungs. Since this increase is due to the activity of the muscles, it is necessary that these obtain a greater supply of oxygen, and that they be able to rid themselves of the carbon dioxide which is a waste product of their activity. Every other organ requires an increased blood supply when it becomes active, so that blood has to be diverted from the inactive to the active tissues, and the least important activities of the body have to be subordinated to the one which is most needed at the time in question. This action is brought about partly by the central nervous system, acting through its afferent and efferent nerves on the musculature of the blood vessels of the body, and partly by means of chemical substances which are produced at an early stage of the activity itself.

The Vasomotor Nerves.—It was discovered in the middle of the past century by the French physiologist, Claude Bernard, that section of the cervical sympathetic nerve in the neck of the rabbit causes a marked dilation of the blood vessels of the ear, and that during stimulation of the nerve with an electric current, the blood vessels become very small, and the ear consequently colder. This experiment shows that the nervous system plays an important rôle in the control of the flow of blood through the tissues, and from it many important truths about the nervous control of the blood vessels may be deduced. If cutting a nerve will cause the blood vessels to dilate, and stimulating the same nerve with an electric current will cause the vessels to constrict to much less than their normal size, it follows that the blood vessels must be normally held in a state half way between extreme dilation and constriction by stimuli received from the nervous system. The nerve fibers which carry the stimuli, because of their power of producing constriction of the blood vessels, are known as *vasoconstrictor nerve fibers*. They are com-

parable in action to the accelerator nerves to the heart, since stimulation of either type of nerve tends to produce an increase in the blood pressure, the one by quickening the heart rate and the other by constricting the blood vessels and increasing the resistance to the flow of blood.

The presence of the vasoconstrictor fibers in the sympathetic nerves is easily shown by the fact that stimulation of these nerves to any part of the body produces a marked diminution in the size of the part to which the nerves are connected. At the same time there is an increase in the general blood pressure, because the freedom of outflow of blood from the arterial system is somewhat reduced. The large nerves which supply the limbs also contain vasoconstrictor nerves. These are derived from fibers coming from the ganglia of the sympathetic chain in the thorax and abdomen and joining with the roots of the spinal nerves in order that the fibers may be distributed along with the cerebrospinal nerves to the part in question (see p. 277).

After section of the spinal cord, the blood vessels of the part of the body supplied with vasoconstrictor nerves below the level of the section of the cord, become dilated, and may be constricted again if a stimulus be applied to the lower end of the cord. The effect of such a stimulus is to increase the blood pressure, since the resistance offered to the flow of blood is increased.

The organ in which the changes taking place in the blood vessels under various conditions can be most easily demonstrated is the kidney. It is not hard to enclose one kidney in an air-tight box, and by means of rubber tubing to connect the box with an instrument called a *tambour*, which will record on a smoked drum any change in the amount of air in the box, i. e., any increase in kidney volume will cause air to pass out of the box, or the reverse in case the kidney volume decreases. The instrument is called a *plethysmograph*. The instrument applied to the kidney of anæsthetized animals records each heart beat, or, in other words, shows a pulse. Any change in blood pressure will also cause a change in kidney volume, but the nature of the change will depend on the cause of the change of blood pressure. (See Fig. 26).

The vasomotor nerves to the kidney and the abdominal viscera are for the most part supplied by the lower thoracic nerves. These sympathetic fibers are combined and enter the abdomen in what are known as the *splanchnic nerves*, which terminate about nerve cells in a ganglion behind the stomach, which is called the *semilunar ganglion* of the *solar plexus*. If while the normal volume of the kidney is being recorded, the splanchnic nerve of the corresponding side of the body is cut, the kidney will show increase in volume, due to the loss of the vasoconstrictor nerve control on its vessels. On the other hand, stimulation of the cut end of the splanchnic nerve leading towards the kidney, will produce a great decrease in the kidney volume, and a marked increase in the systemic blood pressure, due to a diminution in the volume of the vessels of the kidney and of the whole splanchnic area, since the splanchnic nerves supply not only the kidneys, but the whole intestinal tract with vasoconstrictor fibers.

Vasodilator Nerves.—There is another class of efferent nerve fibers to the arteries, which are known as the vasodilator nerves. When stimulated they bring about a dilatation of the arterioles, and allow a greater amount of blood to pass through the vessels. Vasodilator nerve fibers are found in all the spinal nerves, and they run to the blood vessels along with the nerve trunks supplying the various organs. Unlike the vasoconstrictor nerves, they do not seem to be continually exerting an influence or tonic action on the blood vessels. Because their action is hard to elicit, not so much is known of their normal functions as is known of the vasoconstrictor nerves. In some nerves, however, they predominate and their action is easily seen. Such is the case in the chorda tympani, a nerve coming from the seventh cranial nerve and supplying the submaxillary gland with fibers, which when stimulated bring about an increase in the flow of saliva and marked dilatation of the blood vessels of the gland (see p. 41). The arterioles normally may be supposed to be held in a state midway between dilatation and contraction. Stimulation of the vasodilator nerves probably inhibits the tonic action of the vasoconstrictor nerves and the muscles of the vessels are extended by the force of the arterial blood pressure.

After section of the sciatic nerve, the constrictor fibers soon die, and the dilator fibers, which live for a time, may be shown to be present by the fact that the volume of the leg increases when the nerve is stimulated.

Vasomotor Reflexes.—In the same manner that the heart is influenced by afferent stimuli reaching cardiac centers from peripheral parts of the body, we find afferent stimuli affecting the size of the blood vessels reflexly by way of the vasomotor center—located in the medulla near the vagus center—and the vasomotor nerves. Some of the afferent impulses cause dilation of the blood vessels, while others cause constriction. Perhaps the most important of the sensory nerves, which, when stimulated, produce a dilation of the blood vessels, is the cardiac depressor, which we mentioned in connection with the afferent nerves of the heart. It will be remembered that this nerve has sensory endings in the left ventricle and in the aorta, and that these are stimulated when the blood pressure in the arterial system reaches too great a height for the safety of the individual. The stimuli originating in the sensory endings of this nerve are carried to the cardiac center and are then transmitted to the heart through the vagus nerves. Besides the slowing of the heart which is thus produced, there also occurs a dilation of the peripheral vessels brought about by the action of the stimuli on the vasomotor center. This is easily demonstrated by electrically stimulating the cardiac depressor nerve after both vagi have been cut in the neck and the reflex vagus action thus removed. The fall of blood pressure which is obtained under these conditions is due to an inhibition of the constrictor center and a stimulation of the dilator center of the vasomotor nerves.

The stimulation of many of the afferent or sensory nerves of the body is followed by a change in the blood pressure. Just what this change may be it is often impossible to predict. Strong sensory stimuli of short duration may produce a marked rise in blood pressure, the constrictor center being the most affected. On the other hand, if the stimuli are very strong or continued over a long period of time, the constrictor nerves may become exhausted, as it were, resulting in a dilation of the arteries and

a fall in the general blood pressure. Like phenomena are often seen following fright, pain, grief, and excitement. The patient becomes suddenly pale, dizzy, and may faint, losing consciousness entirely. This is due to a fall in the arterial blood pressure produced by a temporary inhibition of the vasoconstrictor nerves and perhaps also by a slowing of the heart, due to vagus stimulation. If the person be standing, the blood naturally flows to the vessels of the abdominal viscera and dependent portions of the body, and the brain is thereby rendered bloodless. The treatment of these cases is to elevate the feet and abdomen and to lower the head.

In case the depression of the blood pressure slowly develops because of the gradual onset of fatigue in the vasomotor and other nervous centers, a condition known as *surgical shock* supervenes. The treatment of this condition demands plenty of air, stimulants, saline or blood transfusion, and measures to maintain the body temperature.

The Pressure Effects of Gravity on the Blood Flow vary according to the posture of the body. In the upright position the blood vessels of the feet support a column of blood of relatively great height, but when the individual is lying down this ceases to be the case. In spite of this, by means of the delicate adjustments which the nervous system can bring about in the heart and the blood vessels, there is little difference in the pressure of the blood in the arteries in any position which the person may assume. The blood vessels and nerves soon lose this power if it is not continuously exercised. This is illustrated in patients who have been confined to their beds for a time. If they try to walk or to stand up suddenly, they become very dizzy and may faint, which means that the blood has left the vessels of the brain and is gathered by the force of gravity in the vessels of the dependent parts of the body. With a normal vasomotor mechanism, the vessels of the feet and viscera would quickly constrict to such an extent that the blood pressure would remain at its normal height in the vessels of the brain.

The fact that stimulation of sensory nerves by the gross methods of the laboratory results in very profound changes in the

blood pressure and in the velocity of the circulation of the blood, suggests that normally the vasomotor and cardiac nerves play an important rôle in the proper distribution of blood in the various parts of the body. It may be supposed that normally the nerves of the vascular system function to control the blood flow through the various organs according to their respective needs. Whenever the work of an organ is increased, the blood flow likewise is augmented in the part, while in the rest of the body the blood flow is diminished to a greater or less extent. The blood supply is continually changing according to the call of the various tissues for blood; now the muscles, now the digestive organs, now the brain demand more blood, and this is supplied in the proper amount by the nervous system commanding some arterioles to dilate and others to constrict.

Hæmorrhage.—The action of the vasomotor mechanism is beautifully shown in the case of hæmorrhage. As blood is withdrawn, the vasomotor nerves are stimulated by the falling pressure in the brain. This brings about a more powerful tonic constriction of the vessels through the action of vasoconstrictor nerves, the vascular area becomes smaller and smaller in size, and less blood is required to maintain the blood pressure. Because of this mechanism a relatively large amount of blood can be lost without affecting the general blood pressure (Fig. 26, No. V).

The Regulation of the Blood Supply by Chemical Stimuli.—The caliber of the blood vessels may be influenced by other means than through their nervous mechanism. Acids in very small concentrations cause a vascular dilatation. For example, lactic acid and carbonic acid, both of which are formed during muscular work, may produce a local dilatation of the blood vessels, the phenomenon thus constituting an automatic mechanism for delivering more blood to a part when it is needed. On the other hand, the secretion of the adrenal and of a portion of the pituitary gland (see p. 131) produces a constriction of the vessels and thus tends to maintain the normal blood pressure. Recently it has been shown that during periods of excitement and sensory pain the amount of the adrenal secretions may be increased and

the arterial blood pressure raised as a result of general vasoconstriction (p. 190). Because of its vasoconstricting properties, extract of the adrenal glands (“*adrenalin*” or “*epinephrin*”) is used in local anesthetics, as in cocain solution, to prevent bleeding and to minimize the absorption of the cocain into the general circulation (Fig. 26, No. IV).

Asphyxia.—Whenever the amount of oxygen which the blood must supply to the tissues falls below the minimum amount required, a condition known as asphyxia develops. If the nervous centers are intact, any interference with the respiratory function, as by obstruction of the respiratory passages, lack of oxygen in the atmosphere, or the presence of irrespirable gases in the atmosphere—such as carbon monoxide, which reduces the oxygen capacity of the hæmoglobin—interferes with the blood supply of the brain and will produce a train of phenomena in which the respiratory and circulatory changes are prominent. In ordinary asphyxia two factors may be involved, a deficiency of oxygen and an excess of carbon dioxide in the blood. The phenomena following each are essentially the same, and may be divided into three typical stages. In the first stage, that of hyperpnœa, the respirations are increased in rate and amplitude. This stage merges into the second, which consists of exaggerated expiratory efforts, and loss of consciousness; stimulation of the vascular centers in the brain, causing general vasoconstriction accompanied with vagus slowing of the heart also occurs. The net result is a rise in blood pressure. In the third stage, the expiratory efforts give way to slow deep inspirations followed by expiratory convulsions. The pupils dilate widely, the heart becomes very weak from lack of oxygen and overwork, and death occurs from cardiac failure. The changes produced in the respiratory movements, as well as those of the vascular system, are caused by the direct stimulation of the respiratory (see p. 220) and vascular centers, by excess of carbon dioxide and by the lack of oxygen in the blood.

Nitrous Oxide.—The circulatory and respiratory changes accompanying the administration of nitrous oxide gas are very similar to those produced in asphyxia. The asphyxia produced

by the lack of oxygen and the excess of carbon dioxide in the blood during gas anesthesia, stimulates the vasoconstrictor center, producing a rise in blood pressure. The narcotic action of the gas depresses the inhibitory effects of the vagus cardiac center on the heart. The heart is therefore quickened and tends still further to increase the blood pressure. For these reasons it is not wise to use nitrous oxide in the case of elderly patients with weakened sclerosed arteries, or in the case of those suffering from cardiac disease. When oxygen is given along with the nitrous oxide the asphyxial phenomena are reduced.

Cocain.—The effect of cocain injections on the circulation are both central and peripheral, and vary according to the dose and the individual susceptibility. Very small doses generally cause a slight fall in blood pressure, due to slowing of the heart from stimulation of the vagus. The vasomotor center is likewise stimulated, but the resulting vasoconstriction does not compensate for the fall in pressure caused by the decreased action of the heart. Moderate doses depress the vagus function and increase the heart rate, which, together with the vasoconstrictor stimulation observed in the case of the smaller doses, causes a marked rise in the blood pressure. Large doses paralyze the vital centers in the medulla, and a great fall in blood pressure results. With small doses the respirations are accelerated, but in fatal doses the respiratory center (see p. 219) is paralyzed and death ensues.

CHAPTER XXI.

THE RESPIRATION.

Oxygen is one of the essential substances required by every living organism, in the cells of which it combines with the carbon to form carbon dioxide, and with hydrogen to form water. All the phenomena accompanying the supply and utilization of oxygen and the excretion of carbon dioxide are included under the subject of respiration.

In the simplest forms of life the exchange of oxygen and carbon dioxide gas occurs directly with the air, but in more complex organisms this sort of exchange is impossible, since practically none of the cells composing the organism is in direct communication with the air. Some sort of respiratory apparatus becomes necessary, so that each cell may be supplied with oxygen and have its carbon dioxide removed. In the higher animals this is accomplished through the agency of the blood, which is well adapted to transport the oxygen and carbon dioxide, first because it contains chemical bodies with which the gases can unite, and secondly because it comes in close contact with the tissue cells in the peripheral portions of the body, and with the atmospheric air in the capillaries of the lungs. The study of the respiratory function therefore includes the mechanism of the gas exchange between the tissues and the blood, or internal respiration, and also that between the lungs and the blood, or external respiration.

Internal Respiration.

The energy which the body expends in the performance of the functions of life, including the heat which is required to maintain the body temperature, is produced in the cellular chemical reactions, in which the oxygen of the air combines with the hydrogen and carbon of the foodstuffs to form water and carbon dioxide gas.

Oxidation in the Tissues.—The actual mechanism which unites the oxygen with the carbon and hydrogen of the food-stuffs within the tissue cells, is not entirely known. In spite of the fact that the processes of combustion of hydrocarbon matter outside the body yield the same end products as the oxidations taking place within it, the two processes are not strictly analogous. An important point of difference lies in the fact that the intracellular materials—fats, proteins, and carbohydrates—are oxidized with relatively great rapidity at low temperatures (98.4°), whereas the same reactions outside the body require a very high temperature.

Let us take as an example the cell of the yeast plant, in which there is a substance, under the influence of which, the sugar molecule becomes split up, at a temperature below that of the body, to produce carbon dioxide and water. Similar substances are present in the tissue cells of plants and animals; they are the ferments or enzymes (see p. 34), and they act as catalytic agents. The function of these bodies is to increase the velocity of many chemical reactions which otherwise proceed so slowly that they may be said in some cases not to exist. A class of these substances is present within the tissue cells, which at the demand of the tissues control the extent and the velocity of the union of oxygen with the hydrocarbons of the food. Such enzymes are known as oxidases.

What evidence have we, however, that this oxidation takes place within the tissues and not within the blood itself? It is conceivable that the substances that are to be oxidized are collected from the tissues by the blood, and that the oxygen combines with them in this fluid. It is quite possible that some oxidation takes place in the blood, for it is essentially a tissue and has a metabolism of its own, but this is not true for the oxidation which concerns the tissues, since this takes place in the tissues themselves, as can be shown by the following fact: The blood of a frog may be replaced with saline solution in which oxygen is dissolved under pressure, without killing the animal. It is hardly conceivable that oxidation similar to that occurring within the body can take place in a solution of sodium chloride.

RELATION OF OXIDATIVE PROCESS TO ACTIVITY.—Under ordinary conditions the blood has a supply of food and oxygen sufficient for the needs of the body. An excess of either does not intensify the oxidative process. An animal will give off the same amount of carbon dioxide in an atmosphere of pure oxygen as it will under ordinary conditions. This fact indicates that the oxidative processes are governed not by the supply of food or oxygen, but rather by the actual needs of the tissues. A muscle freshly removed from the body may be made to contract, and will give off carbon dioxide for some time in the entire absence of oxygen in the surrounding medium. Another feature of this experiment is that for a time after the muscle has ceased to contract, it will produce heat and take up a large amount of oxygen. Indeed the maximal intake of oxygen and output of heat often occurs after the actual period of work. In this respect the muscle can be likened to a storage battery which is charged by the actual expenditure of energy and delivers quickly the energy stored up when the circuit is closed. If the volume intake of oxygen and output of carbon dioxide is measured, it will be found that the amounts are greatly increased during periods of tissue activity. Experiments have demonstrated that a muscle at full work will use up its own volume of oxygen in ten minutes. To supply such an amount of oxygen requires a very high degree of efficiency on the part of the distributing agent, the blood.

PHYSICAL LAWS GOVERNING SOLUTION OF GASES.—A brief review of the physical laws governing the solution of gases in water will help us materially to understand the mechanism of the transportation of oxygen and carbon dioxide by the blood and the respiratory mechanism in general.

Gases differ from solid and fluid materials in that the particles which compose them repel more than they attract each other, thus permitting the gas to diffuse throughout the atmosphere. The repelling force exerted by the molecules of gas on the walls of the container produce the phenomena of *gaseous pressure*. It follows, therefore, that the pressure which a gas exerts varies with the number of molecules of the gas present in the atmosphere. The various gases diffuse out into space

until this diffusion pressure is balanced by the force of gravity. The weight of a substance is the force which gravity exerts on it. The weight of a gas would therefore be an indication of the diffusion pressure of the gas in the atmosphere, and also indirectly of the number of molecules of gas present. The weight of a gas or the pressure of the gas, on the earth's surface is measured by an instrument called a barometer, in which the atmosphere is balanced against a long column of mercury, and the weight expressed in the number of millimeters of mercury which the atmosphere will support. At sea level and at 15.5° Centigrade, the pressure which the atmosphere exerts on the surface of any fluid is sufficient to support the weight of a column of mercury 760 millimeters in weight.

The solubility of a gas in a fluid is measured by the number of cubic centimeters of gas which one cubic centimeter of fluid will dissolve under standard conditions of temperature and pressure. Such a figure is known as the coefficient of solubility. For example, pure carbon dioxide gas under standard conditions of temperature and pressure (760 mm. pressure and 15.5 degrees Cent.) will dissolve to the amount of one c. c. in one c. c. of water. Under like conditions only 0.04 c. c. of oxygen will be dissolved. The coefficient of solubility of carbon dioxide is therefore 1.0 and of oxygen 0.04.

The amount of gas which will go into solution in water depends on three factors: the temperature of the water, the solubility of the gas in water, and the pressure which the gas exerts on the surface of the water. As a rule, the higher the temperature of the water, the less gas will go into solution, or in other words, the solubility of a gas varies inversely with the temperature.

If, in place of having pure gases over a fluid, a mixture of several gases be present, then we find the solubility of each of the gases varying directly with the pressure it exerts on the surface of the fluid. Suppose that in place of exposing a cubic centimeter of water to oxygen at 760 mm. pressure, we expose it to oxygen at a pressure of 152 mm. mercury, which is the normal pressure of oxygen in the air ($\frac{1}{5}$ of an atmosphere) it would absorb $\frac{1}{5}$ of .04 c. c. or .008 c. c. of oxygen. The presence of

other gases does not enter into consideration, for according to Dalton-Henry's law, when two or more gases are mixed together, each of them produces the same pressure as if it separately occupied the entire space and the other gases were absent. When the fluid has taken up all the gas it can, an equilibrium becomes established between the gas in the atmosphere and the gas within the fluid. The pressure which the gas in the fluid exerts on the gas in the atmosphere is known as the tension of the gas, and equals the pressure of the gas in the outside atmosphere to which it is exposed. This can be easily measured.

Since the pressure of the oxygen in the air in the lungs is less than that in the outside atmosphere, it is apparent that if the blood should carry the same amount of oxygen as water does, the amount would be very small indeed. Analysis of the amount of oxygen in arterial blood shows that it contains 40 times the amount per c. c. that water can dissolve under like conditions. For example, let us imagine human blood to be water. It would carry then only 1/40 of the volume of oxygen that it does, and the tissues of the body would need a vascular system the size of an elephant's in order to obtain as much oxygen as normally is supplied by the blood. Therefore it is obvious that the laws for simple solutions can apply only in a slight degree to the gases in the blood. They would account at the most for only 0.7 per cent of the total oxygen and 2 per cent of the carbon dioxide found in the blood.

Hæmoglobin.—The extraordinary ability of the blood to carry oxygen and carbon dioxide lies in the presence of substances capable of chemically uniting with and storing up large amounts of the gases. The iron-containing protein substance called hæmoglobin, found in the red blood cells, carries the oxygen, and the alkalies and proteins of the blood carry most of the carbon dioxide. Analysis of samples of arterial and venous blood gives the following average figures, which represent the volumes of the gas found in one hundred volumes of blood.

	Oxygen	CO ₂	Nitrogen
100 vol. arterial blood contains.....	20	40	1-2
100 vol. venous blood contains.....	10-12	45-50	1-2

The small amount of nitrogen present in the blood in spite of the large percentage found in the atmosphere ($4/5$ of the barometric pressure being due to nitrogen) is due to the absence of any chemical body within the blood plasma which will unite with nitrogen. Of the 20 volumes per cent of oxygen found in arterial blood only 0.7 per cent is in solution in the plasma.

RELATION OF OXYGEN TO HÆMOGLOBIN.—In order to understand the affinity of oxygen for hæmoglobin, we must investigate the various conditions which favor the union of hæmoglobin with oxygen and the break-down of the resulting oxygen compound, oxyhæmoglobin, into oxygen and hæmoglobin. Equal quantities of *pure hæmoglobin solution* are placed in a series of glass vessels containing variable quantities of oxygen mixed with nitrogen at atmospheric pressure. After shaking, the solutions are removed and the amount of oxygen in each sample is measured.

The hæmoglobin solutions in the tubes containing a partial pressure of oxygen which is within two-thirds of that present in air (between 90 and 152 mm. of mercury) are all almost saturated with oxygen. In other words, at these pressures the hæmoglobin exists entirely in the form of oxyhæmoglobin. In the tube containing one-half the pressure of oxygen in air (i. e., almost 76 mm. Hg.), the hæmoglobin solution is 90 per cent saturated. At about one-fourth the normal oxygen pressure in air (i. e., 40 mm. Hg.), it is about 84 per cent saturated. At lower partial pressures of oxygen, the ability of hæmoglobin to unite with oxygen very rapidly decreases.

From these observations we must conclude that, as the pressure of oxygen in contact with the hæmoglobin solution increases above zero, by graded stages, the amount of oxygen, per unit of increase of oxygen pressure, that combines with hæmoglobin at low pressures is large, but becomes relatively less at higher pressures. Or, conversely, if the hæmoglobin saturated with oxygen be subjected to decreasing oxygen pressure, the combined oxygen is set free at first slowly and then more rapidly.

If the oxygen-combining power of *blood* be investigated in exactly the same way as described above and the results compared with those of a pure hæmoglobin solution, a marked difference

will be observed. At low pressures the oxygen is more easily released from the hæmoglobin of the blood than from pure solutions of hæmoglobin. An inquiry into the cause of this difference has revealed the following facts. The rate at which oxyhæmoglobin breaks down into oxygen and hæmoglobin, depends on

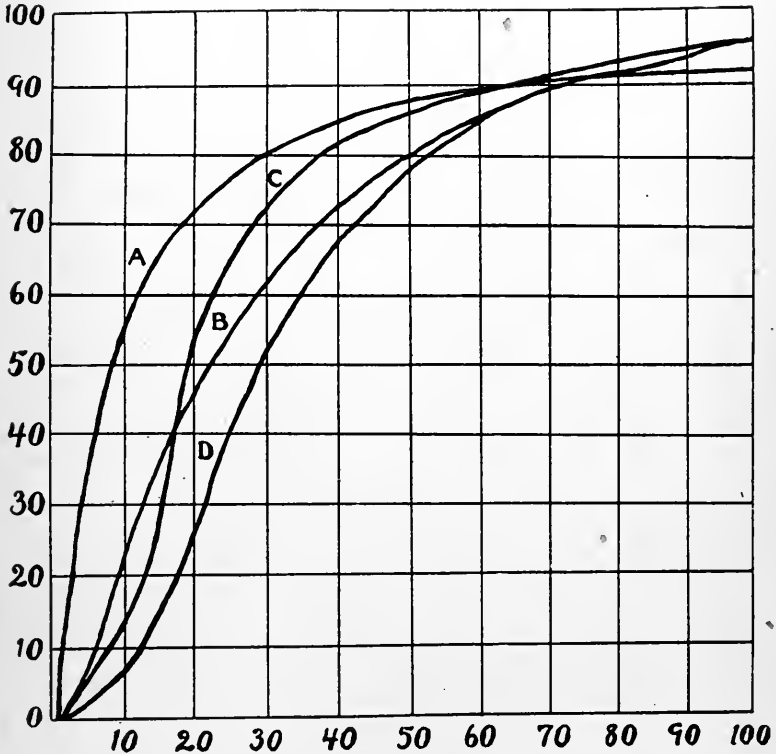


Fig. 27

Ordinates—Percentage saturation of hæmoglobin with oxygen.

Abscissæ—Tension of oxygen in mm. of mercury.

Curve A—Degree of saturation of pure hæmoglobin solutions at varying pressures.

Curve B—Modification of degree of saturation caused by presence of salts in the blood.

Curve C—Effect of 20 mm. CO₂ pressure on above solution.

Curve D—The saturation curve in normal blood at 40 mm. carbon dioxide pressure.

other factors besides oxygen pressure. These are: (1) temperature, (2) the presence of inorganic salts, and (3) carbon dioxide or other weak acids in the blood. If hæmoglobin be dissolved in a saline solution containing the same concentration of inorganic salts as is found in blood, it will take up oxygen in a manner somewhat similar to blood under like oxygen pressures. The similarity will become perfect if the saline solutions of hæmoglobin be subjected to the same pressure of carbon dioxide as that present in the sample of blood, that is, provided the temperature is the same in the two cases. Of the curves shown in Fig. 27, *a* represents the degree of dissociation of oxygen from pure oxyhæmoglobin solution at varying oxygen pressures; *b*, the modification in the degree of the association produced by the presence of the salts of the blood; *c*, the effect of carbon dioxide on the oxygen content of the hæmoglobin in a saline solution; and *d* is the dissociation curve of normal blood with a carbon dioxide tension of 40 mm.

The effect of carbon dioxide is of special interest. It is seen that the greater the concentration of carbon dioxide, the more readily is the oxygen dissociated from the oxyhæmoglobin. Thus, at an oxygen pressure of 20 mm. of mercury, the amount of oxyhæmoglobin formed is 67.5 per cent of the total hæmoglobin at a carbon dioxide pressure of 5 mm., whereas at a pressure of 40 mm. of carbon dioxide the amount of oxyhæmoglobin is only 29.5 per cent. Inasmuch as the amount of carbon dioxide is constantly changing in arterial and venous blood, the presence of this gas would seem to be an important factor in the control of the oxidation or the dissociation of the hæmoglobin compounds. At any rate, it would help to account for the ease with which oxygen is broken from the oxyhæmoglobin molecule in the capillaries which are imbedded in the tissues where the carbon dioxide is formed, and its pressure is correspondingly high.

The Mechanism of the Respiratory Exchange.—The oxygen in the alveoli or air passages of the lungs comprises about 14 to 15 per cent of the total air, and exerts on the cells of the respiratory epithelium a pressure of about 100 mm. mercury, more or less. Venous blood when it reaches the lungs contains about 50

per cent less oxygen than does arterial blood, and can take up from 6 to 8 c. c. of oxygen for every one hundred c. c. of blood. Hæmoglobin solutions are almost completely saturated with oxygen at pressures of oxygen much less than 100 mm. of mercury. There are, therefore, very favorable conditions in the lungs for hæmoglobin to take up oxygen from the air. It must be understood, however, that the hæmoglobin does not obtain oxygen directly from the air. The hæmoglobin is held in the blood corpuscles which are floating in the blood plasma. Between the plasma and the air in the lungs lie two thin membranes, the capillary wall and the wall lining the air sac of the lung. The oxygen must first be dissolved by the fluid in the lung epithelium; from this the cells of the capillary walls take oxygen, and the plasma in turn takes the oxygen from the capillary cells. The plasma loses the oxygen thus obtained because the hæmoglobin is very greedy for oxygen. There is accordingly a difference in the oxygen pressure in the plasma of the capillaries of the lungs sufficient to account for the absorption of oxygen by the hæmoglobin of the blood. The blood leaving the lungs is delivered into the left heart, from which it is distributed over the body. Since oxidation takes place within the tissue cells, oxygen is being continually called for, and the lymph surrounding the cells must continually gain a fresh supply of oxygen from the plasma of the blood. This reduces the tension of oxygen in the plasma and causes an evolution of oxygen from the oxyhæmoglobin, which is taken up by the plasma to be passed on to the lymph and then on to the cell. There is thus a descending scale of pressure or tension of oxygen from the air of the lungs, where its pressure may amount to 100 mm. of mercury, until it reaches the tissue elements, where the pressure may be considered zero. Under ordinary conditions the circulation is fast enough to prohibit the complete reduction of the oxyhæmoglobin. In case it is not, or in case the oxygen supply is short, the phenomena of asphyxia develop (see p. 195).

EFFECT OF CARBON DIOXIDE ON OXYHÆMOGLOBIN.—As a result of the oxidative changes which take place within the cells, carbon dioxide is produced, and the tension of this gas rises in the tissues. It will be remembered in the discussion of the dissociation

of oxyhæmoglobin, that the effect of increased tensions of carbon dioxide is to increase the rate of reduction of oxyhæmoglobin into oxygen and hæmoglobin. Since there is a high tension of carbon dioxide present in the tissues and at the site of the capillaries, the effect on the reduction of oxyhæmoglobin is very marked, and has a great influence on the rate at which oxygen is supplied to the tissues. Just as there is a descending pressure of oxygen from the air in the lungs to the cell, so is there a decrease in pressure from the carbon dioxide in the cells to the air of the lungs. This gas therefore passes through the lymph to the plasma and out of the plasma through the pulmonary epithelium by the simple process of diffusion.

THE EXCHANGE OF CARBON DIOXIDE.—Analysis of venous blood shows that 100 c. c. contains about 45 to 50 c. c. of carbon dioxide, and that the gas exerts a pressure or tension of about 40 mm. mercury, which is equal to about five per cent of an atmosphere. Now water will dissolve under these conditions about $2\frac{1}{2}$ c. c. of carbon dioxide per 100 c. c. This would leave the most of the carbon dioxide of the blood unaccounted for, in case the blood has the same solvent power for the gas that water has. The rest of the carbon dioxide therefore must be accounted for as being in chemical combination with the constituents of the plasma and corpuscles. The major part is probably held in the form of sodium carbonate and bicarbonate, the remainder being combined with the proteins of the plasma and the red corpuscles. The most satisfactory explanation of the manner in which carbon dioxide is dissociated from the above mentioned compounds in the blood, is that there are substances in the plasma, such as the blood proteins, which act as weak acids, and gradually drive off the carbon dioxide when, as in the air in the lungs, its escape is rendered easy by a lowered carbon dioxide pressure outside the plasma.

CHAPTER XXII.

THE RESPIRATION (Cont'd).

The External Respiration.

Anatomical Considerations.—The constant call of the tissues for oxygen and the formation of the waste gas, carbon dioxide, demands a mechanism by which the blood can continually renew its supply of oxygen and excrete its excess of carbon dioxide. This exchange, as we have seen, is effected in the lungs, which are built up in the following way:

The nasal and oral cavities lead to the pharynx, from which open two tubes: one posterior, the œsophagus, going to the alimentary tract, and the other, anterior the trachea, going to the



Fig. 28.—Diagram of structure of lungs showing larynx, bronchi, bronchioles and alveoli.

lungs (Fig. 28). At the beginning of the trachea is placed the larynx, or the voice box, the opening of which is guarded by a flap of tissue, the epiglottis. Within the larynx are the vocal cords. The trachea, or windpipe, is a relatively large tube, about four and one-half inches long, which, after its entrance into the thorax, divides into two tubes, the bronchi, each of which subdivides again and again, the branches gradually growing smaller until they are mere twigs, and are known as bronchioles, or small

bronchi. The lumen of the trachea and bronchi is maintained patent by cartilage plates, which are imbedded in the walls of the tubes. The bronchioles, however, have no such plates, their walls being composed of fibrous and elastic tissue, in which is a layer of smooth muscle. The whole system of tubes is lined with a layer of ciliated epithelium.

The bronchioles terminate in wide air sacs or cavities, the infundibuli, from the walls of which extend numerous minute cavities, the alveoli. The walls of the alveoli are very thin but strong, and are composed of a layer of elastic tissue lined with a single layer of flattened epithelium. It is estimated that the epithelial surfaces of the alveoli, if they were spread out on a flat surface, would cover about 1,000 square feet. Such a large area exposed to the air of the lungs offers the best of facilities for the rapid exchange of the respiratory gases, and in fact the walls of the alveoli are the true respiratory membrane of the lung, for through them the exchange of gases between the air and the blood takes place. Below the epithelial cells of the alveoli lie the capillaries of the pulmonary artery in a regular meshwork; so numerous, indeed, are they that each individual erythrocyte is able to come in close contact with the air in the alveolus, separated only therefrom by the lining of the alveolus, the wall of the artery, and the plasma of the blood. This arrangement makes possible the rapid exchange of gases which must take place within the lungs.

The two lungs in company with the heart occupy the thoracic cavity, which is bounded above and on the sides by the ribs and their attached tissues, and below by the diaphragm, a muscular sheet of tissue which divides the body cavity into a thoracic and an abdominal portion (Fig. 29). The lungs are suspended at their roots, which are composed of the trachea and the pulmonary blood vessels, and they lie free in the thoracic cavity in close apposition with the walls of the thorax. Covering the outside of the lungs and the inside of the thoracic cavity, which is in contact with the lungs, is a thin endothelial membrane known as the pleura, the surface of which is kept moist by a secretion of lymph. This smooth membrane allows the surface of the lungs

to move easily over the inner surface of the thorax during the changes in the size of the cavity which accompany the respiratory movements.

Mechanism of Breathing.—Normal breathing has the object of bringing about a constant renewal of air in the lungs, and it is effected by movements of the thorax and diaphragm. Whenever the cavity of the thorax is enlarged, as in the act of inspiration, the lungs must increase in size to fill the space, and air is

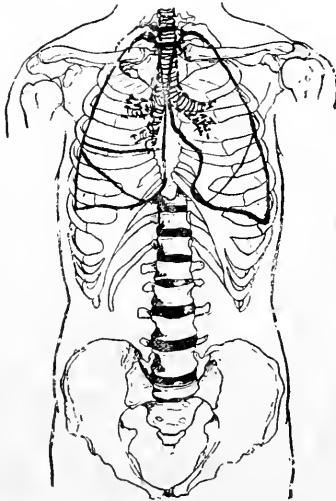


Fig. 29.—The position of the lungs in the thorax. (T. Wingate Todd.)

pushed into the respiratory tubules and the air sacs by the pressure of the outside atmosphere. At expiration the reverse takes place, and the air is expelled. A very good conception of the mechanism by which this is brought about may be had by reference to Fig. 30. Any increase in size of the bottle, as by pulling down the bottom rubber membrane, will cause air to expand the rubber sacs coming in by the tube passing through the cork of the bottle. When the size of the cavity is decreased by releasing the membrane, the reverse takes place and air is expelled from the rubber sacs.

With every inspiration the thorax is increased in size in all

diameters, from above downwards by the contraction of the diaphragm, and in the transverse diameter by the movement of the ribs.

THE PART PLAYED BY THE DIAPHRAGM.—The diaphragm is a circular sheet of muscle which divides the body cavity into two compartments, the upper being the thorax, the lower the abdom-

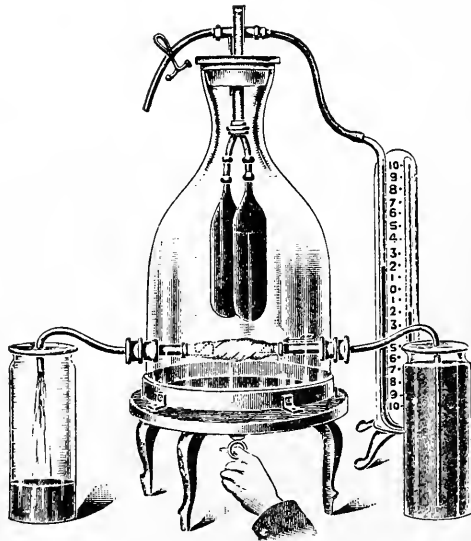


Fig. 30.—Hering's apparatus for demonstrating the action of the respiratory pump. The thorax is represented by a bottle, the diaphragm by a sheet of rubber forming its bottom, the trachea by a tube passing through the cork, and the lungs by two thin rubber bags. A thin piece of rubber tubing crosses the bottle. This represents the heart. The action of the diaphragm pumps air in and out of the lungs and water through the heart. The lungs and heart are thin rubber bags. (From Baird and Co.'s catalogue.)

inal cavity. In the upper compartment are the lungs and heart with the accompanying blood vessels and air passages. The abdominal cavity contains the digestive organs and glands, as the liver, kidneys, spleen and reproductive organs. The peripheral edges of the diaphragm are attached to the lumbar vertebræ at the back, to the lower border of the ribs on the sides, and to the tip of the sternum in front. The muscular fibers radiate to-

wards the center and end in a tendinous sheet of tissue called the central tendon of the diaphragm. When these fibers are relaxed, the diaphragm is pushed up into the thoracic cavity, forming a dome-shaped arch. This is caused by the pressure of the abdominal organs, supported by the muscular walls of the abdomen, on its lower surface, a suction pressure on the upper surface of the diaphragm being maintained by the natural tendency of the lungs to contract. The central tendon is pulled downwards and the arched dome is flattened on contraction of the diaphragm,

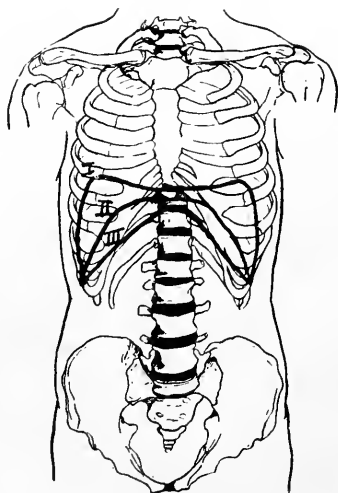


Fig. 31.—Diagram to show movement of diaphragm during respiration: I, expiration; II, normal inspiration; III, forced inspiration.

thus increasing the size of the thoracic cavity (Fig. 31). Another result of the lowering of the diaphragm is the slight protrusion of the abdomen due to the pressure exerted on the viscera. This type of breathing is therefore known as abdominal or diaphragmatic breathing.

THE PART PLAYED BY THE THORAX.—The action of certain muscles attached to the ribs also produces an enlargement of the thoracic cavity. Each pair of corresponding ribs, which are ar-

articulated posteriorly with the vertebral column and anteriorly with the sternum, forms a ring directed obliquely from behind forwards and downwards. Any muscles whose action would bring about a raising of the anterior ends of the ribs, would therefore lessen the oblique position and increase the distance between each pair of ribs, and also add to the antero-posterior diameter of the thorax. Each rib increases in length from above downwards, and as the ribs are raised, the lower longer rib occupies the place previously held by its shorter neighbor. This movement therefore causes the dome or apex of the thorax to become more flat and broad. And also the lower ribs are so articulated with the spinal column that they exhibit an upward rotary movement, which resembles that made by a bucket handle, and which increases the lateral or transverse diameter of the thorax.

The muscles which are responsible for the inspiratory elevation of the ribs are mainly the external intercostals, aided by other muscles of the thorax, some of which are called into use only when very powerful respiratory movements are necessary.

Normal expiration is almost entirely a passive act. The recoil of the stretched elastic tissue of the lungs, after the inspiratory muscles have ceased to act, returns the diaphragm and thoracic cage to the expiratory position. This is aided somewhat by the actions of the internal intercostal muscles which lower the ribs. By increasing the size of the thoracic cavity, inspiration causes a corresponding increase in volume of the thoracic organs; viz., the lungs and the vascular structures, because the thorax is a closed cavity, and whenever it expands it must either produce a vacuum between the organs which fill it and its own walls, or the volume of the organs must increase. It is the latter process which mainly occurs, the result being that air is pushed into the lungs by the atmospheric pressure whenever the thoracic cavity is increased in size.

THE MOVEMENTS OF THE LUNGS.—The changes produced in the size of the thoracic cavity and the lungs during normal respiration or in disease, are easily determined by noting the sounds which are produced by tapping or percussing with the fingers the

thoracic walls during inspiration and expiration. A low-pitched resonant sound is elicited over the lungs containing air, whereas a high-pitched non-resonant or tympanitic hollow sound is heard over the solid viscera and abdominal organs. In disease when changes take place in the substance of the lungs, as in tuberculosis, pneumonia, etc., alterations occur in the tone elicited on percussion. These alterations are of great diagnostic importance. In pleurisy, a condition in which the pleural surfaces are roughened, a friction rub or vibration, produced by the rubbing of the roughened surfaces of the pleura of the lungs on that of the thorax, may be detected by placing the ear over the affected area. The pain following a broken rib is caused by the irritation of the pleural membrane by the broken edge of the rib. It is alleviated by making the ribs immovable by tightly strapping the thorax with adhesive plaster over the region of the pain.

RESPIRATORY SOUNDS.—Accompanying inspiration a rustling sound, described as a vesicular sound, may be heard over most of the lung area. It is produced by the dilatation of the alveoli and fine bronchi. Over the larger air passages a high, sharper tone is heard, called bronchial breathing. In diseases in which the alveoli are destroyed and the lungs are filled with fluid, etc., the bronchial breath sounds replace the vesicular sounds.

Effect of Respiration on the Movement of the Blood and on Blood Pressure.—Within the thorax the changes in pressure accompanying each respiration affect the heart and so influence somewhat the movement of the blood. In thin individuals it is easy to confirm this by observing the effect of breathing on the blood flow through the jugular vein. At each inspiration the jugular vein is seen to empty, and during expiration to fill. If simultaneous records are taken of the blood pressure and respiratory movements in ordinary breathing, it will generally be observed that during inspiration there is a rise and during expiration a fall of blood pressure. This phenomenon is explained as follows: During inspiration the heart is better supplied with blood and can fill more quickly and perfectly than during expiration, because the decrease in the pressure in the thorax at this period serves to accelerate the movement of venous blood

into the thorax by expanding the larger veins. The expansion of the lungs at inspiration also dilates the capillaries and arterioles imbedded in these tissues, hence a greater volume of blood can pass through them in the same unit of time. If the heart beat remains constant in strength and rate, the increased amount of blood pumped during inspiration will cause the blood pressure to rise.

It is well to bear in mind that under abnormal conditions the respiration may affect the blood pressure to a dangerous extent. For instance, in the attempt to force air from the lungs under pressure into a vessel, as in blowing up a football or testing the strength of expiration on a machine made for the purpose, the air pressure can be increased within the thorax to more than equal the pressure in the vessels of the lungs, and the circulation is temporarily stopped in the pulmonary vessels. The blood becomes dammed up in the venous system and forced out of the lungs by the pressure of air. This experiment is dangerous in one who has not a first-class heart and vascular system. The effects on the lungs and blood pressure of sucking, inspiration and expiration can be conveniently reproduced on an artificial schema which represents the thoracic cavity, lungs, heart and related vessels, as shown in Fig. 31.

Variations occur in the respiratory movements under various emotional and physical conditions. Any foreign or irritating body within the air passages will cause a *cough*. This consists in a forced expiration, during the first portion of which the glottis is closed. The irritating substance is likely to be expelled by the sudden opening of the glottis. The presence of irritating substances in the nasal cavity gives rise to *sneezing*, a sudden and noisy expiration through the nasal passages preceded by a rapid and deep inspiration. In *crying*, inspirations are short and spasmodic, followed by prolonged expirations, whereas laughing is quite the reverse. *Yawning*, the expression of drowsiness or ennui, consists in long deep inspirations followed by a short expiration. *Hiccoughing* is due to spasmodic contractions of the diaphragm, the peculiar sound being due to sudden closure of the glottis.

Artificial Respiration.—In cases of suspended respiration in human beings caused by drowning, excess of anæsthesia, or other injury, artificial respiration is often necessary to restore normal breathing. The most efficient of these methods is described by Schäfer, and is known as Schäfer's method (Fig. 32). He describes the method as follows: It consists of laying the subject in the prone posture, preferably on the ground, with a thick folded garment underneath the chest and epigastrium. The operator puts himself athwart or at the side of the subject, facing



Fig. 32.—Position to be adopted for effecting artificial respiration. (Schäfer.)

his head (Fig. 32) and places his hands on each side over the lower part of the back (lower ribs). He then slowly throws the weight of his body forward to bear upon his own arms, and thus presses upon the thorax of the subject and forces the air out of the lungs. This being effected, he gradually relaxes the pressure by bringing his own body up again to a more erect position, but without moving his hands. These movements are repeated regularly at a rate of twelve to fifteen per minute until normal respiration begins.

Volumes of Air Respired.—At each inspiration the lungs take in about 500 c. c. of air, which is given out again at expiration. This is known as the *tidal air*. After the completion of the ordinary inspiration, it is possible by a forced inspiration to take

1500 c. c. more air into the lungs. This amount is known as the *complemental air*. Likewise after a normal expiration about 1500 c. c. more air can be expelled from the lungs. This is known as the *supplemental air*. In spite of forced expiration there will still remain within the lung about 1000 c. c. of air which fills the alveoli and air tubes, known as the *residual air*. This air remains in the air spaces after the forced expiration because the lungs cannot relax to their fullest extent, being held open by the suction pressure of the thorax. In other words, the thoracic cavity is larger in the expiratory position by 1000 c. c. than the lungs are. That this is the case is shown by the immediate contraction of the lungs into a small volume when the thorax is opened, for then the atmospheric pressure becomes equalized on the outside and inside of the lungs, and the elastic tissue contracts and forces out the residual air. From this it is obvious that the elastic recoil of the stretched lungs must always tend to pull the organ away from the chest wall and thus create a negative or suction pressure within the thoracic cavity. Anything which destroys this relation makes breathing impossible, because the lungs are no longer held against the chest walls. It is for this reason that wounds in the chest are very dangerous.

The trachea, bronchi, etc., require quite a little air to fill them, so that only a part of the tidal air reaches the alveoli. In other words, it is only a portion of the air we expire that comes in contact with the respiratory epithelium and undergoes any change in composition.

It is estimated that about 140 c. c. represents the actual volume of the air tubes. This leaves 360 c. c. of air which reaches the alveoli. This amount is used to dilute the 1000 c. c. of residual air and 1500 c. c. of supplemental air already in the alveoli. In fact the function of breathing may be said to consist in continually diluting the alveolar air with a quantity of fresh air in order that its composition may remain more or less constant.

The inspired or atmospheric air is a mixture of oxygen, carbon dioxide and nitrogen, and is relatively constant under ordinary conditions. The expired air varies somewhat according to

the rate and depth of respiration. The following table gives the average percentage composition of inspired and expired air:

	Nitrogen	Oxygen	CO ₂
Inspired air	79	20.96	0.04
Expired air	79+	16.02	4.38

The above analysis shows that there is a marked difference between the inspired and the expired air. It shows us further that of the oxygen taken up by the blood, only part appears again combined with carbon in the gas CO₂. The retention of oxygen is due to the oxidation of substances which do not appear in the expired gases. This subject is fully discussed under the head of *respiratory quotient* in the chapter on metabolism (p. 91).

These observations do not enable us to decide whether the laws of diffusion of gases apply to the gaseous exchange of the lungs. To do this we must know the actual pressures of the respiratory gases in the venous blood coming to the lungs and in the air of the alveoli. Many types of experiments have been devised to obtain these values, and although the actual figures vary somewhat in the hands of different investigators, the results as a whole indicate that the gaseous exchange of the lungs is dependent solely on the presence of a higher pressure of oxygen and a lower pressure of carbon dioxide in the alveolar air than are present in the blood coming to the lungs. The ability of hæmoglobin to take up oxygen with great readiness at oxygen pressures which exceed 50 or 60 mm. mercury pressure indicates that the blood can still obtain oxygen from air which contains only one-half of the normal pressure of oxygen. In whatever way we estimate it, the oxygen pressure in the alveoli is always greater than this.

We will not go into details regarding the methods which have been employed in solution of these problems; suffice it to say that a very fair sample of alveolar air can be secured by collecting a sample of air from a tube through which a forced expiration has been made. The last portions of such expired air must obviously be alveolar air.

Mechanism of Gaseous Exchange in Lungs.—We have seen that in the blood the pressure or tension of the oxygen is greater,

whereas that of the CO_2 is less than in the tissues. These relations will account for the gas exchange which occurs between the blood and tissues if we apply the physical law of the diffusion of gases, which states that two gases under different pressures and separated by a membrane through which they may pass freely, will mix with each other until the tensions on both sides of the membrane are equal. Before this law can be applied to explain the exchange of gases between the blood and air within the lungs, we must prove that the tension of the oxygen is less, and of the CO_2 greater in the venous blood than in the alveolar air. A consideration of these problems is included under the subject of *external respiration*.

CHAPTER XXIII.

THE RESPIRATION (Cont'd).

Nervous Control of Respiration.—Under normal conditions we breathe from 14 to 18 times a minute. According to the demand of the tissues for oxygen, we breathe fast or slow, but the respirations are rhythmic in time and under like conditions are equal in volume. The respiratory movements, unlike those of the heart are initiated by impulses transmitted to the respiratory muscles from the central nervous system. These arise from the so-called respiratory centers in the medulla oblongata (p. 256). Anatomically these centers cannot be sharply localized, but destruction of the portion of the medulla in which they exist causes an immediate cessation of respiratory movements. The centers are connected with the diaphragm by the phrenic nerves, and to the muscles of the ribs, larynx and nares by spinal or cranial nerves. Like all other nerve centers, the respiratory center is influenced by afferent impulses, the chief ones of which come from the lungs by way of the vagus, but there are many others. In fact all the sensory nerves of the body, as well as the higher centers of the brain, are able to influence the respiratory center. Disease of the phrenic nerves causes paralysis of the diaphragm, and impairs the ventilation of the lungs. Likewise paralysis involving the spinal cord below the exit of the phrenic nerves may paralyze the nerves of the thoracic muscles, and throw the whole work of respiration on the diaphragm.

If the vagus nerves of a dog or cat are cut in the neck, the respiration becomes deeper and slower, yet the volume of air respired per minute is not greatly altered. This change is due to the elimination of stimuli normally coming from the lungs by way of the vagi to the respiratory center, which serve to control the depth of respiration. It can be experimentally demonstrated that the collapse of the alveoli of the lungs which occurs at the

end of normal expiration, and the stretching of the alveolar walls which occurs at the end of normal inspiration, cause stimuli to be passed along the vagi to the center, and that these stimuli bring on the next phase of respiration. The breaking of the connection between the lungs and the alveoli destroys this influence and the respirations become deep and slow.

In the absence of the vagi, the higher centers assume partial control of the regulation of the respiratory movements. If they also are destroyed, however, breathing becomes inadequate to maintain life, although the center itself is still able to keep up a modified, rhythmic respiration.

REFLEX RESPIRATORY MOVEMENTS.—The cutaneous nerves, especially those of the face and abdomen, have a marked influence on respiration. These can be excited by heat or cold or pain; for instance, a cold bath will cause a deepening or quickening of the respiration. Another example is found in the forced expiratory effort made on inhalation of acid or sharp smelling substances, which not only affect the olfactory nerves, but also the sensitive endings of the fifth nerve in the nasal mucous membrane.

Chemical Control of Respiration.—In spite of this very effective method of nervous control of the respiration, there is another no less important means of respiratory control, which depends on the ability of chemical substances in the blood to stimulate the respiratory center. The substances which most readily affect the center are acids, such as carbon dioxide (which in solution forms a weak acid,) and lactic acid, which is formed under certain conditions in the body. Lack of oxygen, if it be considerable, also causes the center to show marked signs of activity. In the introductory chapter the physico-chemical properties of the blood and tissue fluids were discussed. It will be recalled that these are practically neutral fluids, that is, they show an almost exact balance in the number of hydrogen and hydroxyl ions, a condition which determines the neutrality of a fluid. Any increase in the amount of carbon dioxide in the blood would form proportionately more carbonic acid, which yields hydrogen ions, and thus tend to destroy the neutral balance of the blood. This

increase in the hydrogen ion concentration in the blood is sufficient to stimulate the respiratory center and augment the rate and depth of respiration in order to expel the carbon dioxide and thus reduce the acidity of the blood. All acids which yield hydrogen ions in solution have this effect on respiration when they are injected into the blood. Lactic acid, which is formed when the oxygen supply to the tissues is diminished or inadequate, is perhaps the most important factor coming into play in the stimulation of the respiratory center which occurs during exercise. The carbon dioxide tension of the blood during exercise may be actually decreased owing to the increased ventilation of the lungs as a result of the presence of lactic acid in the blood.

The increase in breathing due to lack of oxygen is not nearly so easily elicited as that caused by excess of acids. In fact, the percentage of oxygen may be diminished to about one-half of that found in the atmosphere before breathing is markedly affected.

In disturbances of the gaseous exchange of the lungs, the respiratory center attempts to compensate for the change by increasing the number and the depth of the respirations. If the gas exchange be markedly insufficient, the breathing becomes very much exaggerated, and practically all possible respiratory muscles are called into play. This is the case during an attack of asthma, in which the muscles of the arms and abdomen are used by the patient in his efforts to obtain enough air. Difficult breathing of this kind is known as *dyspnœa*. If the gas exchange is very insufficient, the phenomenon of *asphyxia* sets in.

The control of the respiration, therefore, may be said to be two-fold, dependent not only on the nerve supply of the respiratory center from the afferent sensory and cerebral nerves, but also on the chemical constitution of the blood, which stimulates the center directly. Each factor plays an important part in the control of the respiratory movements.

The *bronchial muscles* are supplied through the vagi with nerve fibers which produce dilatation and constriction of the bronchi. Just what the normal conditions are which call for the action of these nerves is not known. It is generally thought that

asthma is caused by the constriction of the bronchioles by spasm of the bronchial muscles. Atropin, a drug which paralyzes certain nerves, is of therapeutic use in this disease, since it paralyzes the nerve endings in the bronchial muscles. Adrenalin is also sometimes of use.

The Effect of Changes in the Respired Air on the Respiration.

A very slight increase in the percentage of carbon dioxide in the *alveolar air* is accompanied by a very marked quickening of respiration. On the other hand, the carbon dioxide content of the *atmosphere* may be increased to about one per cent without embarrassing the respiratory function, except during muscular work, and it is only at concentrations of carbon dioxide of three or four per cent of an atmosphere that the respiratory function is seriously impaired. The reason for this is that the inspired air becomes greatly diluted before it reaches the alveoli, so that a slight increase—up to one per cent of carbon dioxide—in the atmosphere only quickens and deepens the respiration sufficiently to maintain the pressure of carbon dioxide at its normal level in the alveoli.

An increase in the oxygen pressure has no such effect. In fact pure oxygen has scarcely any influence on the rate of breathing in the normal man. In persons suffering with heart failure or diseases in which the respiratory function of the lungs is impaired, however, the presence of a high concentration of oxygen in the alveoli may make it possible for the oxygen-starved blood to obtain enough of this gas to saturate it and thus improve the general condition. The reason for these effects of oxygen is that under normal conditions the pressure of oxygen in the atmosphere is more than sufficient to saturate the hæmoglobin of the blood, so that an increase in the oxygen pressure will add only a small amount more of oxygen to that dissolved in the plasma already. On the other hand, the oxygen pressure in the atmosphere may be reduced to less than half that found at sea level without destroying life. This brings up the interesting question of mountain sickness.

MOUNTAIN SICKNESS.—At an altitude of 5,000 meters (about 16,000 feet) the air is reduced to a little over half an atmos-

phere, and the oxygen tension is therefore only about eleven per cent of an atmosphere in place of twenty per cent. Therefore, in order to supply the needed oxygen, respiration must become more rapid. This, however, by washing out the carbon dioxide, serves to reduce the tension of carbon dioxide in the alveoli and blood to such an extent that the action of this gas on the respiratory center is weakened, and breathing may be very slow or cease for a time, producing a condition known as apnea. The lack of oxygen weakens the heart, the slightest muscular movements are accomplished with difficulty, and the individual suffers from nausea, vertigo, headache and general weakness. After living for some time at such altitudes a person becomes accustomed to the rarity of the atmosphere and in some manner is able to compensate for the lessened oxygen in the air.

VENTILATION.—The disagreeable odor of a crowded room and the symptoms which accompany it are well known and are usually attributed to the rebreathing of air. In support of this the historical incident of the Black Hole of Calcutta, in which many people perished from lack of air, is often cited. We have already seen that atmospheres up to one per cent of carbon dioxide, or containing less than half of the normal percentage of oxygen, can be respired with no ill effects. But the percentage of carbon dioxide in the worst ventilated room does not, as a rule, rise above five-tenths per cent, or at most over one per cent, of an atmosphere. That this amount affects our body metabolism is impossible, since the carbon dioxide in the alveolar air is kept at a constant level of from five to six per cent by the control which the respiratory center exercises on the respiratory movements. Moreover perfectly normal respiration can take place in a room where the oxygen content is so low that a match will not burn.

Because of these facts it was suggested at one time that a toxic substance might be present in the expired air, but this has not been confirmed by subsequent investigators. In spite of the fact that there is a normal percentage of oxygen and carbon dioxide, a room may be unbearably close if it is too warm and the air is saturated with moisture. So long as the body can radiate its heat quickly into the atmosphere, the room does not feel stuffy, but

when evaporation is slow, because of saturation of the air, and heat is no longer given off quickly by the body, the individuals in the room become very uncomfortable. An electric fan, which distributes the air evenly over the room and thus quickens the removal of the warm moist air immediately surrounding the body, adds much to the comfort of the person. In addition to insisting upon fresh air in public offices and private houses, it is necessary that the ventilating engineer should pay heed to something besides the percentage of oxygen and carbon dioxide in the room. He should also direct his efforts towards cooling and increasing the circulation of the air that surrounds the bodies of the individuals, by setting the air in motion by means of fans.

The conditions of temperature, the moisture, and the windless atmosphere found in public rooms and homes diminish the heat loss of the body and thus the heat production, which means that the activity of the occupants must be less. A reasonable temperature with a relatively low percentage of moisture, and ordinary care in providing fresh air, will maintain the proper hygienic conditions of a room.

The Voice.

The voice-producing mechanism in man consists of the trachea, through which the air is blown from the lungs; the larynx, the modified upper portion of the trachea, which contains the vocal cords; and the pharynx, and upper air passages. The larynx forms the entrance into the trachea. It is composed of a number of cartilaginous plates which are united in a manner to form a box. Stretched from front to back on each side across the upper portion of the larynx are thin sharp-edged membranes, the *vocal cords*. The attachments of the muscles to the cartilages and the articulations of the several cartilages with each other, are so arranged as either to tighten or loosen the tension, or increase or decrease the opening between the edges of the cords. The cleft between the cords is called the glottis. The length of the vocal cords varies from 11 to 15 mm., being longer in men than in women and children. Branches of the vagus and the spinal ac-

cessory nerves supply the muscles of the larynx with motor nerves. The sensory nerves, arising in the epithelium of the larynx, are also branches of the vagus. Mechanical stimulation of the mucous membrane of the larynx or electrical stimulation of the superior laryngeal nerve will cause a cough or a forced expiratory movement.

The Changes Which Occur in the Position of the Vocal Cords during the production of certain sounds may be studied by the use of the *laryngoscope*, the principle of which is shown in Fig. 33. The view obtained from such an instrument is shown in Figs. 34 and 35. The base of the tongue appears at the top; be-

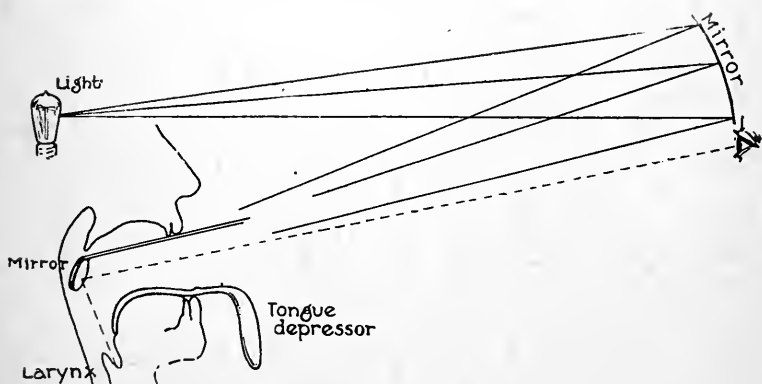


Fig. 33.—Diagram of laryngoscope.

low this is the edge of the epiglottis, the flap of tissue guarding the entrance to the larynx; and below in the middle line are seen the true vocal cords as white shining membranes. Just above these, on either side, are two pink flaps of tissue, the *false vocal cords*. These secrete a fluid which moistens the true cords.

The Production of the Voice.—If the vocal cords be put in a state of tension and the aperture between them be narrowed, causing them to offer a resistance to the passage of air issuing from the lungs, they may be made to vibrate and to produce sounds. It has been experimentally determined that a pressure of expired air of from 140 to 240 mm. of water is required to

produce a sound of the ordinary pitch and loudness, while in loud shouting much greater pressures are necessary.

The sound of the voice, like any other sound, may vary in pitch, loudness and quality. The range of pitch of the voice is generally about two octaves, the *pitch* itself being determined primarily by the lengths of the cords. This accounts for the high-pitched voice of children, in whom the cords are short, and the low pitch of the voice in men, in whom they are long. In

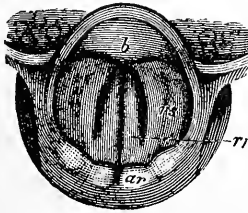


Fig. 34.—Position of the glottis preliminary to the utterance of sound. *rs*, true vocal cord; *ar*, arytenoid cartilage; *b*, pad of the epiglottis. (From Stewart's Physiology.)

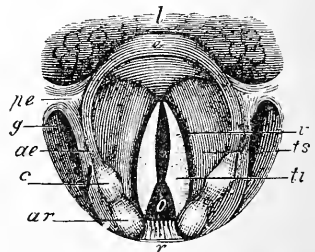


Fig. 35.—Position of open glottis. *l*, tongue; *e*, epiglottis; *ae*, ary-epiglottidean fold; *c*, cartilage of Wrisberg; *ar*, arytenoid cartilage; *o*, glottis; *v*, ventricle of Morgagni; *ti*, true vocal cord; *ts*, false vocal cord. (From Stewart's Physiology.)

singing, three registers can be distinguished, the head, middle and chest registers. The deeper notes of the singer come from the chest register, and are produced by the vibrations of the entire cords, whereas in the upper registers only the inner edge of the cords vibrate.

The intensity or *loudness* of a vocal sound depends upon the amplitude of the vibrations of the vocal cords, and this is proportional to the strength of the expiratory blast. The pitch of a note rises and falls somewhat with the intensity of the pressure of the air, and for this reason high notes are usually loud notes. The *quality* of the voice, like that of a musical instrument, depends on the overtones, or harmonics, that it produces. For example, when a stretched string is made to vibrate, it not only vibrates as a whole, but portions of it vibrate independent-

ly and give off separate tones which are known as overtones. Since the tone which the string produces by the vibration of its entire length is the loudest and lowest in pitch, it is picked out as the fundamental tone. The fundamental tones of instruments may be exactly the same, but the tones yet differ from one another because of the number and the intensity of the overtones.

Speech.

The pure, musical tones produced by the vocal cords are modified by changes in the character of the air passages above them. The various combinations which are produced give rise to sounds which make up speech. Many of the simple combinations are found in all languages, but every language is characterized by certain sounds which are peculiar to it.

The sounds produced in speech may be divided into two groups, the vowels and the consonants. The vowel sounds are continuous and are formed in the lower air passages with the help of the glottis. The consonants are produced by more or less complete interruptions of the outflowing air in different portions of the vocal tract.

All the vowels can be produced in the whispered voice, that is, they can be produced without the actual vibration of the vocal cords. The mouth cavity, however, assumes the same position in the case of the whispered vowel as it does for the spoken vowel. By changing the shape of the air passages, the various vowel tones are produced. In Fig. 36 are seen the various positions of the tongue and palate for the production of the different vowels. When vowels are being uttered, the soft palate closes the entrance to the nasal cavity.

The consonants are named according to the position at which the interruption of the air current takes place. The labials are formed at the lips: p, b; the dentals, between the tongue and the teeth: t, d. The gutturals, k, g, ch, arise between the posterior portion of the arched tongue and the soft palate; and the German r is produced with the help of vibrations of the uvula.

Sounds like m, n, ng, are termed nasal consonants, since they are sounded through the nasal cavity (see Fig. 36).

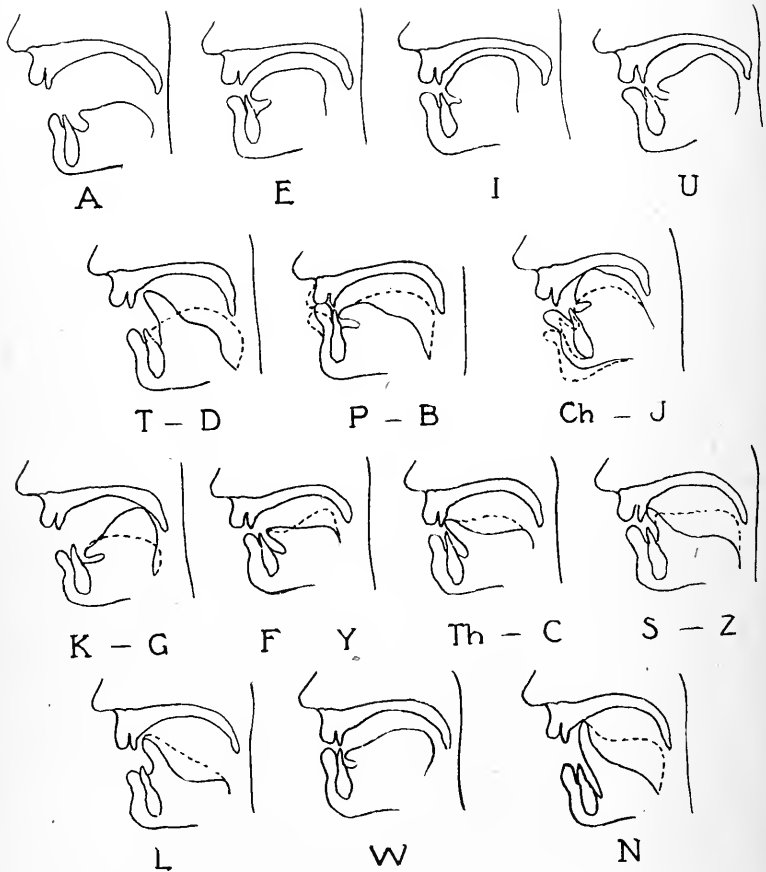


Fig. 36.—The position of the tongue and lips during the utterance of the letters indicated.

CHAPTER XXIV.

THE FLUID EXCRETIONS.

The Excretion of Urine.

The Composition of the Urine.—The waste substance resulting from the processes of metabolism in the tissues are eliminated from the body in a gaseous, fluid, or solid state. With the exception of the carbon dioxide and water of the expired air, and certain substances which are excreted into the intestines or appear in the secretions of the skin glands, the metabolic products are eliminated in the urine.

The composition of the urine is therefore rather complex and varies greatly with the nature of the food and the amount of water taken. By careful analysis of the urine from a number of individuals on ordinary diet, the average amount of the various constituents in what may be considered a normal urine can be estimated. Normal human urine is a clear yellow fluid, a little heavier than water, having a specific gravity of 1.016 to 1.02. If tested with litmus paper it usually shows an acid reaction, mainly due to the presence of acid salts, such as sodium dihydrogen phosphates, but partly also to acid substances derived from proteins. Herbivorous animals secrete an alkaline urine, which is no doubt caused by the presence of the large amount of alkaline earths and the relatively small amount of protein matter in their diet. Human urine becomes alkaline in reaction when vegetables are the main ingredients of the diet.

The character of most of the urinary constituents and the manner by which they are derived from the foodstuffs have been described in the chapter on metabolism, and in the following account only a brief review of their physical and chemical nature is necessary.

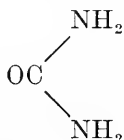
THE ORGANIC SUBSTANCES OF THE URINE.—These comprise a number of nitrogenous compounds. The following figures, ob-

tained from the results of the analysis of a number of normal average urines, show how the nitrogen is distributed among these compounds.

Urea	85 to 90%
Ammonia	2 to 4%
Creatinin	3%
Uric acid	1 to 2%
Unclassified nitrogen	5 to 6%

Urea.—From the above figures it is seen that the greater part of the nitrogen eliminated by man appears as urea. The relative amount of urea eliminated depends very largely on the diet, being 90 per cent or more of the total nitrogen excretion on a full protein diet, and 60 per cent or less during starvation. The total amount excreted is about 30 grams per 100 grams of protein in the diet.

Chemically urea has the following formula:



If prepared pure it forms long colorless needles or four-sided prisms. It is very soluble in water. Hot alkalis, such as sodium hydroxide, decompose it into ammonia and carbon dioxide. The same reaction occurs in case of bacterial decomposition by the micrococcus urea, and accounts for the ammoniacal odor of urine after standing in the air. The significance of urea in regard to protein metabolism and the method of its formation are discussed on page 108.

Ammonia.—This, combined with chlorine or other acid radicles, is normally found in small amounts in the urine. It is one of the important agencies in maintaining the neutrality of the tissues, since with acids it forms ammonia salts, which are neutral in reaction and which are eliminated in the urine.

Creatinin.—The amount of this substance found in the urine

is very constant from day to day, and is independent of the diet. It is largely a product of the metabolism of the body tissues.

Uric Acid.—Uric acid is a purine body and its relationship to the other purines, and its mode of formation and significance are fully discussed in the chapter on metabolism (p. 110). It is relatively insoluble in water, and when allowed to crystallize it forms small rhombic crystals. It can unite with an alkali, such as sodium hydroxide, to form two salts: a neutral or diurate of sodium ($C_5H_2N_4O_3Na_2$) and the biurate or acid urate of sodium ($C_5H_2N_4O_3HNa$). The *biurates* are neutral in reaction and constitute the urates normally found in the blood and urine. They exist in two isomeric forms (*a* and the *b*). The *b* is more soluble than the *a* form. It may be that the deposition of urate tartar on the teeth, and the deposits of urates in the joints of a patient suffering with gout, are due to the change of the *b* form into the less soluble *a* type.

There are a number of other nitrogenous bodies in the urine which are included in the item of unclassified nitrogen in the above analysis. The most important of these is urinary indican, which is derived from the indol produced in the intestines by the action of bacteria on the amino acid tryptophane. The yellow color of the urine is produced by a pigment called urochrome, which is believed to be derived from the pigments in the blood.

THE INORGANIC CONSTITUENTS OF THE URINE.—The urinary salts are chiefly the chlorides, sulphates and phosphates of sodium, potassium, calcium and magnesium. The potassium and sodium salts are found in greatest abundance, since they form the main inorganic constituent of the food, and moreover the greater portion of the salts of the heavier metals, as calcium, iron, bismuth, mercury, etc., is excreted by the intestines. There is very little retention of salts by the body except during the formation of bone, so that the amount of the inorganic constituents of urine varies from day to day with the diet. The chlorides are formed for the most part from the inorganic chlorides of the food; the phosphates and the sulphates are derived from the sulphur and phosphorus of the nucleo-protein molecules. If the urine is neutral or alkaline in reaction, there is apt to be a de-

posit of calcium or magnesium phosphate. This will dissolve when the urine is rendered faintly acid.

ABNORMAL CONSTITUENTS OF THE URINE.—Many of the substances found in the blood occur in minute traces in the urine. When any of these bodies are increased to an unusual amount in the urine, they become what we may term pathological constituents. The bodies most commonly affected are the proteins and sugars. The finding of a protein, such as albumin, in more than the faintest trace, is an indication of *nephritis* or *Bright's disease*. The presence of albumin may be detected by heating in a test tube a slightly acidulated sample of urine.

Normal urine contains the faintest trace of the blood sugar dextrose, but in abnormal conditions, as in the disease *diabetes* or after a meal rich in sugars, a large amount of dextrose appears in the urine as a result of an increase in the sugar of the blood. The condition probably represents the inability of the tissues to make use of their carbohydrate food in the proper manner, and the kidney therefore excretes the sugar as if it were a waste material.

The Organs of Excretion, The Kidneys.

Lying upon the posterior wall of the abdominal cavity at the level of the lower ribs and on each side of the vertebral column are the kidneys, the organs of urine excretion. Each kidney is of the nature of a tubular gland of a very complex structure, anatomically adapted to bring a large amount of blood at a high pressure in close relation with the excreting epithelial cells which line the walls of the gland *tubules*. The tubules empty into a pouch-shaped sac on the inner edge of the kidney, the *pelvis* of the kidney, and this is connected with the urinary bladder by means of a small tube, the *ureter*.

A brief review of the essential parts of the uriniferous tubule and the organs of micturition is necessary in order to understand the mechanism of urine excretion, and the student is advised to consult his textbook of anatomy and histology for a more comprehensive description than is here given. The uriniferous tubules may be divided into the excretory portion and the collecting portion. The tubules arise in the outer part of the kidney,



Fig. 37.—Diagram of the uriniferous tubules (black), the arteries (red) and the veins (blue) of the kidney.

in the region called the cortex, as a body called the Malpighian corpuscle. This corpuscle consists of the dilated end of a tubule which is invaginated to form a cup-shaped vessel, within the cup of which lies a tuft of capillaries. The capillaries compose the structure known as the glomerulus, and the tubular part is known as the capsule of Bowman.

From Bowman's capsule a short neck leads into what is known as the convoluted tubule, which is a very tortuous vessel lined with large epithelial cells. This structure lies in the cortex of the kidney and is nourished by the blood which has already been through the glomerular capillaries. A loop of the tubule leads down into the center or medullary portion of the kidney and back again to the cortex, where the cortex again becomes very tortuous, and finally empties, in company with many other similar vessels, into a common collecting tubule, which leads to the pelvis of the kidney.

THE BLOOD SUPPLY OF THE KIDNEY is very large compared with that of the other organs of the same size. The renal arteries come from the aorta and distribute their blood directly to the glomeruli and the inner medullary portions of the kidney. The vessels of the glomerulus are collected into an afferent vein, which again breaks up into capillaries to supply the remaining structures of the cortical portions of the kidney (Fig. 37).

THE NERVES OF THE KIDNEY.—The kidney is very richly supplied with vasomotor nerve fibers, which are carried to it in the splanchnic nerves. Whether there are nerve fibers in either the vagus or splanchnic nerves which have a secretory influence on the kidney cells, is at present an unsettled question.

The Nature of Urine Excretion.—In spite of repeated attempts to explain the nature of urine excretion, there remain many steps in the process which are not fully understood. The constituents of the urine are formed by other organs than the kidney, and are present in the blood plasma. The function of the kidney is to remove these substances from the blood. Many bodies are present in the blood plasma which are not found in the urine, and again some of the urinary constituents are found in far greater concentration in the urine than in the blood plasma.

To explain these facts, Ludwig, a famous physiologist of the nineteenth century, formulated what is known as the mechanical theory of urine excretion. Impressed by the peculiar relationship of Bowman's capsule and the glomerular capillaries, he concluded that the Malpighian corpuscle is a filtering apparatus which separates, in dilute solution, a portion of all the diffusible substances of the blood. The absence of such diffusible substances as sugar in normal urine and its presence in the blood in a relatively large amount, he believed to be due to the ability of the epithelium of the tubules to reabsorb these substances from the dilute urine. Likewise, the high concentration of salts and nitrogenous bodies, such as urea, he explained by reabsorption of water, through the tubules into the blood. In support of this theory Ludwig demonstrated that the urine excretion varied directly with the blood flow and the blood pressure of the kidney. In other words, the greater the supply of blood and the greater its pressure, the more rapidly will the watery solution of the urine be filtered from the blood. He was not able, however to bring any satisfactory proof of the reabsorption of water or other substances by the epithelium of the urinary tubules. Indeed, most experiments show that this does not occur.

It is impossible to explain all the facts of urinary excretion by simple physical laws. For example, urea and dextrose are both found in the blood and both obey the same physico-chemical laws; nevertheless the one is excreted in the urine and the other is retained in the blood. Furthermore, when certain pigments are injected into the blood, they are excreted by the kidney cells, but do not appear in those of other parts of the body.

That an increase in the pressure of blood in the renal vessels has a very marked accelerating effect on the excretion of urine, is not necessarily evidence that the increased blood supply is the cause of the excretion. That other factors are concerned is demonstrated by the action of drugs which cause an increase in renal excretion. For example, digitalis, a drug stimulating the circulatory apparatus, causes a marked diuresis in cases of a weak heart where the pressure has been totally inadequate to maintain a urine excretion, but has little or no action on the normal kidney.

On the other hand, sodium sulphate injected into the blood causes a diuresis without marked change in rate of blood flow or blood pressure by direct stimulation of the renal epithelium. In almost every case, moreover, an increase in the excretion of urine is followed by an increase in the amount of oxygen used up by the kidney. It is a general law that every increase in cell activity is accompanied by an increase in the amount of oxygen used by the organ, and the increased blood flow accompanying most forms of diuresis is readily explained on the basis of the physiological need of the tissue for water and oxygen. If physical laws were sufficient to explain all the phenomena of excretion, there would be no need for oxygen in increased amounts during periods of increased urine formation. A conception of the actual amount of work which the cells must do to excrete the urine may be obtained by comparing the osmotic pressure of the urine with that of the blood. The osmotic pressure of the blood is only half that of the urine, and for each one thousand cubic centimeters excreted, it is sufficient to call for the expenditure, on the part of the renal cells, of a force capable of lifting a pound through one thousand feet.

We may conclude that the nature of the excretory mechanism cannot be explained by the physico-chemical laws as we now know them, i. e., the phenomena of osmosis, filtration, absorption, etc., but rather that it must be due to a vital action on the part of the renal cells. It is this vital function of the cells which enables them to remove one substance from the blood and to leave another which is identically the same so far as physico-chemical properties are concerned.

Micturition.—The urine discharged from the collecting tubules of the kidney into the pelvis, is carried to the urinary bladder through the ureters (Fig. 38). The muscular coats of the ureter have a movement similar to that of the digestive canal and by peristaltic waves force the urine down through the ureter into the bladder. The urine thus collected by the bladder is retained for a time and is at intervals ejected through the urethra by the act of micturition. This consists of strong contraction of the bladder walls, together with the contraction of the diaphragm-

matic and abdominal muscles, the effect of which is to reduce the size of the bladder cavity and to expel the urine with pressure, through the urethra.

The act is under nervous control, the motor nerves being derived from nerve cells found in the lumbar region of the cord. The stimuli here produced co-ordinate the muscular movements of the act. The afferent or sensory stimuli which initiate the act are excited by the distention of the bladder, or by the passage of a few drops of urine into the first portion of the urethra. These stimuli pass to the center in the cord and are returned to

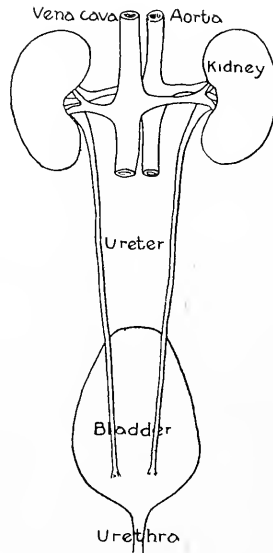


Fig. 38.—Diagram of urinary system.

the muscles of the bladder also causing the sphincter, which closes the bladder to be relaxed. In the voluntary act the motor nerves are stimulated by impulses from the higher centers.

The Function of the Skin.

The skin serves a double function, that of protecting the body from the outside environment, and that of excreting essential

fluids from its glands. Contrary to general belief, the glands of the skin do not excrete the waste substances of the body, or at least do so only to a very limited degree. Their functions are: to regulate the internal heat of the body (sweat glands); to lubricate its surface and hairs (sebaceous glands); and to provide the best form of nourishment for the newborn animal (mammary glands).

The Sweat Glands.—These are simple coiled tubular structures, found practically everywhere in the cutaneous tissue of the body, being especially numerous in certain parts, as in the palms of the hands and the soles of the feet. The excreting cells line the lower portions of the tubules, and are composed of granular, columnar epithelium. The glands are richly supplied with nerve fibers.

The amount of sweat given off in a day varies greatly, since it is influenced by many things, as heat, moisture, exercise, clothing, etc. (see p. 135). The perspiration of which we are unconscious amounts to a considerable number of grams (700 to 900 grams) in a day. Although it is very difficult to obtain pure sweat unmixed with the secretions of the other glands of the skin, we know that it consists for the most part of water, having a specific gravity of about 1.004. The salty taste is due to inorganic salts and to the impurities which the sweat dissolves on the surface of the skin. There is only a trace of urea and related substances, and probably the sweat glands never aid the kidneys in the excretion of these bodies.

The most important function of the sweat glands is to control the temperature of the body by regulating the rate of its heat loss. Dry air is a poor conductor of heat, and to vaporize water requires a large amount of heat. As the water of the sweat is evaporated, the body loses heat rapidly. This principle is practically applied by the housewives of tropical countries. The water is placed in porous pots and the rapid evaporation on the outside of the pot cools the water within.

The secretion of sweat, like the secretion of saliva, is under the control of the central nervous system, as can be demonstrated by electrically exciting the nerves supplying the paw of a cat or

dog. Following such stimulation drops of sweat are found on the paw. The secretion is not due to an increased blood flow, as can be shown by stimulating the nerves in a limb severed from its blood supply, in which case a few drops of sweat will still appear. A center in the brain and subsidiary centers in the spinal cord have been found which, when stimulated, produce a secretion of sweat.

Some drugs have the peculiar action of exciting the secretion of sweat, either reflexly through the nerve center or by stimulation of the nerve endings about the cells of the glands. To the former class belong such drugs as strychnine and picrotoxin, and to the latter, pilocarpin. Atropin, on the other hand, inhibits the secretion by paralyzing the secretory nerve mechanism. An increase in the external temperature will cause a secretion of sweat only when the sensory and motor nerves of the part are both functional. To stimulate the sweat nerves, heat therefore must act reflexly through the sensory nerves and the centers of the brain or spinal cord.

THE SEBACEOUS GLANDS.—Besides the sweat glands there are numerous other glands in the skin. These are associated with the hairs, and are called sebaceous glands. They secrete an oily semiliquid material which affords protection to the hair and the skin. Its oily nature prevents the hair from becoming too brittle, and protects the skin from moisture.

THE SECRETION OF MILK.—The mammary glands are modified sebaceous glands which secrete a nutrient fluid, milk. The glands are much better developed in the female than in the male, and are excited to physiological activity at the birth of a child. Human milk is a white or yellowish fluid, without odor and with a peculiar sweet taste. It contains protein substances called caseinogen, lact-albumin, and lact-globulin; also a sugar called lactose or milk sugar, and fats and inorganic matter, as the chlorides of sodium, potassium and calcium. Human milk is by far the best food for the infant, and should be replaced by other food only when absolutely necessary.

CHAPTER XXV.

THE NERVOUS SYSTEM.

The General Functions and Structure of the Nervous System.

—When a unicellular organism, such as the amœba, is stimulated it responds by a movement because its protoplasm possesses among its other properties those of excitability, conductivity and contractility. In the case of multicellular organisms, some cells are set aside for the assimilation of food, others for movement, others to receive stimuli from the outside, others to compose tougher protective tissues on the surface, and still others, in many animals, to compose definite organs of offense. This location of specific functions in a certain group of cells makes it necessary, for the welfare of the organism as a whole, that some means of communication be provided between the different parts of the animal, for otherwise the cells which are occupied, say, in absorbing food, would be unable to move away when some destructive agency approached them, and indeed the moving (muscle) cells could never know when they ought to become active. In some of the lower organisms these messages are carried by chemical substances present in the fluids that bathe the cells. These belong to the group of hormones which we have already studied in connection with the ductless glands (see p. 124). The responses mediated in this way are, however, too slow for the quick adaptation which it is necessary that the organism should undergo in its battle for life. If it had to depend on such a mechanism alone, the organism would already be within the clutches of its enemy before it could make any attempt to defend itself.

Some more sensitive mechanism, both for receiving and for transmitting impulses throughout the organism, becomes necessary. This is furnished by the nervous system, which, in its simpler form, consists of a cell on the surface of the animal so specialized that it responds to changes in the environment. This

receptor cell, as it is called, is prolonged inside the animal as a fiber, the *nerve fiber*, which passes to *effector cells* specialized either as muscle fibers or gland cells. When a stimulus acts on the receptor cell it therefore sets up a nerve impulse which causes effector cells to become active, so that the animal either moves away or prepares to defend itself by secreting some poisonous substance or making some defensive movement. There are, however, very few, even of the lowliest organisms, which have so simple a nervous system as this, for the nerve fibers from different receptors usually join together to form a *nerve plexus* and they do not run directly to the effector cell, but to another cell,

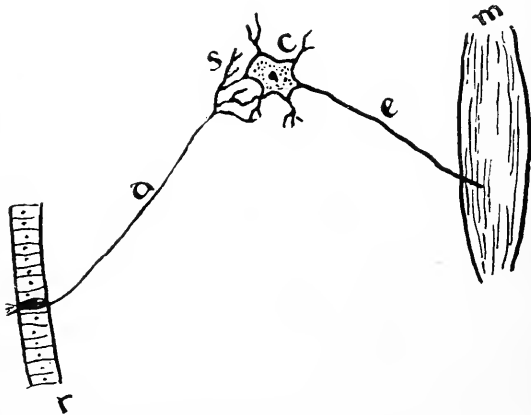


Fig. 39.—Schema of simple reflex arc; *r*, receptor in an epithelial membrane; *a*, afferent fiber; *s*, synapsis; *c*, nerve cell of center; *e*, efferent fiber; *m*, effector organ.

the *central nerve cell*, which is specialized as a junctional or distributing center, and which then transmits the impulse by a fiber of its own to the proper effector organs.

Thus we have the essential elements of the so-called *reflex arc* (Fig. 39), that is, a receptor connected with a nerve fiber called *afferent*, running to a central nerve cell which is again connected with a nerve fiber called *efferent*, which passes to some effector organ. In certain of the lower organisms these nerves and nerve cells are continuous throughout, but in the higher animals the fibers originating from each cell do not actually join with those

of others, but only come in close contact with them. They are contiguous but not continuous, and the nerve impulses pass from one to another by contact rather than by transmission through continuous tissue.

Every nerve cell gives off at least one process called the axon, and it is this which forms the axis cylinder of the nerve fiber. There are usually other processes, but they differ from the axon in that they branch freely and do not run for any distance from the cell. They are called *dendrites*. The axon may also occasionally give off a branch, often called a *collateral*, but it is not until it has reached the effector organ or some other nerve cell that the branching is pronounced. It now breaks up into a mass of fine branches. When these occur at a second nerve cell, they closely encircle the cell, forming a basket-like structure around it. This is called a *synapsis*. The nerve impulse can travel from the fiber through its synapsis on to the nerve cell which this surrounds, but it cannot travel in the opposite direction. This valve-like action at the synapsis explains why a nerve impulse travels along a reflex arc in one direction only. Each nerve cell with its axon and dendrites is called a *neurone*. Reflex arcs are therefore composed of two or more neurones, and the nervous system is built up of great numbers of reflex arcs.

The nerve cells which constitute the centers are usually collected in groups called *ganglia*. In the segmented invertebrates, such as the worms and crustaceans, there is one such ganglion for each segment, each ganglion being connected with its neighbors by nerve fibers, thus forming a chain along the ventral aspect of the animal, and also having numerous nerve fibers connecting it with the various receptors and effectors of the segment (Fig. 40). At the head end of the animal several of these ganglia become fused together to form a larger ganglion, which lies just behind the gullet and from which two fibers pass around the gullet to unite in front of it in a large ganglion, which usually shows three lobes. These larger head ganglia receive the afferent nerve fibers from the adjacent projicient sense organs, namely, the eyes, the ears, the organ of smell, and the antennæ or feelers; these being really receptors which have become

highly specialized for the purpose of receiving impressions from a distance. Many of the efferent fibers which arise from the cells of the head ganglia go to the muscles which move the head end of the animal, others, however, do not run directly to effectors, but they run down the nerve chain to make synaptic connection with the cells of some of the segmental ganglia. This connection of the cells of the head ganglia with those supplying the segments enables the former to exercise a dominating influence over the activities of the latter, the purpose being that approaching dangers may have a greater influence in determining the response of the animal than stimuli that are merely local. When, for example some sight or sound of an approaching enemy is received by the head ganglia, these will transmit impulses down the ganglion chain which so influence the various nerve cells as to produce, in all of them, a co-ordinated action for the purpose of getting the animal out of danger. Even should some local stimulus be acting on one or more of the segments, the stimulus which is received through the head ganglia will obtain the upper hand and annul or inhibit the local influence. The part will become subservient to the whole. This illustrates the *integration of the nervous system*, which, as we pass to higher animals, we shall find to become more and more developed and intricate.

So far, however, the nervous reaction is purely of the nature of a reflex; but in the higher animals other factors, namely, *memory* and *volition*, come to exercise a dominating influence on the nature of the response. The



Fig. 40. — Diagram of nervous system of segmented invertebrate; *a*, supraesophageal ganglion; *b*, suboesophageal ganglion; *oe*, oesophagus or gullet.

afferent stimulus arriving, let us suppose at nerve cells controlling the movements of the leg, may fail to cause a response of the corresponding muscles because of impulses meanwhile transmitted from higher memory centers, for the animal may have learned by experience that such a movement as the local stimulus would in itself call forth, is hurtful to its own best interests. This experience will have become stored away as a memory in the higher (memory) nerve centers, so that whenever the local stimulus comes to be repeated, impulses are discharged from these memory centers to the local nerve center and the reflex response does not occur, or is much modified in nature. For storing away these memories and for related psychological processes of volition, etc., the anterior portions of the nervous system in the vertebrates become very highly developed so as to constitute *the brain*, and the simple chain of ganglia of the invertebrates comes to be replaced by the *spinal cord*.

As we ascend the scale of the vertebrates, the brain becomes more and more developed, until in the higher mammalia, such as man, very few reflex actions can occur independently of the higher centers which are located in it. In other words, the reflex are now involves, not one nerve center, but several, and of these the most important are located in the brain.

CHAPTER XXVI.

THE NERVOUS SYSTEM (Cont'd).

Reflex Action.

The Nerve Structure Involved in the Reflexes of the Higher Mammals.—In general, as already mentioned, these include a receptor, an afferent fiber, a nerve center, an efferent fiber and an effector organ.

THE RECEPTOR.—The receptor exists as one of the sensory nerve terminators situated in the skin (extero-receptors) or in the deep tissues, such as the joints, the muscles or the viscera (proprio-receptors). Many receptors are highly specialized so as to respond only to one kind of stimulus, and each special kind of receptor is located where it will be of most use. Thus, there are special receptors for sensations of heat, others for cold, others for touch, others for pain. The *pain receptors* are distributed more or less uniformly over the body. They are present in the deeper structures, such as the teeth, the joints and the serous coverings of the viscera. Sometimes, as on the cornea and in the pulp of the teeth, they are the only kind of receptor present. The *touch receptors* are collected in small areas called "touch spots," which are much more numerous on the tip of the tongue, the lips, or the tips of the fingers than on the skin of the legs, the arms or the back of the trunk. The frequency of touch spots on the tip of the tongue makes a foreign body in the mouth appear to be larger than when we feel it with the fingers. The touch spots on the finger tips may acquire great acuity of perception by education, as in the case of a blind person, who has to use his fingers for reading. The remarkable irregularity of distribution of touch spots may be very beautifully shown by finding out how far apart the points of a pair of calipers must be from each other in order to be distinguished as separate. This distance is not more than 3 mm. for the tips of the fingers,

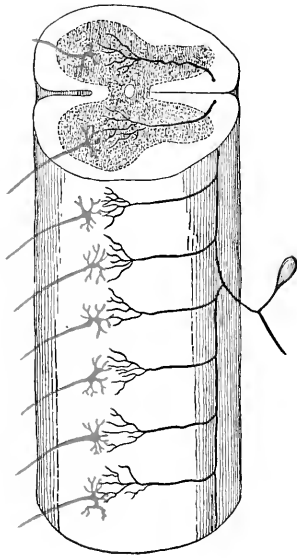


Fig. 41.—The simplest reflex arc in the spinal cord. (After Kölliker.) The afferent fiber in the posterior root (in black) gives off collaterals, which end by synapses around the cells of the anterior horn (in red), the axons of which form the efferent fibers of the anterior roots. (From Howell's Physiology.)

but it is over 60 mm. for the skin of the back of the neck. The *temperature receptors* are still more definitely located in areas, some being specialized for heat and others for cold. These so-called heat and cold spots are most frequent on the portions of the body that are covered by clothing, for example, the skin of the thorax, than on those that are exposed, for example, the face. They are fairly frequent on the skin of the dorsum of the hand, where their existence can be very easily demonstrated by slowly drawing a pencil gently over the skin. At certain places the point of the pencil feels hot, at others cold, and in others it causes no temperature sensation whatsoever.

All varieties of receptors are present on the skin of the hand, but in certain diseases of the nerves or spinal cord, one kind of receptor may become inactive, thus causing, when the absent sensation is that of pain, the condition called *analgesia*, which must be distinguished from that of *anesthesia*, when all sensations are paralyzed. In analgesia a pin prick causes only a sensation of touch. When the nerves of the arm are cut and the cut ends then sutured together so that the nerve fibers regenerate, the skin sensations do not all return at the same time. Those of pain and of extreme degrees of heat and cold return in from six to twenty-six weeks, whereas those of touch and the finer degrees of temperature do not return until after one or two years. The power of localizing the point of application of the stimulus is also late in returning; thus, if we touch the finger of such a person and ask him to tell us where, he may indicate some spot that is quite a distance away from the one actually touched. Certain drugs, such as cocaine, have the power, when applied locally, of rendering all the receptors insensitive.

THE AFFERENT FIBER.—Another name for this is the sensory nerve, because it carries the sensations received by the receptors up to the nerve center. All afferent fibers enter the spinal cord by the *posterior nerve roots*, on each of which, it will be remembered, is situated a ganglion, the posterior root ganglion. The cells of this ganglion are connected with the afferent fibers by a short branch running at right angles to the latter (Fig. 41). The function of the cells is to maintain the nutrition of the affer-

ent fibers, for if these be divided before they reach the ganglion, the peripheral or far away end undergoes degeneration, whereas if the cut be made between the ganglion and the cord, degeneration occurs central-wards, that is, towards and into the cord. This degeneration always occurs in the portion of the nerve fiber which has been disconnected from the nerve cell. It therefore furnishes us with a ready method for finding out whether the fiber is running towards or away from the brain. In the former case, the fiber is said to be ascending, and it degenerates above the section; in the latter case, it is descending and it degenerates below the section. Since degenerated nerve fibers give characteristic staining reactions, we are thus furnished with a means of finding out what becomes of the afferent fibers after they enter the cord.

To further trace the course and connections of the afferent fibers in the cord, we must therefore cut the posterior roots between the ganglion and spinal cord and after a few weeks kill the animal and make microscopic examination of the cord, stained in special ways. If we take a series of such sections above the level at which the posterior roots have been cut, we shall find that opposite the point of entry of the cut root, the degenerated fibers occupy an area near the tip of the posterior horn of grey matter. As we examine sections taken higher and higher up, the degenerated area will be found to shift gradually towards the median fissure, occupying, first of all, the so-called posterolateral column, and later the postero-median (Fig. 42). When we get to the *medulla oblongata* or "bulb," the degenerated areas disappear because the fibers have terminated by forming synapses around the cells of the two large ganglia which form the bulgings seen on the posterior aspect of this structure. The fresh relay of nerve fibers do not degenerate after section of the posterior roots, but by other means of investigation they have been found to become collected into a bundle called the *fillet*, which crosses, or decussates, to the other side of the medulla and runs up through the *pons varolii* and *crura cerebri*, some of the fibers ending near the *optic thalamus*, whilst others run on to the grey matter of the motor areas of the cerebrum.

The posterior root fiber, shortly after entering the cord, gives off a branch at right angles (called a collateral), or in its course up the cord it may give off several collaterals, their destination being the grey matter of the cord, in which they terminate by

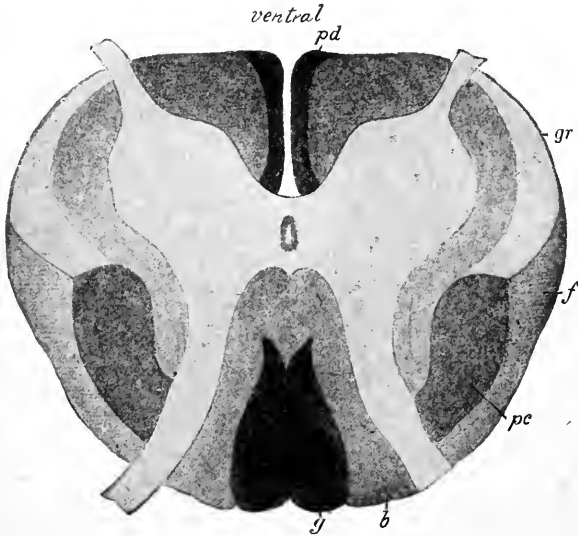


Fig. 42.—Diagram of section of spinal cord, showing tracts. (After Kölliker); *j*, posterior median, and *b*, postero-lateral columns; *p.c.*, crossed pyramidal, and *p.d.*, direct pyramidal tracts; *f*, cerebellar tract. (After Howell.)

synapses around nerve cells. Certain of these may be cells of the anterior horn. These cells give rise to the efferent fibers, which leave the spinal cord by the anterior or motor roots (see Fig. 41). Other collaterals run to intermediary cells, which then communicate with the anterior horn cells (Fig. 43).

THE NERVE CENTER AND INTERMEDIARY NEURONES.—When the entering nerve impulse travels by a collateral to an anterior horn cell, we have the simplest type of reflex action, namely, one involving a receptor, a sensory nerve fiber, the posterior root, a collateral, the anterior horn cell, the anterior root, a motor nerve fiber and an effector organ. But such a simple reflex seldom

occurs in the higher animals. The afferent impulse when it enters the cord is more likely to travel up the posterior columns and then, as already outlined, to the cerebrum, where it is transmitted to the large pyramidal nerve cells of the grey matter.

From the pyramidal cells spring the fibers of the *pyramidal tracts*, which, as they pass downward through the white matter of the cerebrum, crowd closer and closer together until, by the time the basal ganglia are reached (optic thalamus on the inside, and corpus striatum on the outside), they form a narrow bundle which occupies the middle portion of the strip of white matter, which lies between these ganglia. This white matter is called the *internal capsule* (Fig. 46), and it is of very great clinical interest because, being in the neighborhood of a large artery (branch of middle cerebral), which sometimes bursts in elderly people, it is apt to become torn up by extravasated blood, thus destroying the pyramidal fibers and causing paralysis. This is what occurs in *apoplexy*. Below the internal capsule the fibers run into the *crura cerebri*, then into the pons, thence into the medulla oblongata, in the front of which they form a distinct bulging called *the pyramid*; hence their name pyramidal fibers (see Fig. 45).

In the lower portion of the medulla, a most interesting thing occurs, namely, three-fourths of the fibers cross to the opposite side, thus constituting the *decussation of the pyramids* (Fig. 44). These crossed fibers run down in the lateral columns of the spinal cord as the crossed pyramidal tracts. The pyramidal fibers which do not cross in the medulla form the direct pyramidal tracts of the cord, and they gradually cross in the cord itself. The pyramidal fibers end by synapsis around the cells of the anterior horn, so that all fibers from the cerebrum ultimately cross to the opposite side before they reach the anterior horn cells, for which reason it happens that a lesion involving the pyramidal tract anywhere above the decussation, such as a hæmorrhage in the internal capsule above referred to, always causes paralysis of the *opposite side* of the body (hemiplegia).

These facts regarding the course of the pyramidal fibers have been ascertained by microscopic examination of sections from

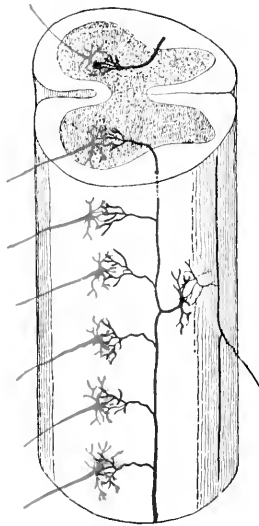


Fig. 43.—Reflex arc through the spinal cord, in which an intermediary neurone (in blue) exists between the afferent and efferent neurones. (From Howell's Physiology.)

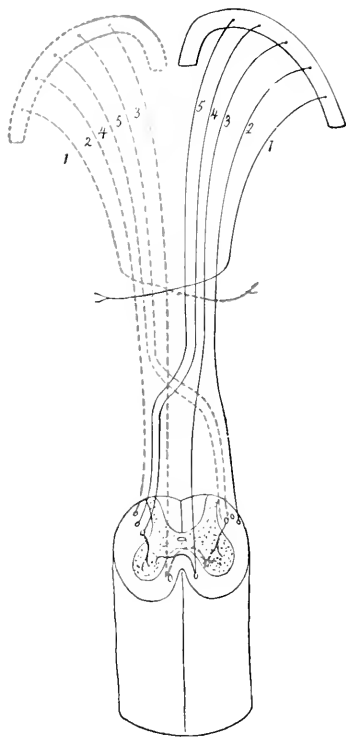


Fig. 44.—Course of the pyramidal fibers from the cerebral cortex to the spinal cord: 1, fibers to nuclei of cranial nerves; 3, fibers which do not cross in the medulla (direct pyramidal tract); 4 and 5, fibers which cross in medulla (crossed pyramidal tract). (After Howell.)

various levels of the spinal cord some time after destruction of the Rolandic area of the cerebrum (see p. 270). The pyramidal fibers are degenerated and they occupy the areas indicated in Fig. 42. Since the degeneration occurs below the destruction, it is called descending degeneration, in contradistinction to ascending degeneration, which we saw to follow section of the posterior roots between their ganglia and the cord (see p. 246).

To sum up, the sensory impulse on entering the spinal cord by the posterior root, by traversing a collateral, may take the shortest possible pathway to the efferent nerve cell of the anterior horn, or it may avoid this and travel up the posterior columns of the cord to the medulla, thence by the fillet to the cerebral cortex of the opposite side, and thence down the pyramidal tracts to the anterior horn cells. In this long cerebral route there are at least three places where the impulse must pass by means of a synapsis from nerve fibers on to nerve cells, and then along the nerve fibers arising from these. These three places are: (1) in the medulla, (2) in the cerebral cortex, (3) in the anterior horn.

This long cerebral route, as it is called, is by no means the only one along which afferent impulses may travel to the brain. Some may be carried by collaterals to certain cells of the grey matter of the cord, and from these cells fibers may run up the cord to the cerebellum or lesser brain. These *cerebellar tracts* are located in the lateral columns of the cord outside the crossed pyramidal tracts (see Fig. 42). They do not degenerate when the posterior roots are cut, but do so after section of the cord itself (this distinguishing them from the fibers in the posterior columns). The impulses which they transmit to the cerebellum have to do with certain subconscious sensations concerned in the maintenance of the tone of the muscles. There are also certain pathways in the white matter of the cord which transmit descending impulses from the cerebellum.

The main bundles of ascending and descending fibers in the spinal cord are charted in Fig. 42, which should be carefully studied.

THE EFFERENT FIBER, OR NEURONE.—As already explained

the cell of this neurone is located in the anterior horn of grey matter of the cord. These anterior horn cells are distinguished from the other nerve cells of the grey matter by their large size and angular shape, and they become greatly increased in number in the portions of the cord from which the nerves going to the extremities originate. The fibers springing from them pass out in the anterior roots. If the cells are destroyed or the anterior roots cut, degeneration occurs below the lesion, and paralysis of the effector organs (muscles) to which they run results, but this paralysis is very slight in degree unless the lesion affects several roots, or the cells of several adjacent levels of the cord. The reason for this is that the nerve cells of one level of the cord only partially supply a given muscle or group of muscles with nerve fibers, thus showing that even the small muscles receive their nerve fibers from several adjacent levels of the cord. The anterior horn cells sometimes become destroyed by disease, namely, in infantile paralysis (poliomyelitis anterior). The resulting paralysis is never recovered from.

Types of Reflexes.—Having traced the paths through which reflexes occur in the higher animals, we may now proceed to consider certain typical forms of reflex action and the conditions which may cause them to become altered. We must first of all confine our attention to the characteristic reflexes of the so-called *spinal animal*, for it is only after we have done so that it will be possible for us to determine what influence the brain has in modifying the spinal reflexes. The spinal animal (dog, for example) is prepared by cutting across the spinal cord somewhere below the origin of the phrenic nerves. After the immediate effects of the operation have been recovered from, the regions of the animal's body lying below the level of the section of the cord, suffer from a condition called *spinal shock*. All reflex movements are absent, the sphincters are paralyzed so that incontinence of urine and feces exists, and various "trophic" or nutritive changes occur in the skin (abscesses form, hair falls out, etc.). After some time, the length of which depends on the position of the animal in the animal scale, the sphincters regain their tone and the reflexes gradually reappear

in the paralyzed region, the first to do so being the protective reflexes, of which the *flexion reflex* is the type.

The flexion reflex is elicited by any stimulus which would cause pain in an animal capable of feeling. Such stimuli are called nocuous and the reflex response is always of such a nature—usually flexion—as to cause the injured part to be removed from further damage. The return of the flexion reflex is soon followed by that of the *knee jerk*, which is elicited by tapping the patellar tendon after putting it on the stretch by passively bending the knee joint. Somewhat later in many animals (e.g., dog) the *scratch reflex* appears, so-called because it consists of a scratching movement of the hind leg in response to mechanical irritation of the flank of the animal. It is a reflex of very great interest because it illustrates to what a remarkable degree the spinal cord, unaided by the brain, is capable of bringing about complicated and purposeful co-ordinated movement. Later still, in the lower animals, practically all the reflex movements which a normal animal exhibits may reappear.

When the cord becomes severed in man, as by spinal fracture, spinal shock is extremely profound, and in order to keep the patient alive great care must be taken, on account of the incontinence of urine, to prevent infection of the bladder and kidneys and to protect the skin from ulceration (bed sores). Even in such cases, however, many of the reflexes recover in the paralyzed regions, but the recovery is slow and the limbs invariably atrophy. It is particularly important to note that the time of reappearance of the reflexes bears a relationship to the degree of development of the cerebral hemispheres, thus rendering it evident that spinal shock is due to a break in the nerve paths which lead to and from the brain. The higher the animal, the more frequently do all reflex acts involve a cerebral path instead of taking the short cuts available through the collaterals (see p. 243). From usage, as it were, the cerebral paths become so well developed that when they are suddenly severed, the reflex action becomes impossible until the entering afferent impulse has learned to use the hitherto unused short cuts available through collaterals. When completely recovered from spinal shock, an

animal, say a dog, in so far as voluntary movement is concerned, is entirely paralyzed in all portions of the body below the level of the section of the cord. It cannot voluntarily move the affected parts, it cannot walk, it feels no pain or any other sensation below the lesion, and yet when appropriately stimulated, the paralyzed limbs may reflexly undergo various, often very complicated movements.

The Essential Characteristics of Reflex Action.—As studied on a perfectly recovered spinal dog these are as follows:

1. For a certain interval after applying the stimulus there is no response, the duration of this "latent period" depending partly on the nature of the reflex (short in the protective reflexes, long in the scratch reflex) and partly on the strength of the stimulus.

2. The response may persist for some time after the stimulus is removed (after response).

3. The degree of the response is roughly proportional to the strength of the stimulus, except in certain of the protective reflexes, such as the conjunctival, which consists in the closing of the eyelids when anything touches the eye.

4. The response is often rhythmical in character, even though the stimulus be continuously applied. This is well seen in the scratch reflex.

5. There are certain ways, apart from an alteration in the stimulus, by which we may cause a reflex movement to become increased or decreased. Thus, taking the flexion reflex as an example, the flexion may be *diminished*: (1) By stimulating some other reflex movement which involves the same muscles, but which is antagonistic to flexion, e.g., by stimulating the opposite limb and causing the so-called crossed extension reflex. (2) By causing strong afferent impulses to pass through other levels of the spinal cord, e. g., pinching the tail. A similar "*interference*" is well illustrated in the case of man by stimulating the fifth nerve by firm pressure on the upper lip at a time when there is an inclination to sneeze. The sneezing, which is a reflex due to irritation of the mucosa of the nose, can usually be prevented. Expressing this phenomenon of reflex interfer-

ence in popular language, we may say that when the attention of a segment of the cord, or its extension in the brain is taken up by some other stimulus, a reflex already in action, or about to act, is depressed. Pain, such for example as toothache, may likewise be lessened by applying counter-irritation such as a blister to some neighboring skin area. (3) By means of certain drugs known as anesthetics, which depress the excitability of the nerve cells. (4) By fatigue.

The reflex movement may be *increased*: (1) by applying a second stimulus to some other area of skin of the same hind leg or by applying electrical stimulation to the central end of one of its sensory nerves; (2) by raising the excitability of the nerve centers by certain drugs, such as strychnin ; (3) by first of all causing the movement to disappear, though the stimulation causing it is maintained, by exciting some other part of the body (see above). When the reflex reappears it is much more pronounced than formerly.

Muscular Tone and Reciprocal Action of Muscles.—Having learned some of the general characteristics of the reflex movements, we may now proceed to inquire into the method by which the spinal cord is enabled, by itself, so to direct the afferent impulses which enter it, that the nerve cells of the anterior horn discharge suitable impulses to bring about such complicated movements as have just been described. When a motor nerve or an anterior spinal root is stimulated, the muscles which contract are not grouped in such a way as to cause any purposeful or co-ordinated movement. Contractors, extensors, adductors and abductors are quite likely all to contract at once and by thus opposing one another to effect no definite movement. When such stimulation is extensive (e.g., involves a considerable number of motor fibers), it is common to find that the extensor muscles predominate over the others, so that the limb becomes extended. Such is the case when some poisonous substance causes irritation of the nerve centers in the spinal cord.

To cause a co-ordinated movement it is necessary that one group of muscles should become relaxed whilst their antagonistic group is undergoing contraction. Now, it might at first sight be

imagined that this relaxation is merely a passive act, that is to say, that the uncontracting group of muscles do nothing more than remain quiescent and permit themselves to be stretched. But such is not the case; on the contrary, they become actively extended. This they are enabled to do because of the fact that, even when apparently relaxed, a muscle is really not so, but exists in a condition called *tone*, that is, in a slightly contracted state. This tone becomes greatly diminished during sleep, and it can be caused almost to disappear by deep anesthesia. It is for this purpose, as well as to abolish pain, that anesthetics are administered before attempting to reduce a dislocation.

Tone is maintained by the nerve cells of the anterior horn of the spinal cord. When therefore an afferent impulse brings about flexion at the knee joint, it does so by exercising two diametrically opposite influences on the anterior horn cells: it stimulates those which preside over the flexor muscles and *depresses* the tonic influence of those supplying the extensors. This tone-depressing action recalls the inhibitory influence which the vagus nerve exercises over the heart beat (see p. 185), and since it always occurs along with a contraction of antagonistic muscles it is called *reciprocal inhibition*. Certain poisons, particularly strychnine and tetanus toxin, cause this reciprocal action to break down so that all the muscles around a joint contract at the same time and produce an extension. Tetanus toxin is the poison produced by the tetanus bacillus, and its interference with the reciprocal inhibition of the muscles of the lower jaw causes lockjaw.

Symptoms Due to Lesions Affecting the Reflexes.—From what we have learned regarding the functions of the spinal cord, it is easy for us to explain the following symptoms and conditions resulting from pathological destruction or stimulation of various parts of it:

1. In destruction of the continuity of the afferent or efferent fibers of the reflex arc, the reflexes are absent. This occurs in chronic inflammation of the nerves (neuritis) and in the disease called *locomotor ataxia*, in which the lesion consists of a destructive pathological process involving the posterior columns

of the spinal cord. One of the first symptoms of locomotor ataxia is absence of the knee jerk, which, it will be remembered, is elicited by tapping the patellar tendon after putting it passively on the stretch, either by sitting with the feet swinging on the edge of a table, or by crossing one knee over the other. Pains, called crises, are also usual in various parts of the body. Later symptoms are inability to stand without falling when the eyes are shut, inco-ordinated walking, in which the foot is lifted too high and is brought down to the ground again too violently, loss of sensation of the skin of the foot and leg, and changes in the pupillary reflexes of the eye (see p. 284). The joints also become swollen and the articular surfaces roughened so that a grating sensation is experienced when the joint is bent (Charcot's joint). The condition gradually gets worse, so that the patient becomes bedridden. Death is usually due to complications.

2. Destruction of the anterior horn cells not only causes absence of reflex action, but is followed by marked atrophy of the affected muscles. It has been supposed that this points to a so-called trophic influence of these nerve cells, that is to say, a power of influencing nutrition. Such changes occur in infantile paralysis (poliomyelitis anterior).

3. Stimulation of the above fibers may cause exaggeration of the reflexes, as in the earlier irritative stages of neuritis, in tumors pressing on the nerve roots, or when the membranes of the cord become inflamed, as in meningitis.

4. Removal of impulses coming from the cerebrum by way of the pyramidal tracts causes exaggerated reflexes. Such occur in paralysis of both sides of the body in paraplegia, and on the paralyzed side in hemiplegia.

In a paraplegic patient the weakest stimulus applied to the skin of the paralyzed portion of the body will call forth a widespread and much exaggerated reflex contraction.

CHAPTER XXVII.

THE NERVOUS SYSTEM (Cont'd).

The Brain Stem and the Cranial Nerves.

The Brain Stem.—The medulla, the pons Varolii, and the mid-brain (Figs. 45 and 46), compose the brain stem, which is really an upward extension of the grey matter, and of certain of the columns of the spinal cord, into the base of the brain with special nerve centers and especially large bundles of inter-connecting nerve fibers superadded. It is because of the crossing in various directions of these bundles of fibers that the structure of the medulla, pons and mesencephalon is so difficult to understand. The grey matter, as in the spinal cord, lies deep and the fibers are superficial. Of the latter, the pyramids and fillet, already described, are the most important, and their direction is longitudinal. The most prominent of the connecting or commissural nerve bundles are the upper, middle and lower *peduncles of the cerebellum*, or small brain, which, it will be remembered, lies over and at the side of the pons varolii and midbrain. The lower peduncles spring from the medulla and connect the spinal cord with the cerebellum. They form the lower edges of the fourth ventricle. The middle peduncles enter the sides of the pons, in which they cross at right angles with the pyramidal fibers (p. 248). They connect the cerebellum of one side with the cerebrum of the opposite side. The superior peduncles join the encephalon just under the posterior corpora quadrigemina, and the fibers composing them decussate to the other side to become connected with certain of the so-called basal ganglia.

The *basal ganglia* are the optic thalamus and the corpora striata, two large collections of nerve cells protruding into the third and lateral ventricles of the brain and having the internal capsule between them (see p. 248). The nerve cells composing these ganglia receive impulses from nerve fibers arriving at them both

from below (coming from the spinal cord) or from above (coming from the cerebrum). They then transmit these impulses along their own nerve fibers, which may run to various other

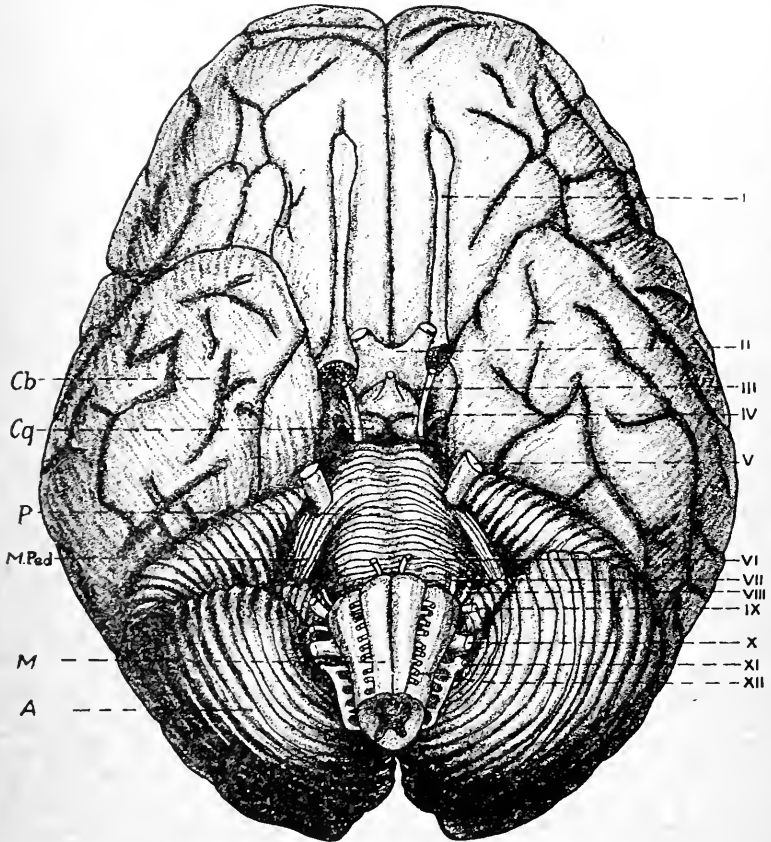


Fig. 45.—Under aspect of human brain. In the center line from below upwards are seen a section of the upper end of the spinal cord, and the medulla oblongata (*m*), with certain of the cranial nerves (as numbered). In front of this is the pons (*p*), with the large fifth nerve arising from it, and the middle peduncles of the cerebellum (*M. Ped*) running into the cerebellum (*A*). The rounder bodies anterior to the pons are the corpora quadrigemina (*Cq*), at the sides of which are the crura cerebri and the origins of the third and fourth nerves. The optic and olfactory nerves are in front. The under surfaces of the cerebrum (*Cb*) and cerebellum (*A*) constitute the remainder of the drawing. (From a preparation by P. M. Spurney.)

parts of the brain. The optic thalamus, as its name signifies, is intimately associated with the optic nerves.

Another important collection of nerve cells occurs in the *corpora quadrigemina*. These exist as four rounded swellings, two on either side, just where the superior peduncles of the cerebellum come together. Their nerve cells serve as distributing centers for visual and auditory impulses, carried to them through tracts of nerve fibers connected with the optic and auditory

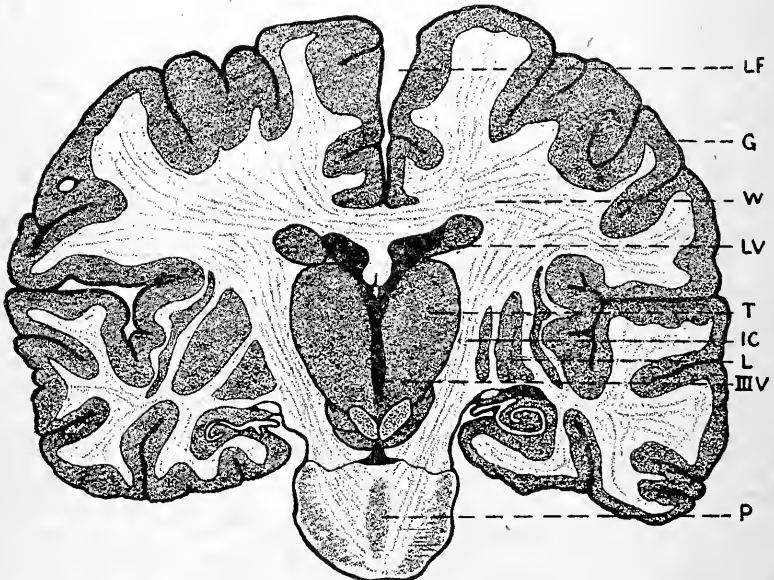


Fig. 46.—Vertical transverse section of human brain. Below is a section of the pons (*P*) showing the fibers which connect the brain stem and cerebrum radiating up through the internal capsule (*IC*), which is bounded mesially by the optic thalamus (*T*), and laterally by the corpus striatum (*L*). The third (*III-V*) and lateral ventricles (*LV*) of the brain are seen in the center (black). The thickness of the grey matter and the infolding of the surfaces, as convolutions, should be noted. (From a preparation by P. M. Spurney.)

nerves. The corpora quadrigemina are usually more developed in the brain of the lower animals than in that of man.

The Cranial Nerves.—On account of the introduction of the new structures described above there is no regularity in the

arrangement of the grey matter in the brain stem as there is in the cord. Instead of forming horns, the grey matter is scattered in colonies or nuclei, many of which are centers for the fibers of the cranial nerves. Some of these fibers are, of course, afferent and some efferent. Since many of the cranial nerves are connected with the nose, mouth and teeth, it is important for us to learn something concerning the location of their centers and the general function of the nerves. There are twelve pairs of cranial nerves, and the last ten of these originate from the grey matter of the medulla, pons or midbrain. The following list indicates the general functions of the nerves:

1. Olfactory.	nerve of smell.	arises from fore-brain.
2. Optic.	nerve of sight.	arises from fore-brain.
3. Oculo motor.	} nerves to the muscles of the eyeball.	arise from midbrain.
4. Trochlear.		
6. Abducens.		
5. Trigeminal.	sensory nerve of face.	arises mainly in pons.
7. Facial.	main motor nerve of face muscles.	arises in pons and medulla.
8. Auditory.	nerve of hearing and of semicircular canals.	arises in pons.
9. Glosso-pharyngeal.	motor nerve of pharynx, sensory nerve of taste.	arises mainly in medulla.
10. Vagus.	efferent and afferent nerve to various viscera.	arises in medulla.
11. Spinal accessory.	mainly blends with vagus	arises with vagus except spinal portion, which extends down into spinal cord.
12. Hypoglossal.	motor nerve for tongue muscles	arises in medulla.

It is important to note that, like the spinal nerves, many of the cranial nerves are composed of two roots, motor and sensory,

each having its own center. This fact justifies the statement which we have already made that the brain stem is really an upward prolongation of the spinal cord, and just as we saw that each posterior root of the spinal cord is characterized by possessing a ganglion, so also is there a *ganglion in the sensory divisions of the cranial nerves*. This ganglion, however, is often difficult to find. The nerve cells which compose it unite with the fibers of the sensory root by a T-shaped junction, and the fibers terminate by synapsis around the cells of the sensory nuclei. The ganglion of the fifth nerve is the Gasserian. Those for the eighth are the ganglia found in the cochlea and internal auditory meatus (Scarpa's ganglion). The ganglia of the ninth and tenth nerves are situated along the course of the nerves.

The approximate position of the various ganglia will be best learned by consultation of the accompanying diagram (Fig. 47).

In the brain stem there are three *sensory or afferent nuclei*, a long, combined one for the ninth, tenth and eleventh nerves, extending practically from the upper to the lower limits of the medulla, one for the eighth in the center of the pons, and a very long one for the fifth, extending from near the upper limit of the pons down into the spinal cord. The *motor or efferent nuclei* for the third, fourth, sixth and twelfth nerves are composed of cells shaped like those of the anterior horn of the spinal cord. They lie near the middle line and extend throughout the whole length of medulla and pons. The motor nuclei of the fifth, seventh, ninth, tenth and eleventh lie outside the above.

It is important that the following *functions of these nerves* be studied by dental students:

THE THIRD NERVE.—The third nerve controls: (1) the muscles of accommodation inside the eye; (2) all of those which are attached to the outside of the eyeball, except the muscle which moves it out (external rectus), and the one which rotates it down and out (the superior oblique); and (3) the elevator muscle of the eyelids (levator palpebræ). When the third nerve is paralyzed, the symptoms are therefore: (1) drooping of the eyelid (ptosis) so that the chin is tilted upward when the patient looks at anything; (2) inability to see clearly unless when

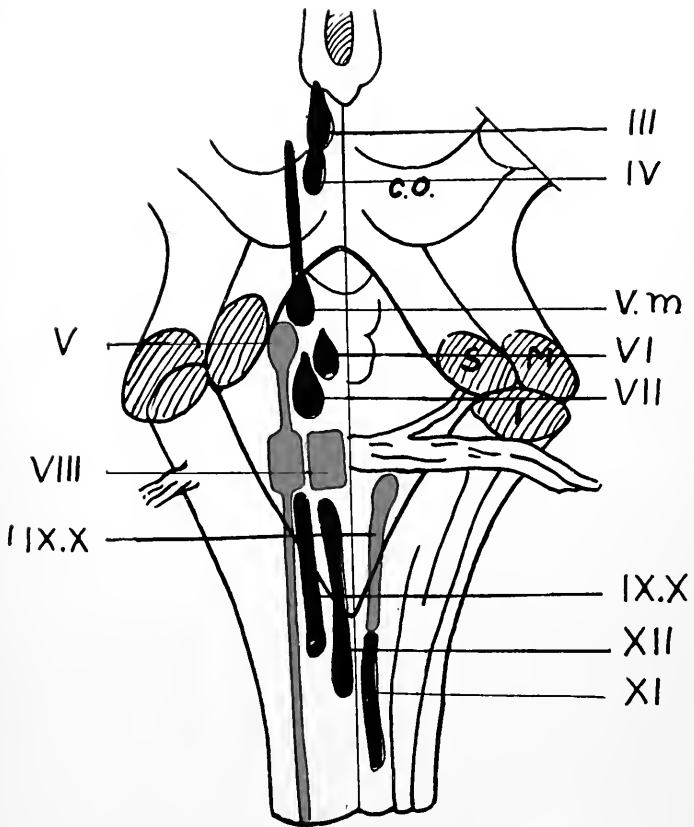


Fig. 47.—Diagram of the dorsal aspect of the medulla and pons showing the floor of the fourth ventricle with the nuclei of origin of the cranial nerves. (After Sherrington.) The sensory nuclei are colored red and are numbered on the left of the diagram, the motor, blue and numbered on the right. The peduncles of the cerebellum—*S.* (superior), *M.* (middle), and *I.* (inferior), are shown cut across. *C.O.*, corpora quadrigemina. The above nuclei are of course present on both sides.

objects are at a distance (long sight); (3) squint of the eye so that it is directed outward and downward.

Such a paralysis of the eye is sometimes accompanied by a partial hemiplegia (see p. 271) of the opposite side of the body, thus indicating that some destructive lesion (hæmorrhage, destructive tumour) exists on one side of the midbrain, so that it involves the nucleus of origin of the third nerve and also the pyramidal fibers lying near. Since the fibers of the third nerve do not cross to the opposite side, but those of the pyramids do (see p. 243), we get a *crossed or alternating paralysis*. Sometimes only one part of the third nerve may be paralyzed, for example, that portion going to the muscles of accommodation.

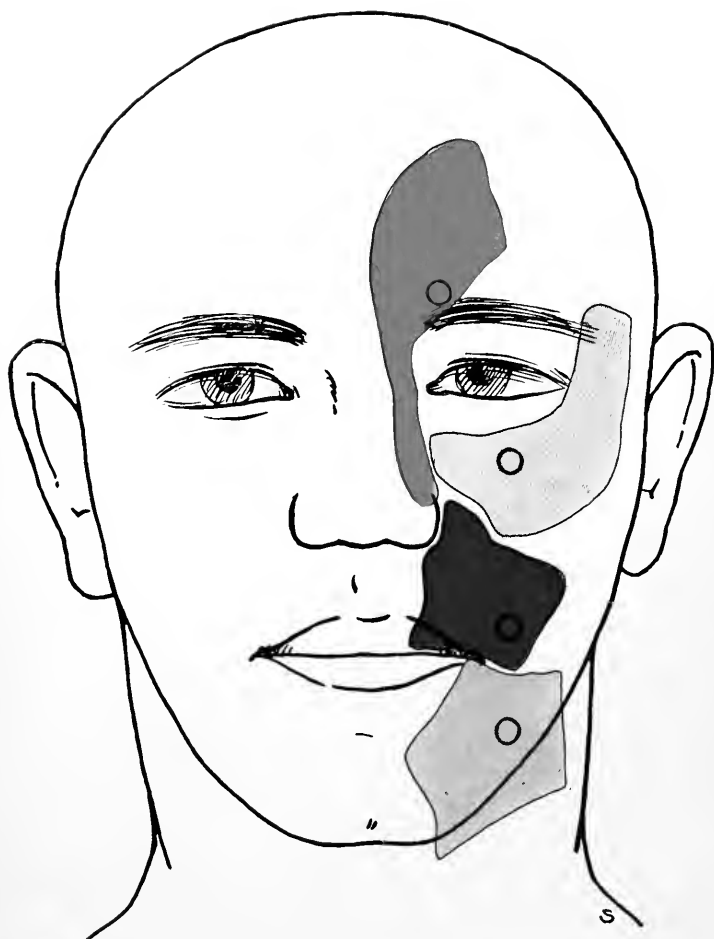
THE FOURTH AND SIXTH NERVES.—The fourth and sixth nerves supply the two extra-ocular muscles not supplied by the third, viz., the superior oblique (fourth) and the external rectus (sixth), respectively.





THE FIFTH NERVE.—The fifth nerve is the largest of the cranial nerves, and is a representative mixed nerve. It supplies the teeth. The *motor branch* runs to the muscles of mastication, the tensor muscle of the palate, the mylohyoid muscle (in the floor of the mouth) and the anterior belly of the digastric. These last two mentioned muscles pull the hyoid bone and therefore the root of the tongue upward and forward during the act of swallowing. Both mastication and swallowing are seriously impaired when this nerve is paralyzed. The *sensory fibers* are connected with the receptors for all the common sensations of the head and face. As already explained, they are connected with the nerve cells of the Gasserian ganglion, which is lodged in a depression near the apex of the petrous portion of the temporal bone. Shortly after leaving this ganglion, the nerve divides into three branches: (1) Upper or ophthalmic, carrying the sensory nerve fibers for the conjunctiva, the mucous membrane of the nasal fossæ, and the skin of the eyebrow, forehead and nose. (2) Middle or superior maxillary, supplying the meninges, the lower eyelid, the skin of the side of the nose and upper lip and all the teeth and gums of the upper jaw. (3) Inferior maxillary, supplying the teeth and gums of the lower

jaw, the skin of the temple and external ear, the lower part of the face and the lower lip.

RELATIONSHIP OF THE FIFTH NERVE TO THE TEETH.—In any inflammatory condition of the teeth, the terminations of the sensory fibers become stimulated, causing extreme pain. This is toothache. The relationship of the fifth nerve to the teeth explains why disturbance in the latter should often cause the pain to be referred not to the tooth that is involved, but to some skin area on the face. This is called *referred pain*. The skin areas corresponding to the different teeth have been worked out by Head, and are indicated in the accompanying diagrams (Figs. 48 and 49). Not only may the pain be referred to the skin area, but this itself may become hypersensitive. There is, moreover, in each area usually a maximal spot at which the pain and tenderness are most marked.

The sensory nerve endings in the teeth are all of the nature of pain receptors; there are no temperature or tactile receptors, these latter sensations being particularly developed in the tongue and lips (see p. 244). The pain receptors of the teeth, like those of the cornea, react practically in full intensity to every strength of stimulus. This explains why a small degree of irritation, as that due to caries, may cause as painful a toothache as an intense irritation. As we have already explained, the purpose of painful or nocuous sensation is protective, causing, for example, withdrawal of the irritated portion of the body or some movement of offense (see p. 251). In the case of the teeth it serves as a warning that something must be done to arrest whatever condition is causing it. The enamel and cement are devoid of nerve endings, which, however, are very abundant in the pulp, and probably also in the dental tubules (Mummery). An inert, sensationless exterior covering, a highly sensitive center, and between these a moderately sensitive tissue, describes the sensitiveness of a tooth. The sensitiveness of the pulp is so great as to suggest that it is partly of the nature of a highly specialized nociceptor, just as the taste buds and olfactory epithelium are specialized receptors for taste and smell. The sensitiveness of the teeth diminishes with advancing age.



- | | | | |
|---|---|---|---|
|  | Fronto-nasal area (maxillary incisors). |  | Maxillary area (maxillary second premolar and first molar). |
|  | Naso-labial area (maxillary canine and first premolar). |  | Mental area (mandibular incisors, canine and first premolar). |

The points of maximum intensity are ringed.

Fig. 48.—Diagram to show areas of referred pain in distribution of fifth nerve due to affections of the various teeth (Front view). (From drawing by T. Wingate Todd.)

The fifth nerve is very commonly the seat of neuralgia, which may affect one or all of its branches. This is called "*tic douloureux*" or tri-facial neuralgia. The attacks come in spasms, and besides the excruciating pain, there is often twitching of the muscles or flushing of the skin of the face. Pressure at the points where the branches of the nerve come out of the skull, as at the supra or infra-orbital notches, is usually especially painful in tic. An unhealthy condition of the teeth is often responsible for the symptoms, but if dental treatment and general medical care do not remove the neuralgia, it is usually advisable to cut out a portion of the nerve or even to remove the entire Gasserian ganglion.

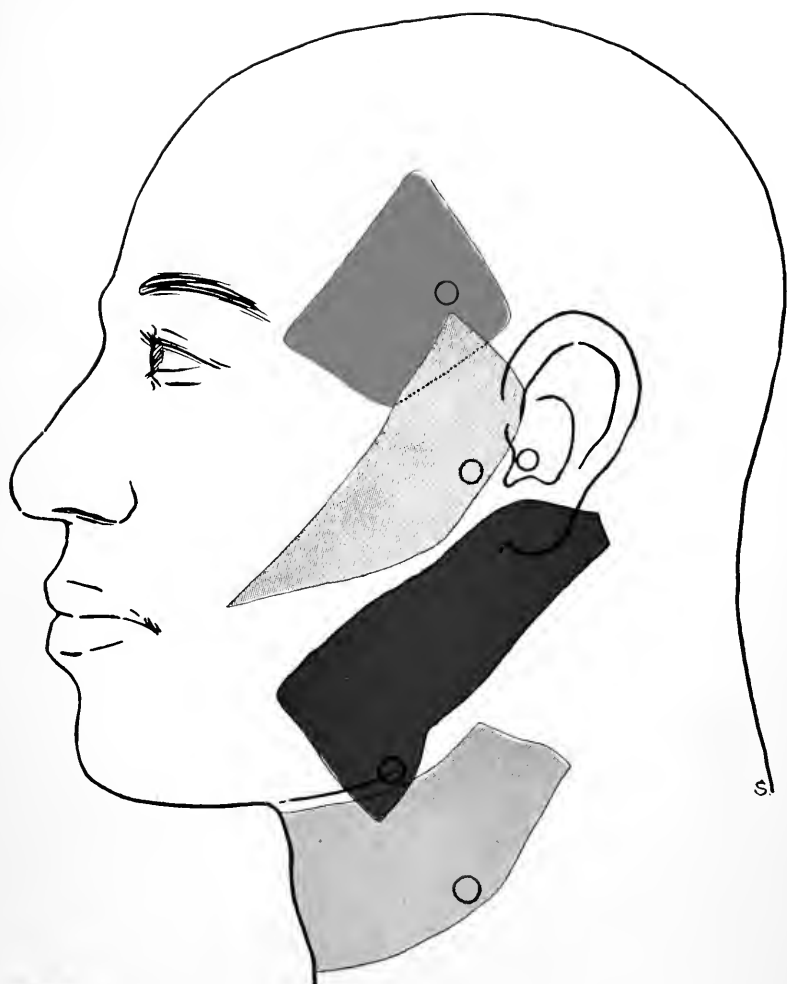
Sometimes the fifth nerve becomes *paralyzed*, causing anesthesia involving the area of its distribution. Tingling, numbness or neuralgic pains often precede the anesthesia. Since the conjunctiva loses its sensitiveness, particles of dust, etc., are not removed from the eye by the tears so that they set up inflammation, which may develop and cause ulceration of the cornea. For the same reason, or perhaps because the nerve independently controls the nutrition of tissues, the gums and cheeks may become ulcerated and the teeth loosened. Partial loss of taste and inability to smell pungent vapors, which act on sensory nerves, are also common symptoms.





THE SEVENTH NERVE.—The seventh nerve is purely motor in function. All the facial muscles, except those concerned in mastication, the platysma of the neck, the posterior belly of the digastric and one of the muscles of the middle ear (the stapedius) are supplied by it. On account of its tortuous course the seventh nerve is peculiarly liable to inflammation and compression. Thus tumors or inflammation located at the base of the brain may involve that portion running between the upper end of the medulla oblongata and the internal auditory meatus, where the nerve enters the aqueduct of Fallopius. In this region it is likely to become involved when there is disease of the internal ear or mastoid sinus (mastoiditis). After its exit from the skull (by the stylomastoid foramen) its close association with the parotid gland renders it liable to be involved in cel-

lulitis of this gland, and on account of its superficial position, it may be injured by blows on the side of the head. Quite commonly the seventh nerve becomes the seat of inflammation after exposure to a draught, as by sitting at an open window. The *paralysis* is almost always one-sided. The eyelid on the affected side cannot be properly closed, a chink remains and the eyeball becomes rotated upward, thus showing the sclera. On smiling or showing the teeth the mouth is drawn up on the healthy side, causing a triangular opening because the lips do not become separated on the paralyzed side. Articulation is difficult and such acts as whistling and blowing are impossible. Because of paralysis of the buccinator muscle, food collects between the cheek and gums. The distortion of the face is much more pronounced in old, than in young persons; indeed in the case of the latter the paralysis may be overlooked until speaking or laughing is attempted.

THE EIGHTH OR AUDITORY NERVE.—The eighth or auditory nerve is composed of two branches, the one called *cochlear*, connected with the organ of Corti (see p. 291), which collects sound waves, and the other, called *vestibular*, with the semicircular canals which, by the movements of the fluid contained in them, record changes in the position of the head (see p. 276). Both branches, being sensory, are connected with ganglia situated in or near the internal ear (ganglion spirale for the cochlear division and ganglion of Scarpa for the vestibular). Paralysis of the auditory nerve causes a degree of deafness which is more profound than that due to disease of the middle ear, for in the latter case a tuning fork can be heard when the end of it is applied to the skull or is held in the teeth, which is not the case when the nerve is diseased. When the eighth nerve becomes irritated (as by inflammation of the ear, or a general condition such as migraine, epilepsy, etc.), various kinds of sounds are heard. This is called *tinnitus*. It is not infrequently followed by deafness.

THE NINTH OR GLOSSO-PHARYNGEAL NERVE.—This nerve is partly motor and partly sensory. The motor fibers supply the muscles of the pharynx and most of those of the soft palate.



- | | | | |
|--|---|---|---|
|  | Temporal area (maxillary second premolar). |  | Hyoid area (mandibular second premolar; first and second molars). |
|  | Mandibular area (maxillary second and third premolars). |  | Superior laryngeal area (mandibular third molar). |

The points of maximum intensity are ringed.

Fig. 49.—Diagram to show areas of referred pain in distribution of fifth nerve due to affections of the various teeth (Side view). (From drawing by T. Wingate Todd.)

The sensory fibers carry impulses of common sensation and of taste from the root of the tongue, the neighboring portions of the pharynx, the tonsils, the soft palate, and the pillars of the fauces. This nerve does not commonly become the seat of local lesions.

THE TENTH OR VAGUS NERVE.—This is the main cerebrospinal nerve supplying the viscera and it is both motor and sensory in function. We shall see later that the nerves to the viscera belong to the so-called autonomic system, which is distinguished from the somatic by two main facts, one anatomical and one functional. The anatomical difference is that every nerve fiber becomes connected through synapses with nerve cells located peripherally (i. e., near the end of the nerve), and the axons of the cells continue the impulse on to the structure; the functional difference is that the autonomic fibers, as their name indicates, control automatically-acting or involuntary functions instead of voluntary movements, as is the case with the ordinary or somatic cerebrospinal nerve fibers.

The most important of the vagus autonomic fibers run to the heart (see p. 185), the œsophagus (p. 57), the stomach (p. 60) and the intestines (p. 79). The vagus also contains afferent fibers which have their cell stations in ganglia situated in the trunk of the nerve. These fibers carry sensory impulses particularly from the larynx and lungs (p. 219). Further details regarding the functions controlled by the vagus are fully given in the references indicated above. When the vagus nerve, or its center, is the seat of paralysis, swallowing is seriously interfered with, and food is liable to pass into the larynx and cause pneumonia. Various forms of paralysis of the vocal cords may also result from paralysis of the vagus.

THE ELEVENTH OR SPINAL ACCESSORY NERVE.—The eleventh or spinal accessory is entirely an efferent nerve, one part of it, the accessory, being derived from the same column of nerve cells as the vagus and being really a part of this nerve; the other arises from the cells of the anterior horn of the spinal cord in the upper cervical region and supplies the trapezius and sterno-mastoid muscles.

THE TWELFTH OR HYPOGLOSSAL NERVE.—The twelfth or hypoglossal nerve is entirely efferent, being the motor nerve of the tongue muscles and of most of the muscles attached to the hyoid bone. When it is paralyzed, as in bulbar paralysis, swallowing of food becomes impossible, the tongue cannot be protruded and soon atrophies because of the removal of the trophic influence of the nerve cells. Rarely the paralysis is unilateral, but this is because of lesions higher up in the nervous system than the medulla and so situated that they destroy the connection of the fibers which run from the higher motor centers in the cerebrum to the hypoglossal nucleus. Such lesions necessarily involve fibers of the same type running to the nerve cells of the spinal cord, so that hemiplegia (p. 248) accompanies and is on the same side as the tongue paralysis. When a patient with such a lesion attempts to put out the tongue, it is directed towards the affected side but it shows no atrophy.

CHAPTER XXVIII.

THE NERVOUS SYSTEM (Cont'd).

The Brain.

The first question which naturally arises is, what influence does the brain have on the reflex movements produced through the spinal cord? These influences may be summarized as follows:

1. The brain enables the animal to will that a particular movement shall or shall not take place, irrespective of the stimulation of spinal reflexes. Much of this influence of the brain is of course voluntary in nature, but some of it is subconscious or involuntary. In general it may be said that the cerebrum, through the pyramidal tracts, usually exercises a damping or inhibitory influence on the spinal reflexes. It is for this reason that the reflex response to a certain stimulus is usually much more pronounced in a spinal, as compared with a normal animal. For example, it is impossible to bring about the scratch reflex in many normal dogs, whereas it is always present in spinal animals.

In man this restraining influence of the pyramidal tracts on spinal reflexes is very evident in the case of knee-jerk, which, it will be remembered, is the extension of the leg which occurs when the stretched patellar tendon is tapped. Ordinarily the kick is moderate in degree, but in patients whose pyramidal tracts are diseased, as in spastic paraplegia, it becomes very pronounced.

2. The brain, being the receiving station for the projicient sensations (p. 279), sight, hearing and smell, adds greatly to the number of afferent pathways by which reflex actions can be excited.

3. Since in higher animals all the afferent impulses usually

travel through the brain (p. 248), many nerve centers become more or less involved in the reflex actions, so that a much higher degree of co-ordination than that seen in a spinal animal attends the muscular response. For example, some of these afferent impulses reach the cerebellum, whose function, as we shall see, is to strengthen some impulses and weaken others, so that a more perfect movement results.

4. The animal becomes conscious not only of the nature and place of application of the sensory stimulus itself, but of the degree to which it has moved its muscles in response.

The Functions of the Cerebrum.

The complicated movements, such as those involved in the scratch reflex, which we have seen that a spinal animal can carry out in the paralyzed region after shock has passed away, become more and more numerous and complicated as the higher centers are left in connection with the spinal cord. That is to say, the higher up in the cerebrospinal axis the section is made, the more capable does the part of the animal below the section become to perform complicated movements. The important centers in the medulla, pons and mesencephalon add their influence to those of the spinal cord itself, so that integration becomes more comprehensive. If the cut is made above the level of the pons, in other words, if the cerebral hemispheres alone be disconnected from the rest of the cerebrospinal axis—*decerebration*, as it is called—we obtain an animal possessing all the reflex actions that are necessary for its bare existence, although it is of course incapable of feeling or, if the basal ganglion be also destroyed, of seeing or hearing. It becomes a mere automaton: it breathes, the blood circulation is normal, it can walk or run or swim, it swallows food if the reflex act of swallowing be stimulated by placing the food in the mouth, but it has not the sense to take food itself even when this is placed near it. All the mental processes are absent; it has no memory, no volition, no likes and dislikes. By seeing that it takes food, it has been possible to keep such a decerebrated dog alive for eighteen months, and the lower we descend in the animal scale, the easier

it becomes to perform the operation and to keep the animal alive. In higher animals, such as monkeys, however, life is impossible without the cerebrum, thus supporting the conclusion, which we have already drawn (see p. 243), that the cerebrum comes to be a necessary part of every reflex action in the higher animals.

Cerebral Localization.—The various functions of the cerebrum are located in different portions of it. This localization of cerebral functions has been very extensively studied during recent years, partly by experimental work on the higher mammalia and partly by clinical studies on man. Careful observations are made of the behavior of the various functions of the animal either after removal or destruction of a portion of the cerebrum, or during its stimulation by the electric current. Important additions to our knowledge of cerebral localization are also being made by correlating the symptoms observed in insane persons with the lesions which are revealed by post-mortem examination.

It has been found that there are roughly three areas on the cerebrum with distinct and separate functions (Fig. 50).

I. In the portions of the cerebrum which lie in front of the ascending frontal convolutions—*prefrontal region*—are located the centers of the intellect (thought, ideation, memory, etc.). This part of the cerebrum is accordingly by far the best developed in man; it is much less so in the apes and monkeys, becomes insignificant in the dog, and still more so in the rabbit. It has been destroyed by accident in man with the result that all the higher mental powers vanished.

II. The next portion includes roughly the region of the cerebrum bordering upon the *Rolandic fissure* (i. e., the ascending frontal and ascending parietal convolutions). Here are located the highest centers for the movements of the various parts of the body. Microscopic examination of the grey matter reveals the presence of large triangular nerve cells, which communicate by synapses (see p. 241) with the afferent fibers that carry the sensory impulses, whose course from the posterior spinal roots we have already traced (p. 246). From each of these cells an efferent fiber runs to join the pyramidal tract

(p. 248), and thus connect with the anterior horn cells of the spinal cord.

In the *Rolandic area*, as it is called, is therefore situated the cerebral link in the chain of neurones (see p. 249) through which the ordinary movements of the body take place. Such movements may be set agoing, either by stimulation of the Rolandic nerve cells through afferent fibers—a pure reflex—or by impulses coming to them from the centers of volition situated

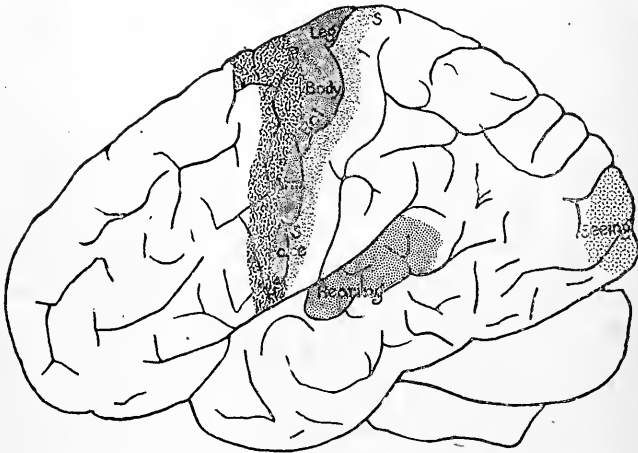


Fig. 50.—Cortical centers in man. Of the three shaded areas bordering on the Rolandic fissure (*Rol.*), the most anterior is the precentral associational area, the middle one is the motor area (the position of the body areas are indicated on it), and the most posterior is the sensory area, to the cells of which the fillet fibers proceed. The centers for seeing and hearing are also shown. The unshaded portion in front of the Rolandic area is the precentral; the portions behind, the parietal and temporo-occipital.

in the prefrontal convolutions. Or, again, the nerve cell, at the same time that it receives a sensory impulse coming up from the spinal cord, may receive one from the prefrontal convolutions which may either interdict or greatly modify the reflex response. Every possible muscular group in the body has a center of its own in the Rolandic area, the determination of the exact location of these centers being one of the achievements of modern medical science. Thus, if we stimulate with a finely

graded electric stimulus, say, the center of the thumb, it will be found that the thumb undergoes a slow, purposeful, co-ordinated movement; and so on for every other center. Or, if instead of stimulating, we cut away one of the centers and allow the animal to recover from the immediate effects of the operation, it will be found that all the more finely co-ordinated movements of the corresponding part of the body have disappeared, although gross reflex movements may be possible, because the spinal reflexes are still intact. If the entire Rolandic area on one side is removed, the muscles of the opposite side of the body, except those of the trunk, become completely paralyzed for some time, after which, however, particularly in the case of young animals, the paralysis becomes recovered from, thus indicating that some other portions of the brain have assumed the function of the destroyed centers. If the stimulus is a very strong one, the movements do not remain confined to the corresponding muscle group, but they spread on to neighboring groups until ultimately the whole extremity or perhaps even all the muscles of that side of the body are involved.

These experimental results find their exact counterpart in *clinical experience*. Thus when some center becomes irritated by pressure on it of some tumor growing in the membranes of the brain (meningeal tumor), or by a piece of bone, as in depressed fracture of the skull, or by blood clot, convulsive attacks (known as Jacksonian epilepsy) are common. The first sign of such an attack is usually some peculiar sensation (aura) affecting the part of the body which corresponds to the irritated area; the muscles of this part begin to twitch and more muscles are involved, until ultimately all those of the corresponding half of the body become contracted. There is, however, no loss of consciousness, as there is in true epilepsy. The evident cause of these symptoms has clearly indicated the proper treatment for such cases, namely, surgical removal of the cause of irritation. For this purpose a very careful study is first of all made of the exact group of muscles in which the convulsions originate; the location of the area on the cerebrum is thus ascertained and a trephine hole is made in the correspond-

ing part of the cranium and through this hole the tumor or blood clot is removed.

III. These so-called motor areas are of course also *sensory* areas in the sense that the afferent stimuli which come up from the spinal cord run to them. They are really sensori-motor centers. For some of the more highly specialized proficient sensations, such as vision and hearing (see p. 279), there are, however, special centers. These, along with an extensive field of associational or junctional grey matter, constitute the third main division of the cerebral cortex and occupy the greater part of the parietal, the temporosphenoidal and the occipital lobes. The *visual* is the most definite of these centers. Thus if the occipital lobe be removed or destroyed by disease on one side, the corresponding half of each retina becomes blind. It is by studying the exact nature of the involvement of vision in such cases that the physician is able to locate the position of a tumor, etc.

The center for *hearing* is in the temporosphenoidal lobe, but its location is not very definite.

It will be seen, however, that the visual and auditory centers take up but a small part of this third division of the cerebrum, the most of it being occupied by *associational areas*. The nerve cells of these areas do not, like those of the motor and sensory centers, send fibers which run as pyramidal or optic fibers to some lower nerve center, but only to other cerebral centers, which they serve to link together. They are specialized to serve as junction points for all the receiving and discharging centers of the cerebrum, so that all actions may be properly correlated or integrated. These junctional centers thus perform the great function of adapting every action of the entire animal to some definite purpose. Together with the nerve cells in the prefrontal areas, the associational cells represent the highest development of cerebral integration, so that we find the areas in which they lie becoming more and more pronounced, the higher we ascend the animal scale.

The Mental Process.—The impression received by the visual center when a young animal looks for the first time at, say a

bell, becomes stored away in nerve cells lying in or close to that center, and when the bell is moved sound memories are likewise stored in the auditory center. At first these remain as isolated memory impressions and the animal is unable to associate the sight with the sound of the bell. But later, with repetition, the visual and the auditory centers become linked together, through nerve cells and fibers which occupy the associational areas, so that the invocation of one memory is followed by association with others. It is evident that the intricacy of this interlacement of different centers will, in large part, determine the intellectual development of the animal, and the possibility of his learning to judge of all the consequences that must follow every impression which he receives or every act which he performs. In man these associational areas are very poorly developed at the time of birth, so that the human infant can perform but a few acts for itself. Everything has to be learned, and the learning process goes hand in hand with development of the associational areas, which proceeds through many years. On the other hand, most of the lower animals are born with the associational areas already laid down and capable of very little further increase, so that, although much more able than the human infant to fend for itself at birth, the lower animal does not afterwards develop mentally to the same extent.

The practical application of these facts concerning the functions of different areas of the cerebrum is in the study of mental diseases. To serve as an example we may take *aphasia*. This means inability to interpret sights or sounds or to express the thoughts in language. In the former variety—called sensory aphasia—the patient can see or hear perfectly well, but fails to recognize that he has seen or heard the object before. He fails to recognize a printed word (word blindness) or to interpret it when spoken (word deafness). The lesion responsible for this condition is located in the associational areas and not in the centers themselves. In the other variety, called motor aphasia, the patient understands the meaning of sounds or sights, of spoken or written words, but is unable to express his thoughts or impressions in language. The lesion in this case in-

volves some of the centers concerned in the higher control of the muscles which are used in speech, and very commonly it is situated in the left side of the cerebrum. In all three forms of aphasia there is more or less decrease in the mental powers.

Cerebellum.

The afferent impulses set up by stimulation of the nerves of the skin in a spinal animal, and due therefore to changes in the environment, after entering the spinal cord travel to the various centers in the cord. Although complicated movements may result (e.g., the scratch reflex), there is an entire absence of the power of maintaining bodily equilibrium, and the animal cannot stand because the muscles are not kept in the degree of tone which is necessary to keep the joints properly stiffened. A similar inability to maintain the center of gravity of the body results from removal of the cerebellum, or small brain, which it will be remembered is situated dorsal to the medulla and pons, with which it is connected by three peduncles. The cerebellum consists of *two lateral hemispheres* and a median lobe called the *vermis*. The remarkable infolding of the grey matter which composes its surface, and the large number of nuclei which lie embedded in its central white matter are structural peculiarities of the cerebellum.

The immediate results of removal of the cerebellum consist in extreme restlessness and inco-ordination of movements. The animal is constantly throwing itself about in so violent a manner that unless controlled it may dash itself to death. Gradually the excitement gets less, until after several weeks all that is noticed is that there is a condition of muscular weakness and tremor, and difficulty in maintaining the body equilibrium. Quite similar symptoms occur when the cerebellum is diseased in man (as by the growth of a tumor); the condition being called cerebellar ataxia, and being characterized by the uncertain gait which is like that of a drunken man.

These observations indicate that the function of the cerebellum is to harmonize the actions of the various muscular groups, so

that any disturbance in the center of gravity of the body may be subconsciously rectified by appropriate action of the various muscular groups. It evidently represents the nerve center having supreme control over other nerve centers, so that these may not bring about such movements as would disturb the *equilibrium of the animal*.

In order that the cerebellum may perform this function it must, however, be informed of two things. In the first place, it must know the existing state of contraction of the muscles and the tightness of the various tendons that pull upon the joints, and in the second, it must know the exact position of the center of gravity of the body.

Information of the condition of the muscles and tendons is supplied through the *nerves of muscle sense*, which run in every muscle nerve and are connected in the muscles with peculiar sensory nerve terminations called muscle spindles. When the muscles contract, or the tendons are put on the stretch, these spindles are compressed and sensory or afferent stimuli pass up the nerves of muscle sense, enter the cord by the posterior roots and reach the cerebellum by way of the lateral columns (see p. 249).

Information regarding the center of gravity of the body is supplied through the vestibular division of the eighth nerve, which, it will be recalled, is connected with the *semicircular canals* and vestibule. In these structures are membranous tubes or sacs containing a sensory organ (called the crista or macula acoustica), which consists essentially of groups of columnar cells furnished with very fine hair-like processes at their free ends and connected at the other end with the fibers of the eighth nerve. The hair-like processes float in the fluid which is contained in the membranous canals or sacs. This fluid does not, however, completely fill these structures, so that it moves whenever the head is moved. This movement affects the hair-like processes and thus sets up nerve impulses which are carried to the cerebellum.

To make the hair cells of this receiving apparatus capable of responding to every possible movement of the head, it is,

however, evident that there must be some definite arrangement of the tubes. This is provided for in the disposition of the semi-circular canals in three planes, namely, a horizontal and two vertical (Fig. 51). Taken together the three canals form a structure which looks somewhat like a chair, the horizontal canals being the seat of the chair and the two vertical canals joining together to form its back and arms. The back of each chair is directed inwards so that they are back to back. At one end of each canal is a swelling, the ampulla, in which the sensory nerve

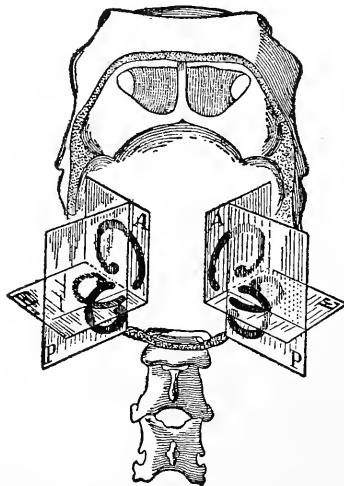


Fig. 51.—The semicircular canals of the ear, showing their arrangement in the three planes of space. (From Howell's Physiology.)

apparatus above described is located. It is evident that when the head is moved in any direction the fluid in some of these canals will be set in motion. It is this movement of the fluid which stimulates the hair cells. That this is really the function of the semicircular canals is proved by the fact that if they are irritated or destroyed, grave disturbances occur in the bodily movements. This is what occurs in Menière's disease, in which attacks of giddiness, often severe enough to cause the patient to fall, and accompanied by extreme nausea, are the chief symptoms, the lesion being a chronic inflammation involving the

semicircular canals. It is believed by some that the constant movements of the fluid in the semicircular canals is the cause of sea sickness. The unusual nature of these movements causes confusion in the impressions transmitted to the cerebellum from the canals, but after a while the cerebellum may become accustomed to them and the sea sickness passes away.

The Sympathetic Nervous System.

Along with the vagus and one or two less prominent cerebrospinal nerves, the sympathetic constitutes the *autonomic nervous system*, so-called because it has to do with the innervation of automatically acting structures, such as the viscera, the glands and the blood vessels. The characteristic structural feature of the nerves of this system is that they are connected with nerve ganglia located *outside* the central nervous system. In these ganglia the nerve fibers run to nerve cells, around which they form synapses, thus permitting the nerve impulse to pass on to the cell, which then transmits it to its destination along its own axon (see p. 241). Before arriving at the ganglion in which the synapsis is formed, the fibers are called preganglionic; after they leave, they are called postganglionic. A preganglionic fiber may run through several ganglia before it becomes changed to a postganglionic fiber. In the case of the vagus and other cerebral autonomic nerves, the ganglia are often situated, as in the heart (see p. 185), at the end of the nerve, but in the case of the sympathetic itself, they are more numerous, and are mainly situated at the sides of the vertebral column, where, together with the connecting fibers, they form a chain—the *sympathetic chain*—which can easily be seen on opening the thorax and displacing the heart and lungs.

Two fine branches connect each of the spinal nerves with the corresponding sympathetic ganglion. It is through one of these branches that the sympathetic chain receives its fibers from the spinal cord. Through the other, fibers run from the ganglion to the spinal nerve. Some of the sympathetic ganglia are situated at a distance from the spinal cord; the ganglia which compose the solar and hypogastric plexuses are examples.

In the thorax, the uppermost ganglion is very large and is called the *stellate ganglion*. Its postganglionic fibers constitute the vasomotor nerves of the blood vessels of the anterior extremity, and the sympathetic fibers to the heart. Some preganglionic fibers run through the stellate ganglion to pass up the neck as the *cervical sympathetic*, their cell station being in the superior cervical ganglion. They act on the pupil (dilating it), on the salivary glands (causing vasoconstriction and stimulating glandular changes), and on the blood vessels of the head, face and mucosa of the inside of the mouth.

From about the fifth dorsal vertebra downwards, branches run from the sympathetic chain on each side to become collected into a large nerve called the *great splanchnic*, which passes down by the pillars of the diaphragm into the abdomen and runs to the ganglia of the coeliac plexus. This nerve supplies all of the blood vessels of the intestines and other abdominal viscera. Its action on these vessels has already been described (see p. 191). It also carries nerve impulses for the control of the movements of the stomach and intestines and for some of the digestive glands. In the abdomen the sympathetic chain gives off branches, which form the *pelvic nerves* and supply the blood vessels of the lower extremity. It is important to note that the connections between the sympathetic system and the cerebrospinal axis are limited to the spinal nerve roots between the second thoracic and the second lumbar. The results which follow stimulation of the sympathetic system are exactly like those which are produced by injections of adrenalin (see p. 130).

CHAPTER XXIX.

THE SPECIAL SENSES.

The sensory nerve terminations, or afferent receptors, that are scattered over the skin are affected by stimuli which come in actual contact with the surface of the body. In order that the stimuli transmitted from a distance, such as those of light, sound and smell, or the projicient sensations as they are called, may be appreciated by the nervous system, specifically designed organs, called the organs of special sense, are required. These organs collect the stimuli in such a way as to cause them to act effectively on receptors which have been especially adapted to react to them.

Although not really a projicient sensation, taste is conveniently considered along with the above.

Vision.

Light is due to vibration of the ethereal particles that occupy space. The vibrations occur at right angles to the rays of light, and these travel at high velocity in straight lines from the source of the light. The rate of vibration of the rays is not always the same, and on this difference depends the color of the light, red light vibrating much slower, and its waves being accordingly much longer, than those of violet light. The terminations of the optic nerve, the retina, have been specially developed to receive the light waves. But in order that a comprehensive picture of everything that is to be seen may be projected on the retina, an optical apparatus, consisting of the cornea and lens, is situated in front of it. The retina and the optical apparatus are built into a globe—the eyeball—which, pivoting on the attachment of the optic nerve, can be so moved that images from different parts of the field of vision may be

focused in turn on the retina. These movements are effected by the so-called ocular muscles.

There are, therefore, three functions involved in the act of seeing: (1) That of the retina, in reacting to light. (2) That of the cornea, etc., in focusing the light. (3) That of the ocular muscles, in moving the eyeball.

The Optical Apparatus of the Eye.

It will readily be seen that the eye is constructed on much the same principle as a photographic camera, the retina being like the sensitive plate. There is, however, an important difference in the manner by which objects at varying distances are brought to a focus on the sensitive surface in these two cases: in the camera, it is done by adjusting the distance between the lens and the focusing screen; in the eye, it is done by varying the convexity of the lens.

In order to understand how the optical apparatus works, it is necessary to know something about the refraction of light. When a ray of light passes from one medium to another, it becomes bent or refracted. When it passes from air to water or glass, for example, it becomes refracted so that the angle which the refracted ray makes with the perpendicular to the surface is less than that of the entering ray. In other words, the ray becomes bent towards the perpendicular. The greater the difference in density between the two media, the greater is the difference between the two angles. A figure expressing the ratio between these two angles is called the *index of refraction*. If the ray of light leaves the denser medium by a surface which is parallel with that by which it entered (as in passing through a pane of glass), it will be refracted back to its old direction, but if, as in a prism, it leaves the denser medium by a surface which forms an angle with that by which it entered, the original refraction will be exaggerated. If two prisms be placed with their broad ends together, parallel rays of light coming from a certain direction will be bent so that, on leaving the prisms, they meet somewhere behind them. Two prisms so arranged are virtually the same as a *biconvex lens*. It is plain that the

focusing power of such a lens will depend on two things: first, its index of refraction, and, secondly, the curvature of its surfaces.

A considerable part of the actual refraction of the rays which enter the eye is accomplished at the curved surface of the cornea, a smaller degree of refraction taking place at the lens itself. The reason for this is that the refractive index from air to cornea is much greater than that between the lens and the humors of the eye in which the lens is suspended, these humors and the cornea having very much the same refractive indices. The entering rays are, therefore, refracted at two places in the eye, namely, at the anterior surface of the cornea and on passing through the lens.

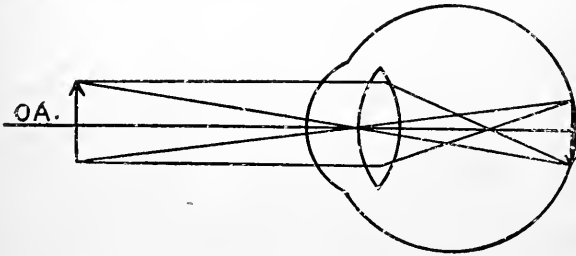


Fig. 52.—Formation of image on retina. O.A. is the optic axis.

Accommodation of the Eye for Near Vision.—When the eye is at rest, its optical system is of such a strength that parallel rays, i. e., rays that are reflected from objects at a distance, are brought to a focus exactly on the retina. The picture thus formed is, however, upside down for the same reason that it is so on the screen of a camera (Fig. 52). When the object looked at is so near that the rays reflected from it are divergent when they enter the eye, it becomes necessary, if the image is still to be focused on the retina, that some adjustment take place in the optical system of the eye. This could happen in one of two ways, either by lengthening the distance between the lens and the retina (the method used in a camera), or by increasing the convexity of the lens. The former process cannot

occur in the eye, but the second is rendered possible by *bulging of the anterior surface of the lens*. There are several ways by which this bulging of the lens can be proven to occur. Thus, if the eye of a person who is looking at some distant object be inspected from the side of the head, that is to say, in profile, it is easy to note the exact position of the iris, which, with the pupil in its center, hangs as a circular curtain just in front of the lens (Fig. 53). If the person is now told to regard some



Fig. 53.—Section through the anterior portion of the eye: *C*, the cornea; *I*, the iris (note the circular muscular fibers cut across at the margin); *L*, the lens; *Ci*, the ciliary process; *S*, the suspensory ligament; *Scl*, the sclerotic or outer protective coat of the eye. (From a preparation by P. M. Spurney.)

object held close to him, it will be seen that the iris is pushed forward nearer to the cornea. That this is really due to a bulging of the anterior surface of the lens can be shown by placing a candle to one side and a little in front of the head and then, from the other side, viewing the images of the candle flame which are cast on the eye. It will be seen that one image occurs at the anterior surface of the cornea, and another, less distinct, at the anterior surface of the lens. This image from the lens

will be seen to move forward—that is to say, closer to the image at the cornea—when the person shifts his gaze from a distant to a near object. By using optical apparatus for measuring the size of the images, the degree to which the convexity of the lens has increased, as a result of the bulging, can be accurately measured.

This change in the convexity of the lens depends on the fact that it is composed of a ball of transparent elastic material, which is kept more or less flattened antero-posteriorly because of its being slung in a capsule which compresses it. The edges of the capsule are attached to a fine ligament (the suspensory ligament), which runs backwards and outwards to become inserted into the ciliary processes (Fig. 53). These processes exist as thickenings of the anterior portion of the choroid, or pigment coat of the eye, and they can be moved forwards by the action of a small fan-shaped muscle, called the ciliary muscle, which at its narrow end originates in the corneo-scleral junction, and runs back to be attached, by its wide end, to the ciliary processes. When this muscle is at rest, the ciliary processes lie at such a distance from the edges of the lens that the suspensory ligament is put on the stretch. When the ciliary muscle contracts, it pulls the ciliary processes forward, thus slackening the suspensory ligament and removing the tension on the capsule of the lens, with the result that the latter bulges because of its elasticity. The ability of the lens to become accommodated for near vision depends, therefore, first, on the elasticity of the lens, and secondly, on the action of the ciliary muscle. Interference with either of these renders accommodation faulty. For example, the lens, along with the other elastic tissues of the body [e. g., the arteries (p. 175)], becomes less elastic in old age, thus accounting for the "long-sightedness" (or presbyopia) which ordinarily develops at this time. Paralysis of the ciliary muscle produces the same effect in even more marked degree, which explains the utter inability to bring about any accommodation after treating the eye with atropin, which is given for this purpose before testing the vision in order to find out the strength of lenses required to correct for errors in refraction.

The Function of the Pupil.—Every optical instrument contains a so-called diaphragm, which is a black curtain having a central aperture whose diameter can be altered to any required size. The object of this is to prevent all unnecessary rays of light from entering the optical instrument, thus materially increasing the distinctness of the image. In the eye, this function is performed by the iris with the pupil in its center. The size of the pupil is altered by the action of two sets of muscle fibers in the iris. One of these runs in a circular manner around the inner edge of the iris; by contracting it causes constriction of the pupil, an event which occurs, along with the bulging of the lens, during accommodation for near vision. The other layer of fibers runs in a radial manner, and by contracting causes dilatation of the pupil. This occurs in partial darkness, or when the eye is at rest (although not during sleep). The circular fibers are supplied by the third nerve, and the radial fibers by the sympathetic. Under ordinary conditions both muscles are in a state of tonic contraction (see p. 253), so that the actual size of the pupil at any moment is the balance between two opposing muscular forces. This renders its adjustment in size very sensitive. For example, it can become dilated either by stimulation of the sympathetic (which occurs when any irritative tumor affects the cervical sympathetic nerve), or by paralysis of the third nerve (as by giving atropin). Conversely, constriction of the pupil may be the result of stimulation of the third nerve (as by a tumor at the base of the brain) or paralysis of the sympathetic.

These local conditions acting on the *afferent* nerves to either pupil are not nearly so often called into play as conditions acting *reflexly* on both eyes at the same time.

Certain of the afferent impulses which call these reflexes into play travel by the optic nerve to the nerve centers for the pupil, such for example as the stimulus set up by light falling on the retina. The afferent pathway concerned in the contraction of the pupil, which occurs in accommodation, must, on the other hand, be a different one because in the disease locomotor ataxia (see p. 254), the pupil contracts on accommodation, but does not

do so when light is thrown into the eyes. The nerve centers for the pupil are very sensitive to general nervous conditions, thus accounting for the dilatation of the pupil which occurs during fright or other emotions, or pain. The pupils are contracted in the early stages of asphyxia or anesthesia, as in the early stages of nitrous oxide administration, but they become dilated when the anesthesia or asphyxia becomes profound. Their condition helps to serve as a gauge of the depth of anesthesia.

Imperfections of Vision.—The optical system of the eye is not perfect. *Some of these imperfections exist in every eye, whilst others are only occasional.* The errors in every eye are those known as spherical and chromatic aberration. *Spherical*

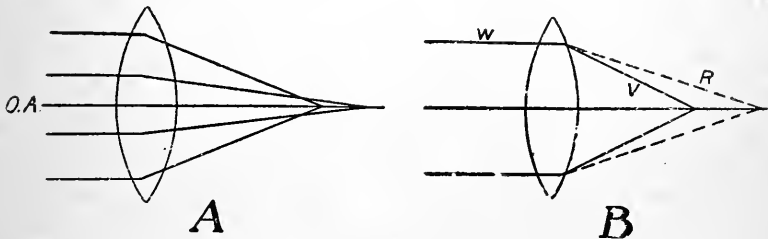


Fig. 54.—*A*, spherical aberration. The rays which strike the margins of the lens are brought to a focus before those striking near the center. *B*, Chromatic aberration. The ray of white light (*W*) is dissociated by the lens into the spectral colors, of which those at the red end (*R*) are not brought to a focus so soon as those at the violet end (*V*).

aberration (Fig. 54), occurs because the edges of the lens have a higher refractive power than the center, so that the image on the retina is surrounded by a halo of overfocused rays. *Chromatic aberration* is due to the fact that white light, on passing through the lens, suffers some decomposition into its constituent colored rays (the rainbow colors), of which certain ones (viz., those towards the violet end of the spectrum) come to a focus sooner than others (viz., those towards the red end), thus creating a colored edge on the focused image. These errors are greatly minimized, although not entirely removed, by the pupil, which cuts out the peripheral rays.

The *occasional errors* are long-sightedness or hypermetropia,

short-sightedness or myopia, and astigmatism (Fig. 55). *Hypermetropia* is due to the eyeball being too short so that the focus of the image is behind the retina. The error is corrected by prescribing convex glasses. *Myopia* is due to the opposite con-

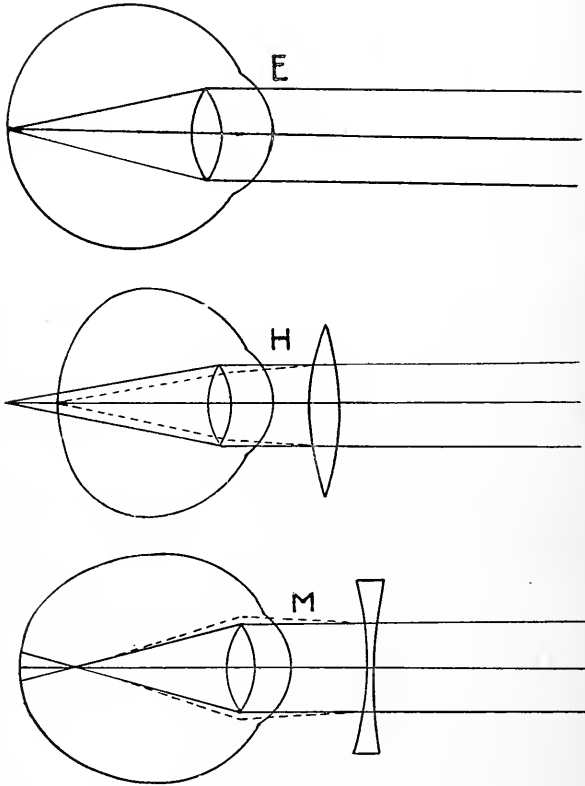


Fig. 55.—Errors in refraction: *E* shows the formation of the image on the retina in the normal or emmetropic eye; *H* shows the condition in long-sight, or hypermetropia, where the eyeball is too short; *M* shows the condition in short-sight, or myopia, where the eyeball is too long.

dition, that is, the eyeball is too long, so that the focus occurs in front of it. Concave glasses correct it. *Astigmatism* is due to the lens or cornea being of unequal curvature in its different

meridians. This causes the rays of light in one plane to be brought to a focus before those in other planes, so that the two hands of a clock, when they are at right angles to each other, cannot be seen distinctly at the same instant, although they can be successively focused. A certain amount of astigmatism exists in every eye, but when it becomes extreme, it is necessary to correct it by prescribing glasses which are astigmatic in the opposite meridian to that of the eye. Such glasses are called cylindrical.

Astigmatism may occur along with either myopia or hypermetropia, and when any of these errors is only slight in degree, the patient may be able, by efforts of accommodation, to overcome the defect. The strain thus thrown on the ciliary muscle is, however, quite commonly the cause of severe headache. The correction of the errors should never be left to untrained persons, but a proper oculist should be consulted, since it is usually necessary to give atropin so that the accommodation may be paralyzed and the exact extent of the error measured. The use of improper glasses may aggravate the defect of vision and do much more harm than good.

The Sensory Apparatus of the Eye.

The Functions of the Retina.—The image which is formed on the retina by the optical system of the eye sets up nerve impulses which travel by the optic nerve to the visual center in the occipital lobes of the cerebrum (see p. 272), where they are interpreted. Microscopic examination of the retina has shown that it consists of several layers of structures, the innermost being of fine nerve fibers which arise from an adjacent layer of large nerve cells, and the outermost of peculiar rod or cone-shaped cells, called the rods and cones. Between the layer of large cells and the layer of rods and cones are several layers composed of other nerve cells and of interlacements of the processes of cells and nerve fibers. The rods and cones are the structures acted on by light, the other layers of the retina being for the purpose of connecting the rods and cones with the large nerve cells from which the fibers of the innermost layer arise.

The fibers all converge to the optic disc, which is a little to the inside of the posterior pole of the eyeball. At this point the fibers of the nerve fiber layer bend backwards at right angles and run into the optic nerve, thus crowding out the other layers and causing the existence of a *blind spot*, which can be readily demonstrated by closing one eye, say the left, and with the other regarding the letter B in the next line. Although the S is

B

S

also distinctly visible in most positions, yet if the book be moved towards and away from the eye, the S will become invisible at a certain distance corresponding to that at which the rays from it are impinging upon the blind spot. As we alter the distance of the book from the eye, the line of vision, or visual axis, being fixed on the B, the image of the S travels from side to side across the inner or nasal half of the retina, and at a certain position strikes the optic disc. Ordinarily we are unaware of the blind spot, partly because we have two eyes and, the blind spot being towards the nasal side of each retina, the image of an object does not fall on it in both eyes at the same time; and partly because we have learned to disregard it. The area or extent of the blind spot may become so increased, as by excessive smoking, that it becomes noticeable.

At another portion of the retina called the *fovea centralis*, all the layers become thinned out except that of the rods and cones, especially the cones. This, as we should expect, is by far the most sensitive portion of the retina, and is indeed the portion on which we cause the image to be focused when we desire to see an object clearly. The remainder of the retina is only sufficiently sensitive to give us a general impression of what we are looking at. Thus when we view a landscape, we can see only a small portion clearly at one time, although we have a general impression of the whole. The portion which we see clearly is that which is focused on the fovea, and we keep moving our eyes in all directions so that every part of the landscape may in turn be properly seen. We see with the fovea what the rest of the retina informs us there is to be seen.

The Movements of the Eyeballs.—In order that we may be enabled to move our eyes so as to see objects in different positions in the visual field, the eyeballs are provided with six little muscles, four recti and two obliques. These muscles are innervated by the third, fourth and sixth nerves (see p. 259). The images in the two eyes cannot of course fall on anatomically identical parts of the retinae, but they fall on parts that are physiologically identical. Thus, an object, say on the right of the field of vision, will cause an image to fall on the nasal side of the right retina and on the temporal side of the left retina. We do not, however, see two objects because by experience we have come to learn that these are *corresponding points* on the retinae. When an object is brought near to the eye, the two eyeballs must converge so as to bring the visual axes on to the corresponding points. This convergence of the eyeballs constitutes the third change occurring in the eyes during accommodation for near vision, the other two being, as we have seen, bulging of the lens and contraction of the pupil. It is interesting that these three changes are controlled by the third nerve. If anything happens to throw one of the images on to some other portion of one retina, double vision is the result. This condition of *diplopia*, as it is called, can be brought about, voluntarily, by pressing on one eyeball at the edge of the eye, or it may occur as a result of paralysis or incoordinate action of one or more of the ocular muscles. This occurs in certain intoxications, as, for example, that produced by alcohol.

Just as in the case of errors of refraction, e. g., astigmatism, slight degrees of diplopia may cause symptoms that are more distressing than when marked diplopia exists, because we try to correct for slight errors and the effort causes pain (headache) and fatigue, whereas with extreme errors we do not try to correct but, instead, we learn to disregard entirely the image in one eye. Whenever the incoordination of ocular movement is permanent, as when due to shortening of one of the muscles, it is called *strabismus*. This condition is usually congenital, and can often be rectified by a surgical operation.

Judgments of Vision.—Besides these purely physiological

problems of vision, there are many others of a physio-psychological nature. Such for example are the visual judgments of size, distance, solidity, and color. Judgments of *size* and *distance* are dependent on: (1) the size of the retinal image, (2) the effort of accommodation necessary to obtain sharp definition, and (3) the amount of haze which appears to surround the object. Judgment of *solidity* depends on the fact that the images produced on the two retinæ are not exactly from the same point of view; they are like the two photographs of a stereoscopic picture. The brain on receiving these two slightly different pictures fuses them into one, but judges the solidity of the object from the differences in the two pictures.

Judgment of *color*, or color vision, forms a subject of great complexity. It apparently depends on the existence in the retina of three varieties of cones, one variety for each of the three primary colors. The primary colors are red, green and violet; and by mixing them on the retina in equal proportions (as by rotating a disc or top on which they are painted as sectors) a sensation of white results; by using other proportions, any of the other colors of the spectrum may be produced. When one of these primary color receptors is absent from the retina, *color blindness* exists. Thus if the red or the green receptors are absent, the patient cannot distinguish between red and green lights. Such persons cannot be employed in railway or nautical work.

CHAPTER XXX.

THE SPECIAL SENSES (Cont'd).

Hearing.

Like light, sound travels in waves, but not as transverse waves of the ether that fills space, but as longitudinal waves of condensation and rarefaction of the atmosphere itself. The magnitude of these waves is much greater and their rate of transmission much slower than the waves of light; therefore we see the flash of a gun long before we hear its sound. The several qualities of sound, such as pitch, loudness and quality or timber, depend respectively on the frequency, the magnitude and the contour of the waves. Sound waves are not appreciated by the ordinary nerve receptors but only by those of the cochlear division of the eighth nerve. These are connected, in the cochlea of the internal ear, with a highly specialized receptor capable of converting the sound waves into nerve impulses. The *cochlea* consists of a bony tube wound two and one-half times as a spiral around a central column, up the center of which runs the end of the cochlear nerve. A longitudinal section of the cochlea (Fig. 56), therefore shows us this spiral tube in section at several places, and it is noticed that there projects into it from the central column a ledge of bone having a C-shaped free margin. From the lower lip of the C, a membrane called the basilar membrane, stretches across the tube, which it thus divides into two canals, of which the upper is again divided into two by another membrane running from the upper surface of the bony ledge.

The basilar membrane is a very important part of the mechanism for reacting to sound waves. Resting on it is a peculiar structure called the Organ of Corti (Fig. 57), which in transverse sections of the cochlear canal is seen to be composed of two rows of long epithelial cells set up on end like the rafters of a roof, with

shorter "hair" cells leaning up against them, particularly on the side away from the central column. The sound waves, which act on the basilar membrane, are transmitted to the fluid, which fills the uppermost of the three divisions of the cochlear tube (see Fig. 56), through a membrane covering an oval-shaped opening (the oval window) in the bony partition separating the internal from the middle ear. After reaching the apex of the cochlea they pass through a small aperture in the basilar membrane into the lowest

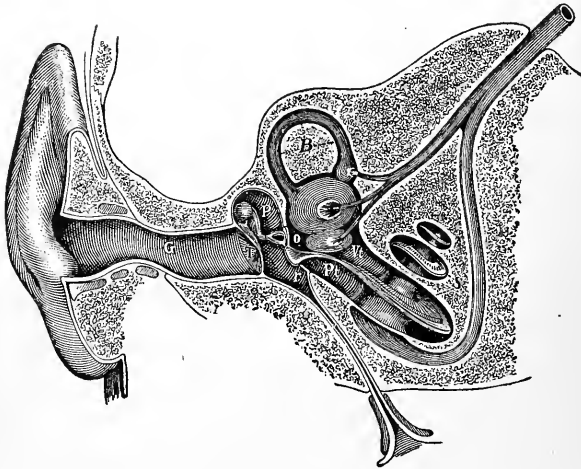


Fig. 56.—Semidiagrammatic section through the right ear (Czermak): *G*, external auditory meatus; *T*, membrana tympani; *P*, tympanic cavity or middle ear with the auditory ossicles stretching across it and the Eustachian tube (*E*) entering it; *o*, oval window; *r*, round window; *B*, semicircular canals; *S*, cochlea; *Vt*, upper canal of cochlea; *Pt*, lower canal of cochlea. (From Howell's Physiology.)

canal, down which they travel to lose themselves against the membrane covering another opening (the round window) situated near the oval window in the same partition of bone. As they pass along these canals the waves cause the basilar membrane to move or vibrate. The vibration affects the cells of the Organ of Corti, and so sets up nerve impulses which are transmitted to the cochlear nerve by means of nerve fibers which connect with each of the main cells of the Organ. A fine membrane (called Tec-

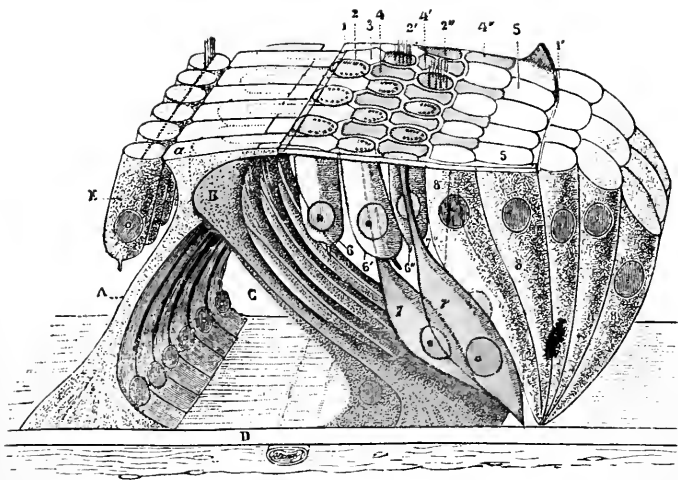


Fig. 57.—Diagrammatic view of the organ of Corti (Testut): *D*, basilar membrane; *A*, *B*, inner and outer rods of Corti; *6*, *6'*, *6''*, hair cells; *7*, *7'*, supporting cells. (From Howell's Physiology.)

torial) rests on the tops of the hair cells, and by rubbing on them when they move, this membrane augments the action of the basilar membrane.

We must now consider how the sound waves are brought from the outside to the oval window. The pinna of the ear collects the sound waves from the outside and directs them into the *external auditory canal*, at the inner end of which they strike the drum of the ear or *tympanic membrane*. This membrane is stretched loosely in an oblique direction across the canal, and is composed partly of fibers which radiate to the edge of the membrane from the handle of the malleus, a process of one of the auditory ossicles, to which it is attached. Because of these properties, the tympanic membrane, unlike an ordinary drum, is capable of vibrating to a great variety of notes, and the vibrations cause the handle of the malleus to move in and out. Between the tympanic membrane and the cochlea is the middle ear, or *tympanum*, consisting of a cavity across which stretches the *auditory ossicles* composed of three small bones, the malleus, the incus and the stapes. Besides the long process or handle already described, the malleus consists of a rounded head situated above and forming a saddle-shaped articulation with the head of the incus and a short process which runs from just below the head to the anterior wall of the tympanum. The incus is somewhat like a bicuspid tooth, the malleus articulating with the crown, and having two fangs, a short one passing backward and a long one vertically downwards. This process, at its lower end, suddenly bends inwards to form a ball and socket joint with a stirrup-shaped bone (the stapes), the foot piece of which is oval in shape and fits into the oval window already mentioned.

The ossicles act together as a bent lever, the axis of rotation passing through the short process of the malleus in front and the short process of the incus behind. If perpendiculars be drawn from this axis to the tips of the handle of the malleus and the long process of the incus, it will be found that the latter is only two-thirds the length of the former (Fig. 58). The amplitude of movement at the stapes will therefore be only two-thirds of that at the center of the tympanic membrane, but one and one-

half times stronger. The increase in force with which the movements of the tympanic membrane are conveyed to the oval window is still further magnified by the fact that the latter is only one-twentieth the size of the former. It is by these movements at the oval window that waves are set up in the fluid occupying the uppermost membranous tube of the cochlea and thus acting on the basilar membrane. The tympanic cavity or

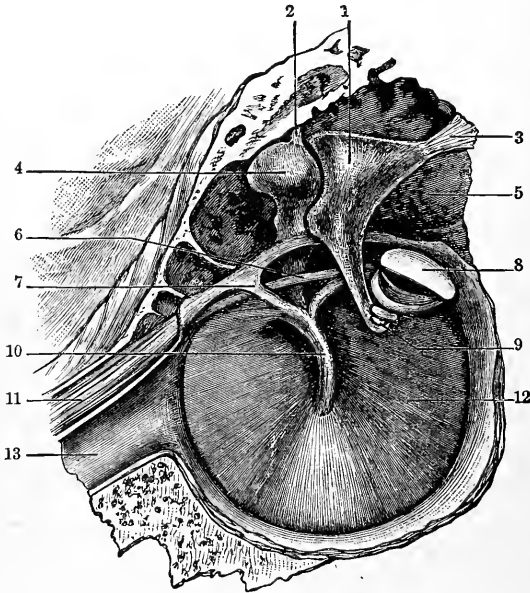


Fig. 58.—Tympanum of right side with the auditory ossicles in place (Morris): 1, incus (like bicuspid tooth) with one process (3) attached to wall of tympanum and the other running downwards to articulate at 9 and 8, the stapes; 10, head of malleus attached to tympanic membrane. (From Howell's Physiology.)

tympanum across which the chain of ossicles stretches is kept at atmospheric pressure by the *Eustachian tube*, which connects it with the posterior nares.

Deafness may be due to the following causes:

1. Rupture of the tympanic membrane.
2. Ankylosis or stiffening of the joints between the ossicles

and the ligaments which hold them in place in the tympanic cavity. Flexibility of the joints between the ossicles prevents sudden jars at the oval window, for the joint between the malleus and incus, being saddle-shaped, unlocks whenever abnormal or excessive movements are transmitted to the malleus.

3. Blocking of the Eustachian tube. This is quite commonly a result of adenoids or it may be due simply to a catarrh of the tube. The result of the block is that the pressure on the tympanic cavity falls below that of the atmosphere because of absorption of oxygen into the blood, and the tympanic membrane bulges inwards and becomes stretched so that it cannot vibrate properly to the sound waves. The deafness in this case is easily removed by reopening the Eustachian tube by forcing air into it. This can be done by attaching a large syringe bulb to one nostril, closing the other nostril, and while the patient is swallowing a mouthful of water, suddenly compressing the bulb.

The auditory distress which is experienced by a person on going into compressed air (as into a caisson) is also due to disturbance in the tympanic pressure, for it takes a few moments before this reaches that on the outside. Blowing the nose usually removes the distress.

In all these conditions, the patient hears perfectly when a tuning fork is applied to the skull or teeth. This is because the sound vibrations are then transmitted to the cochlea through the bones of the head. When the cochlea is diseased, however, the tuning fork cannot be heard either when it is sounded in the air or when it is applied to the skull or teeth.

The Sense of Taste.

Scattered over the mucous membrane of the tongue and buccal cavity, and extending back into the pharynx and even into the larynx, are the *receptors of taste, or taste buds*. They are most numerous in the grooves around the circumvallate papillæ at the root of the tongue, and in the fungiform papillæ. Each taste bud is composed of a mass of fusiform cells packed like a barrel filled with staves. The staves in the center project as hairs beyond those on the outside, and it is evidently by action

on these hairs that certain dissolved substances set up a stimulus of taste. This stimulus is then conveyed by fine nerve fibers which arborize around the taste cells, to the chorda tympani and lingual nerves in the anterior portion of the tongue and the glossopharyngeal in the posterior part. Through these nerves the sensations are carried to the combined afferent nucleus of the fifth and ninth nerves in the medulla oblongata (see Fig. 59).

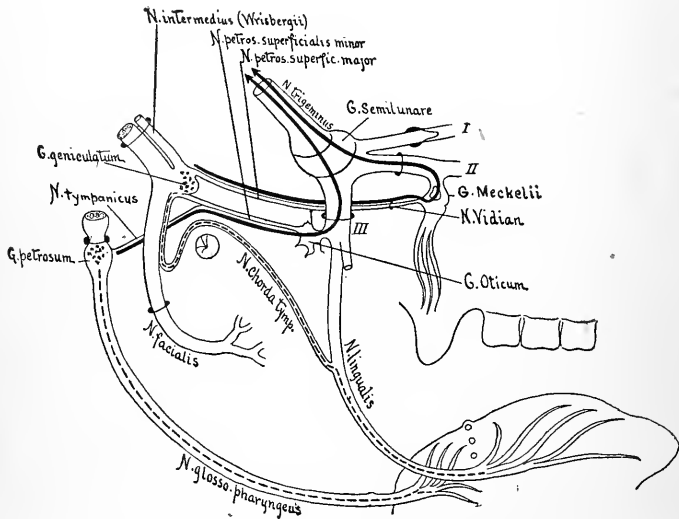


Fig. 59.—Schema to show the course of the taste fibers from tongue to brain (Cushing). The dotted lines represent the course as indicated by Cushing's observations. The full black lines indicate another path by which the impulses may reach the brain. (From Howell's Physiology.)

Substances cannot be tasted unless they are in solution, thus, quinine powder is tasteless. One of the functions of saliva is to bring substances into solution in order that they may be tasted.

There are four fundamental taste sensations: sweet, saline, bitter and sour or acid. The ability to distinguish each of these tastes is not evenly distributed over the tongue, but occurs in definite areas. These can be mapped out by applying solutions,

possessing one or another of these qualities, by means of a fine camel-hair brush, to different portions of the tongue previously dried somewhat with a towel. Bitter taste is absent from all parts of the tongue except the base, hence a mouthful of a weak solution of quinine sulphate has practically no taste until it is swallowed, when however it tastes intensely bitter. Sweet and sour tastes are most acute at the tip and sides of the tongue. Saline taste is more evenly distributed.

This *location of taste sensations* is not a hard and fast one, for neighboring taste buds in, say, the bitter area at the root of the tongue may appreciate different tastes; thus, if a solution containing quinine and sugar be applied to one papilla, it may taste sweet, whereas when applied to a neighboring one, it tastes bitter. With weak solutions one taste may neutralize another; thus the addition of a small amount of salt to a weak sugar solution may remove its sweet taste. This neutralization of one taste by another does not occur when the solutions are stronger; thus a mixture of acid and sugar, as in lemonade, causes stimulation of both "acid" and "sweet" taste buds. The stimulation of one kind of taste bud may cause other taste buds to become more acutely sensitive, which explains the sweetish taste of water after washing out the mouth with a solution of salt.

Attempts have been made to correlate *the chemical structure of organic substances with the taste* which they excite, but with little success. Thus pure proteins have very little taste, whereas half-digested protein is intensely bitter; on the other hand, the pure amino acids, which form a large proportion of the decomposition products in such a digest, are sweet. In the case of acids and alkalies, however, it has been established that the acid taste is due to the H-ion and the alkaline to the OH-ion. Some acids, such as acetic, taste more acid than we should expect from their degree of dissociation into H-ions. This is because of their power of penetration into the cells of the taste buds. When platinum terminals from a battery are applied to the tongue, the positive pole tastes alkaline and the negative acid, because OH-ions accumulate at the former and H-ions at the latter.

THE ASSOCIATION OF TASTE, TOUCH AND SMELL.—The four

fundamental tastes do not nearly represent all the tastes and flavors with which we are familiar. The relish of an appetizing meal, the piquancy of condiments, the bouquet of a fine wine, would remain unappreciated were there no other nerve receptors than those described above. Two other types of nerve receptors are involved, namely, (1) those of common sensation, as in the case of acids, which add an astringent character to the sour taste, and, (2) those of smell, as in wines and flavored foods. The importance of the sense of smell in "tasting" explains the loss of this ability during nasal catarrh or cold in the head. Under such conditions an apple and an onion may taste alike.

Certain *drugs* when applied to the tongue affect taste sensations in different degrees. Thus cocaine first of all paralyzes the receptors of common sensation so that pain is no longer felt and an acid loses all of its astringent qualities and merely tastes sour. A little later the bitter taste also disappears, then salt, then sour, but the saline taste remains even after the cocaine has developed its full effect. Another interesting drug acting on the taste sensations, is a substance present in the leaves of *Gymnema sylvestre*. When these leaves are chewed, the sweet and bitter tastes are absent, those of acid and of salt and ordinary sensation (astringency, etc.) being, however, unaffected.

The Sense of Smell.

In man the sense of smell is very feeble when compared with that of the lower animals, and it is of very unequal development in different individuals. It is, moreover, readily fatigued, as is the experience of every one who has been compelled to live in stuffy rooms. The *receptors* are represented by the columnar epithelium of the superior and middle turbinate bones and the adjacent parts of the nasal septum. This epithelium is composed of large columnar cells, each cell being connected with a nerve fiber which is one of the branches of a fusiform bipolar nerve cell lying immediately beneath the epithelium. The second branch of each nerve cell runs through the cribiform plate to join the olfactory bulb. After making connections with nerve cells here, the pathway is continued along the olfactory tract to the hippocampal

region of the brain. As we would expect, this portion of the brain is highly developed in those animals having a very acute sense of smell.

The olfactory epithelium is kept constantly moist with fluid, and substances cannot be smelled unless the odorous particles which they give off become dissolved in this fluid. These odorous particles diffuse into the upper nares from the air currents which, with each respiration, are passing backwards and forwards along the lower nasal passages. There is no actual movement of air over the olfactory epithelium.

NATURE OF STIMULUS.—It is impossible to state just exactly what it is that emanates from an odorous body to excite the olfactory sense. All we can say is that it does not require to be present in more than the merest trace in the air in order to unfold its action. Thus even in the case of man, with his undeveloped sense of smell, 0.000,000,000,04 of a gramme of mercaptan, suspended in a liter of air, can be smelled, and in the case of the dog, the dilution may no doubt be many thousand times greater. The sense of smell is the most important of the projicient sensations in certain aquatic animals, and is very closely associated with the sexual functions of the animal. Just as in the case of taste, certain substances owe their peculiar odors to simultaneous stimulation of the olfactory epithelium and the receptors of common sensation. Thus the pungency of acids, of ammonia, chlorine, etc., is due to stimulation of the endings of the fifth nerve. Attempts have been made to classify odors, as has been done for tastes, but with no success.

CHAPTER XXXI.

THE MUSCULAR SYSTEM.

The General Properties of Muscular Tissues.—The intimate nature of the physical changes taking place during the contraction of a muscle are not understood, and the histological changes which occur have had various interpretations put on them. For a discussion of these a textbook on histology should be consulted.

The physiological property which distinguishes muscular tissue from other forms of tissue is that of *contractility*. It is to this property that the forcible shortening of the muscles which produces movements is due. The shortening occurs in the long axis of the muscle and is accompanied by a compensatory thickening in the transverse diameter, which keeps the bulk of the muscle constant. After the period of active contraction the muscle remains in the contracted position unless it be pulled back into extension by some force. No isolated muscle can actively expand; it can only do so passively. Muscle does not possess the property of initiating the contraction. This depends on the nervous system acting on another property of muscle, namely, its *irritability*, that is, the ability of the muscle to react very quickly to a stimulus. The amount of stimulus which it requires is very small compared with the reaction brought about in the muscle.

A muscle can be stimulated in other ways than through its nerve, namely, by mechanical, thermal, electrical, and chemical stimuli applied directly to it. By using these artificial stimuli on muscles excised from the body the properties of muscular contraction can be studied.

A record of the contraction of a muscle of a frog may be made by excising it and attaching one end to a suitable clamp and the other end to a light lever the opposite end of which is arranged to trace on smoked paper placed on a rapidly revolving drum. If such a muscle be electrically excited, it will record its contraction as a curve on the smoked surface of the paper, and show

a number of interesting details as to the properties of contracting muscles.

The muscle does not begin to *contract* at the exact moment that the stimulus is applied. A very short latent period (.01 sec.) elapses between the stimulus and the beginning of the contraction. During this time the muscle is undergoing some internal change which must precede the contraction. The period of active contraction is relatively short (.04 sec.) and the period of relaxation somewhat longer (.05 sec.). The ordinary movements of the body cannot obviously be of the nature of a single muscular contraction, for they much exceed one-tenth of a second in duration. They are in fact produced by a prolonged contraction of muscles caused by the fusions of several single contractions. This is known as *tetanic contraction*, and it can easily be produced in the muscle preparation described above by giving it a series of electrical stimuli from an induction coil. If the stimuli be properly timed, a contraction curve somewhat higher and showing no relaxation phase will be produced. When the excitation is discontinued, the muscle returns to its normal length.

The amount of *load* which the muscle lifts has a peculiar effect. Up to a certain point an increase in the load increases the efficiency of the muscle and the muscle will actually perform more work with a moderate load than with no load at all. After a certain load is reached, the efficiency of the muscle begins to diminish and further increase of the load decreases the work accomplished by the muscle. The principle involved here is made use of by fork and shovel manufacturers, who are careful to make their implements carry the load best suited to develop the maximal efficiency of the muscles of a normal average man. Allowing the laborer to choose his own shovel is not always the best for the laborer or for his employer.

Another interesting fact is that a contracted muscle is more *elastic* than a relaxed muscle. Equal weights attached to a contracted and to a relaxed muscle will produce a greater elongation in the contracted than in the relaxed muscle. It is this property which protects the muscle from sudden rupture when attempts are made to lift loads that are too heavy.

The Chemical Changes Which Accompany Muscular Contraction are concerned in the liberation of energy by the oxidation of the organic foodstuffs and the converting of this energy into muscular energy. Just how this change is brought about is not known. During muscular activity a great amount of oxygen is required and a large amount of carbon dioxide is given off. It is very interesting, however, to know that the maximal exchange of these gases does not actually accompany but follows the muscular activity, thus indicating that a muscle becomes charged with energy, so to speak, during rest and discharges itself in much the same manner as a storage battery during a period of activity. If a muscle be made to contract till it becomes fatigued, a large amount of sarco-lactic acid accumulates in the tissue. This poisons the muscle and makes it unable to contract. If this be washed out with saline, the muscle will again contract for a time. *Rigor mortis*, or the rigidity which comes on after death, may be due to the development of sarco-lactic acid in the tissues because they have become deprived of oxygen.

CHAPTER XXXII.

REPRODUCTION.

The most important function of an animal's life is the production of a new individual which in all peculiarities of function and structure is essentially like the parent. The fundamental problems of the process of reproduction which are of physiological importance, are those of fertilization and heredity. Fertilization consists in the union of two parent cells to produce a new cell which is endowed with the power of growth and subdivision. Heredity refers to the phenomenon which directs the cell thus fertilized to develop into an individual like its parents.

Since up to the present time most of our knowledge of these processes is based on anatomical data, we will discuss them very briefly and will pay more attention to what we may term the accessory phenomena of reproduction, which are of more practical interest at present.

Reproduction in the unicellular animals is a simple process. The parent cell divides exactly in halves and two daughter cells are produced. In the multicellular animals this type of reproduction is impossible and the process is delegated to a portion of the animal's body known as the reproductive system. This system in man includes the specialized tissues which produce the cells or eggs from which the new individual develops, and the accessory organs which are concerned in providing favorable conditions for the development of these cells.

Fertilization.—A very simple type of fertilization is seen in unicellular animals, which ordinarily reproduce by simple division. After a series of simple divisions the cell becomes unable to develop more cells until after it has united with another cell to form one large cell. This process is termed *conjugation*. In higher forms, the development of the egg is always preceded by the phenomenon of *fertilization*, which is somewhat similar to

that of conjugation in lower forms. In this process, cells of two types are concerned, the male, or sperm cell, or spermatozoon, and the female cell or ovum. The spermatozoon has the ability to move and to penetrate the ovum. The nuclear elements of both cells unite to form a new nucleus, which is then capable of undergoing a long series of subdivisions. In changes which precede fertilization, the nuclear material originally present in both male and female cells is reduced, and when the cells fuse, the resulting nucleus contains a normal quantity of nuclear material.

The Accessory Phenomena of Reproduction in Man.—The beginning of the active sexual life in man is between the ages of fourteen and sixteen, and is called the age of puberty. In both boys and girls the whole body shows a marked development at this time. The growth of hair on the pubic regions and arm pits, and on the face of boys, the deepening of the male voice, and the development of the breasts in the female, are all accompanying phenomena of the development of puberty. In females this age is marked by the onset of menstruation, which consists of a periodic flow of mucus and blood from the uterus. The flow lasts from four to five days, and recurs with great regularity about every four weeks. In males fully formed seminal fluid, containing live sperm cells, appears.

The Female Organs of Reproduction.—These are the ovaries, oviducts, uterus and the vagina. The ovaries are paired bodies lying in the lower part of the abdominal cavity and held in position by the broad ligament. The cells from which the ova develop are imbedded in the fibrous tissue of the ovary. A number of these cells, better developed than their fellows, and surrounded by a layer of cells, which form a sort of follicle, lie near the surface of the ovary. These are the *Graafian follicles*, in which the ova develop till they are ripe, when they are extruded into the abdominal cavity by rupture of the follicle. In very close apposition to the ovaries is a tube, the oviduct, which leads to the uterus. The outer end of this tube is fimbriated, and it is furnished with cilia, the movements of which cause currents in the fluids of the abdominal cavity, and which direct the ova dis-

charged from the follicle into the oviduct. The uterus is a pear-shaped organ with muscular walls. It is about 7 cm. in length, and consists of an upper dilated portion, called the fundus, and a lower constricted portion, called the cervix. The cervix opens by a small aperture into the vagina, which is a membranous canal about 10 cm. long extending to the vaginal outlet at the external genitalia.

The Male Organs of Generation are the testicles, vas deferens, seminal vesicles, the penis, the prostate gland, and a number of small glands along the urethra.

The testicles consist of two parts, a portion of which is cellular and is concerned in the development of the spermatozoa; and a portion called the epididymis, containing the lower portion of the very long and convoluted duct, the vas deferens. This duct connects the testicles with the seminal vesicles, which lie at the base of the bladder and in close relation to the prostate gland. The seminal vesicles are united by a short duct with the urethra, which is the outlet for the excretions of both the kidney and the testicles.

The spermatozoa are developed in the testicles and find their way to the seminal vesicles through the vas deferens. On their way they become mixed with a number of fluid secretions, the chief of which are derived from the seminal vesicles of the prostate gland and of the glands of Cowper. The resulting mixture is the seminal fluid.

Impregnation.—The seminal fluid containing the spermatozoa is deposited in the vagina during coitus. Attracted by the acid reaction of the secretions of the uterus or under an unknown influence, the spermatozoa soon enter the uterine cavity through its opening into the vagina, and find their way to the oviduct, where they remain waiting for the ovum to appear.

Ovulation.—At about the time of a menstrual period an ovum is discharged from a ripened Graafian follicle and finds its way into the oviduct by way of the fimbriated extremity of the tube, down which it is conducted to the uterus. It is a debated question as to what the exact relation between menstruation and ovu-

lation may be. Whether ovulation precedes or follows menstruation is not known, but the weight of evidence favors the belief that menstruation serves to prepare the uterine walls for the reception of the fertilized ovum should one be discharged. In animals there are periods, called the rutting period, during which impregnation of the ovum with the spermatozoon is possible. Preceding this period there occurs a swelling of the external genitalia and some discharge of mucus. This period probably corresponds to the menstrual period in woman, for there is much evidence to show that impregnation occurs most frequently following the menses.

Menstruation ceases during pregnancy and is generally absent during the period of lactation. It ceases altogether between the ages of about forty-five and fifty. After this time, which is known as the climacteric period, a woman is no longer capable of bearing children.

The union of the spermatozoon and the ovum usually occurs in the oviduct. If the ovum is not fertilized it is cast off. If it is fertilized, a considerable thickening of the uterine mucous membrane takes place from the proliferation of its cells. When the ovum reaches the uterus, it becomes imbedded in the mucous membrane of the fundus of the uterus. This mucous membrane is very vascular and soon becomes fused with the outer layer of the ovum.

Pregnancy.—At first the ovum receives its nourishment directly from the mucous membrane of the uterus, but as the ovum develops and becomes what we term an embryo, the part lying next to the uterine mucosa becomes very vascular; a similar process takes place in the uterine mucosa directly in contact with the embryo. By this process the placenta is formed, the organ through which the embryo obtains nourishment from the mother.

The vascular system of the embryo is, however, entirely separate from the maternal vessels, and the blood of the mother never directly enters the embryo. The interchange between the two must be effected through the cells covering the vessels of the uterine and foetal portions of the placenta. In other words, the embryo may be said to live a parasitic yet entirely independent

life, since through its placental vessels it exchanges its effete products for the oxygen and nourishment contained in the mother's blood.

Birth.—While the ovum is being developed into a human being by division of the original cell of the fertilized ovum, the uterus becomes very much enlarged, and its walls increase in size by the growth of muscular tissue. At the end of approximately 280 days from the date of impregnation of the ovum, the development is complete and birth takes place. This consists in the expulsion of the fœtus by muscular contractions of the uterus.

Directly the child is born, the placenta begins to separate from the uterine wall and is soon expelled. The child deprived of its placental nourishment must now begin an independent life. It must take in its own oxygen and give off carbon dioxide by its respiratory organs. It must take its food through the alimentary canal, and excrete its waste products through its kidneys.

APPENDIX.

Since the amount of time devoted to laboratory instruction and the general equipment of the physiological laboratories in our dental schools varies greatly, detailed laboratory outlines for an experimental course in physiology are out of place. The following is a summary of the experiments in experimental physiology which is given at the present time to the dental classes in the University of Illinois. It is presented here in hope that it may help others in planning a course of like character. The exercises occupy thirty periods of about two hours each. When possible, the experiments are done by the individual students; the more difficult experiments are given as demonstrations.

EXERCISE No. 1.

This period is devoted to a study of the chemical nature of the proteins. The solubility of egg white in distilled water and in salt solution is tested. The coagulation of albumin by heat, and its precipitation by the addition of neutral salts, is shown. The common chemical tests for the proteins are made. The alterations which take place in the chemical and physical properties of protein when partially digested are illustrated by doing the above experiments on solutions of peptone in place of egg white.

EXERCISE No. 2.

The physical and chemical properties of the fats, carbohydrates and inorganic salts found in the body, are studied.

EXERCISE No. 3.

The physical chemical properties of water which are of interest from a physiological standpoint, as for example, its solvent action, specific heat, and latent heat of vaporization, are compared with the same properties of other solvents, such as oil, ether, acid and alkali.

EXERCISE No. 4.

This consists of a demonstration of experiments which illustrate the phenomena of surface tension, osmosis, dialysis and ionization.

EXERCISE No. 5.

The well known experiment showing the nervous mechanism involved in the secretion of the saliva is made upon a dog.

EXERCISE No. 6.

In this exercise each student tests his own saliva for its organic and inorganic constituents. The digestive power of the saliva is estimated by determining the length of time that it takes to change a solution of starch into sugar. The determination of the neutralizing power of the saliva is determined by Marshall's method (see page 49).

EXERCISE No. 7.

The acidity and the digestive power of gastric juice are determined in this exercise. As gastric juice is difficult to obtain, a very good artificial juice can be prepared by dissolving commercial pepsin in 0.4% hydrochloric acid.

EXERCISE No. 8.

The peristaltic muscular movements of the stomach are studied by means of a strip of muscle obtained from the pyloric end of a frog's stomach. The muscle strip is attached to the end of a light lever which traces on the smoked drum of a kymographion.

EXERCISE No. 9.

The secretion of pancreatic juice in a dog following the intravenous injection of the hormone, secretin, is demonstrated. The pendulous and peristaltic movements of the small intestines are also observed.

EXERCISE No. 10.

Each student determines the number of red blood corpuscles per cubic millimeter of blood in another student's blood, by use of the hæmocytometer.

EXERCISE No. 11.

The white sells in each cubic millimeter of blood are determined as in the case of the red cells.

EXERCISE No. 12.

The number of white cells in a cubic millimeter of blood obtained from patients suffering from infections of the mouth, is determined.

EXERCISE No. 13.

This period is used for demonstrating the physical and chemical phenomena of the coagulation of the blood.

EXERCISE No. 14.

The circulation of the blood in the mesentery of the frog's intestines is studied under the microscope.

EXERCISE No. 15.

The principles of the circulation as shown by the Lombard's Heart Model are demonstrated.

EXERCISE No. 16.

This period is devoted to a study of the physiological properties of the turtle's heart muscle. A record of the heart beat is obtained by attaching the heart to a light lever which records its movements on the revolving drum of a kymographion.

EXERCISE No. 17.

A demonstration upon a dog, showing the factors which maintain the blood pressure, occupies this period. Tracings are made of the blood pressure and the heart beat by means of the mercury manometer and the kymographion.

Attention is called to the part which the heart beat and the peripheral resistance of the blood vessels play in the maintaining of the circulation of the blood.

EXERCISE No. 18.

The nervous regulation of the heart beat is graphically shown by determining the effect which section and subsequent stimulation of the peripheral ends of the sympathetic fibers to the heart, and the peripheral end of the vagus nerves have upon the heart beat and the blood pressure. The method of recording these observations is the same as in the previous experiment.

EXERCISE No. 19.

The vaso-constrictor fibers to the ear in the cervical sympathetic nerve of the rabbit are demonstrated. In the same animal the action of the cardiac depressor nerve upon the heart beat and the blood pressure is shown.

EXERCISE No. 20.

The effect of sensory nerve stimulation upon the respiration and circulation is studied. The central end of the fifth nerve in an anæsthetized dog is stimulated with an electric current, while tracings of the heart beat, blood pressure, and the respiration are being taken upon a kymographion. Likewise the effect of stimulating the sensory fibers of the sciatic nerve (by burning the paw of a deeply anæsthetized dog) upon the blood pressure, etc., can be shown. The effects of asphyxia, hæmorrhage and gravity on the circulation and respiration is also demonstrated.

EXERCISE No. 21.

In this experiment the blood pressure is recorded as in the former experiments. The changes in the volume of the kidney are determined by means of the oncometer. The effect of stimulation of the splanchnic nerve upon the kidney volume and the blood pressure and the effect which follows the injection of adrenalin, are compared.

EXERCISE No. 22.

The students, using each other as subjects, determine the tidal, complementary, and supplemental air and the vital capacity of their lungs by means of the spirometer. The various forms of artificial respiration are tested out and the most effective type determined by comparing the respiratory exchange as measured by the spirometer or a gas meter. A graphic record of the respiratory movements is made.

EXERCISE No. 23.

An analysis of the atmospheric and expired air is made and compared.

EXERCISE No. 24.

The blood pressure of each student is determined by the auscultatory and palpation methods. Both systolic and diastolic pressures are taken. The effect upon the blood pressure, of running up and down stairs, is determined.

EXERCISE No. 25.

The student is taught to recognize the heart and the respiratory sounds by the use of the stethoscope.

EXERCISE No. 26.

The effect of the administration of nitrous oxide upon the blood pressure and heart beat is demonstrated. The various stages of the anæsthesia are indicated. The experiment is terminated by showing the effect upon the blood pressure and the heart of injecting a small and a large dose of cocain into the animal.

EXERCISE No. 27.

This period is devoted to the study of the physical and chemical properties of normal and pathological urine.

EXERCISE No. 28.

This is a demonstration experiment of the physiological properties of the skeletal or voluntary muscle.

EXERCISE No. 29.

This exercise is a demonstration of the reflexes which can be elicited in the spinal frog. The common reflexes which can be elicited in man are shown and their physiological significance pointed out.

EXERCISE No. 30.

This period is devoted to some of the simple experiments on the special senses.

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