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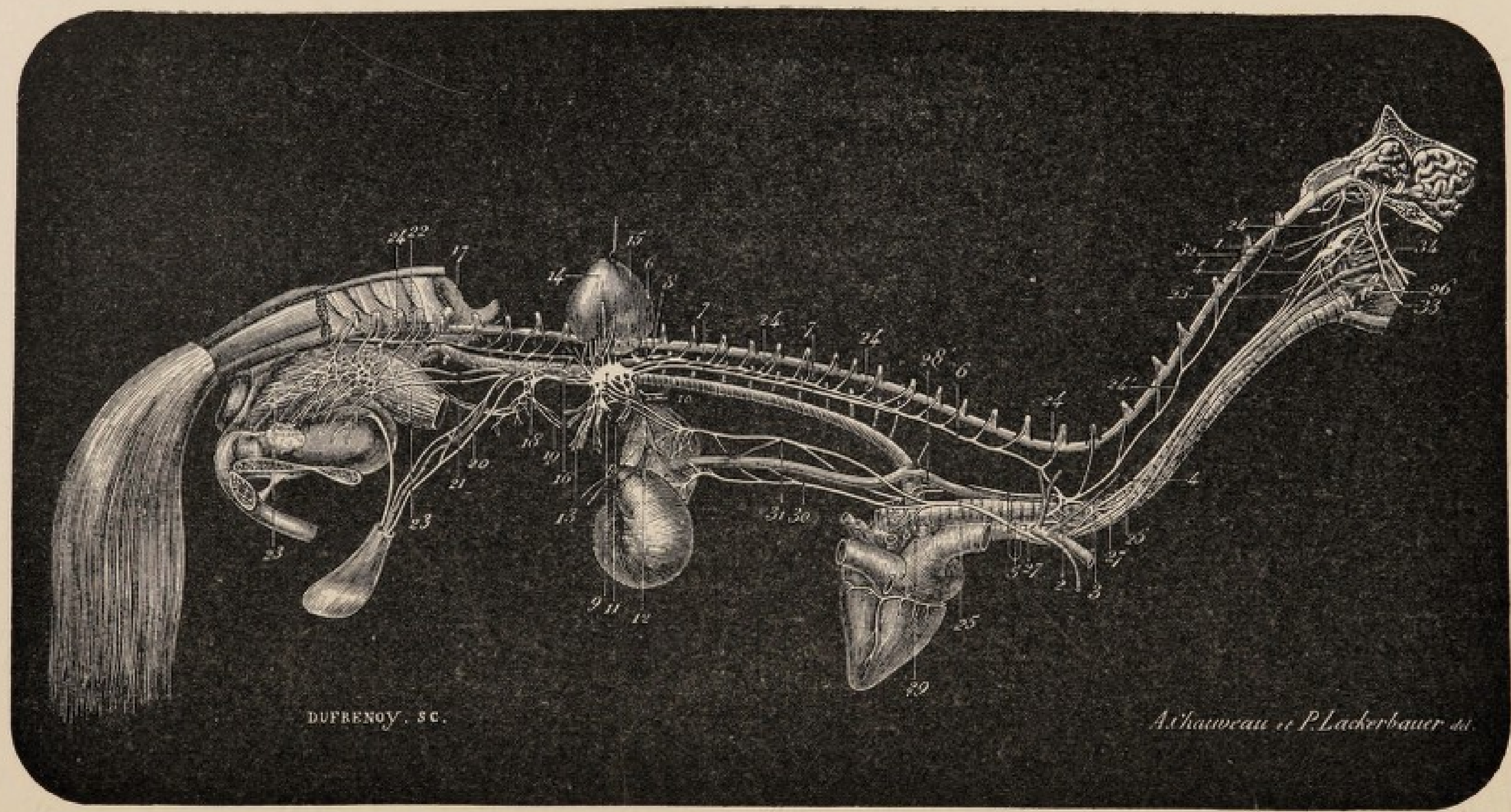
FOR
VETERINARY STUDENTS



DUFRENOY. SC.

A. Chauveau et P. Lackerbauer del.

The Nervous System of the Horse. (CHAUVEAU.)
(See p. 156 *et seq.*)

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ESSENTIALS
OF
PHYSIOLOGY
FOR
VETERINARY STUDENTS

BY

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PREFACE

BETWEEN the Physiology of Man and that of the Domestic Animals there is no fundamental difference, and most of our knowledge of human physiology has been acquired from experiments upon the lower animals. But while the tissues of a man, a dog, and a horse act much in the same manner, the mode of nutrition of these tissues is somewhat different, and requires special attention in the case of each.

In this volume the attempt is made to give the essentials of general physiology and of the special physiology of the domestic animals in a form suitable to the requirements of Students and Practitioners of Veterinary Medicine. The book is not intended to take the place of the demonstrations and practical work from which alone physiology can be properly learned, but merely to supplement these and to focus the information derived from them.

The student must take every opportunity of acquiring a really practical knowledge, and, to facilitate the more direct association of the practical and systematic study of physiology, throughout these pages references are made to descriptions of the experimental and chemical work which the student should try to do for himself or have demonstrated to him. The histological structure of the tissues and organs which is now studied practically in every school is here described only in so far as it is essential for the proper understanding of their physiology.

D. N. P.

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INTRODUCTION

Physiology is really an older science than anatomy, for even before any idea of pulling to pieces, of dissecting the animal machine had suggested itself to our forefathers, crude speculations in regard to the causes and nature of the various vital phenomena must have been indulged in—speculations based upon the vivid belief in the action of spiritual agencies, and perhaps unworthy of the name of science. Still the physiology of to-day is the offspring of such speculations.

Organs and Function.—The first great and true advance was through anatomy. As that science showed how the body is composed of distinct and different parts, it became evident that these parts or organs had separate actions or functions; and hence arose the important conception of the *co-relation of organ and function*.

From the early metaphysical speculations to such true inductions was a great stride, for a scientific method of advance had been established.

Ever since this, until quite recent times, physiology has followed in the footsteps of anatomy, or, to use a more comprehensive term, of morphology. The connection between organ and function having been demonstrated, the questions, Why are these various functions connected with the respective organs? why should the liver secrete bile and the biceps muscle contract? next forced themselves upon the attention.

Tissues and Function.—Again anatomy paved the way for the explanation. The dissecting knife and the early and defective microscope showed that the organs are composed of certain definite structures or *tissues*, differing widely from one another in their physical characters and appearance, and, as physiologists soon showed, in their functions. It now became evident why the liver secreted and the biceps contracted: the one is composed of secreting tissue and the other of contracting tissue.

Cells and Function.—Physiologists and anatomists alike devoted their energies to the study of these various tissues, and, as the structure of the microscope improved, greater and greater advances were made in their analysis, till at length Schwann was enabled to make his world-famous generalisation, that all the tissues are composed of certain similar elements more or less modified, which he termed cells, and it became manifest that the functions of the different tissues are due to the activities of their cells.

The original conception of the cell was very different from that which we at present hold. By early observers it was described as composed of a central body or nucleus, surrounded by a granular cell substance with, outside all, a cell membrane. As observations in the structure of the cell were extended, it soon became obvious that the cell membrane was not an essential part, and later, the discovery of cells without any distinct nucleus rendered it clear that the essential part is the cell substance, and this substance Von Mohl named *protoplasm*, by which name it is since generally known.

Protoplasm and Function.—So far physiology had followed in the tracks of anatomy, but now another science became her guide. Chemistry, which during the last century has advanced with enormous strides, and has thrown such important light upon the nature of organic substances, now lent her aid to physiology; and morphologists having shown that the vital unit is essentially simply a mass of protoplasm, the science of life bids fair to become the science of the chemistry of protoplasm.

The prosecution of physiology on these lines is still in its infancy, but already it has changed the whole face of the science. Physiology is no longer the follower of anatomy. It is become its leader, and at the present time, as we shall afterwards see, not only the various activities, but also the various structural differences of the different tissues, are to be explained in terms of variations in the chemical changes in protoplasm.

In the study of physiology this order of evolution must be reversed, and from the study of protoplasm the advance must be made along the following lines:—

1. **Protoplasm**—the physical basis of life; its activities and nature.
2. **Cells.**—Manner in which protoplasm forms the vital units of the body.
3. **Tissues.**—Manner in which these are formed by cells. Their structure, physical and chemical properties, and vital manifestations.
4. **Nutrition of Tissues.**
    - *a.* Fluids bathing the tissues—
        Blood and Lymph.
    - *b.* Manner in which fluids are brought into relationship with tissues—
        Circulatory System.
    - *c.* Manner in which substances necessary for the tissues are supplied to these fluids—
        Respiratory System.
        Digestive System.
        Food, its nature and quantity.
    - *d.* Chemical changes in the tissues generally—
        Metabolism and Heat Production.
    - *e.* Manner in which the waste products of tissues are eliminated—**Excretion**, *Hepatic*, *Renal*, *Pulmonary*, *Cutaneous.*
5. **Reproduction and Development.**

PART I

SECTION I

Protoplasm

The first step in the study of physiology must be to acquire as clear and definite a conception as possible of the nature of protoplasmic activity in its most simple and uncomplicated form, for in this way an idea of the essential and non-essential characteristics of life may best be gained.

I. Structure.—Protoplasm is a semi-fluid transparent viscous substance. It usually occurs in small individual particles—Cells—more or less associated, but it may occur as larger confluent masses—Plasmodia.

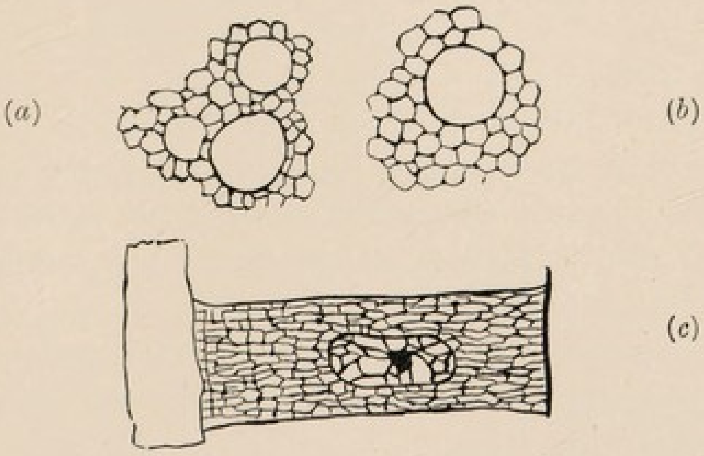


Fig. 1.—(*a*) Foam structure of a mixture of Olive Oil and Cane Sugar ; (*b*) Reticulated structure of Protoplasm ; (*c*) Reticulated structure of Protoplasm in the cell of an earth-worm (*after* Bütschli).

Sometimes protoplasm seems perfectly homogeneous, but generally a reticulated appearance can be made out even in the living condition (fig. 1), and from this it has been concluded that there is a more solid part arranged like the fibres of a sponge, or like the films of a mass of soap-bubbles, with a more fluid interstitial part. In all protoplasm, therefore, there seems to be a certain amount of organisation, and in certain cells this organisation becomes very marked indeed.

II. Physiology.—A knowledge of the essentials of the physiology of protoplasm may be gained by studying the vital manifestations of one of the simplest of living things, the yeast plant (Saccharomyces Cerevisæ).

This plant consists of very minute oval or spherical bodies frequently connected to form chains, each composed of a harder outer covering or capsule and of a softer inner substance which has all the characters of protoplasm.

Its physiology may be studied by placing a few torulæ in a solution, containing glucose, $C_6H_{12}O_6$, and urea, CON_2H_4, with traces of phosphate of soda, Na_2HPO_4, and sulphate of potash, K_2SO_4.

If the vessel be kept all night in a warm place the clear solution will in the morning be seen to be turbid. An examination of a drop of the fluid shows that the turbidity is due to the presence of myriads of torulæ. In a few hours the few torulæ placed in the fluid have increased many hundredfold. The whole mass of yeast has grown in amount by the growth and multiplication of the individual units.

This power of growth and reproduction under suitable conditions is the essential characteristic of living matter.

What are the conditions necessary for the manifestation of these phenomena of life?

1. If the yeast be mixed with the solid constituents of the solution in a dry state no growth or reproduction occurs. *Water is essential.*

2. If the yeast, mixed with the solution, be kept at the freezing point no growth takes place, but this proceeds actively at about 36° C. *A certain temperature is necessary for the vitality of protoplasm.* In the absence of these conditions, protoplasm is only potentially alive, and in this state it may remain for long periods without undergoing any change, as in the seeds of plants and in dried bacteria.

The conditions essential for the manifestations of life being present, in order that the growth of the yeast may take place, there must be :—

(*a*) A SUPPLY OF MATERIAL from which it can be formed.

(*b*) A SUPPLY OF ENERGY to bring about the construction.

(*a*) The chemical elements in protoplasm are carbon, hydrogen, oxygen, nitrogen, sulphur, and phosphorus. These elements are contained in the ingredients of the solution used. If yeast be sown in distilled water, even if it be kept at a temperature of 36° C., it does not grow.

(*b*) The energy is got by the breaking down of the sugar, $C_6H_{12}O_6$, into alcohol, C_2H_6O, and carbon dioxide, CO_2. Such a breaking down of a complex into simpler molecules liberates energy, as is well seen when nitro-glycerine explodes, breaking into carbon dioxide, water, oxygen, and nitrogen—

$$2C_3H_5(NO_3)_3 = 6CO_2 + 5H_2O + O + 6N.$$

The energy can be used for the performance of work of any kind, as, for example, the work of building up a fresh quantity of the yeast plant out of the substances contained in the solution. The history of the yeast plant shows that *protoplasm, when placed in suitable conditions, has the power of breaking down certain complex substances, and of utilising the energy liberated for building itself up.* It is this power which has enabled living matter to exist and to extend over the earth.

How does protoplasm liberate the potential energy of such substances?

The answer to this question has been given by the demonstration by Buchner that the expressed juice of the yeast torulæ acts on the sugar in the same way as the living yeast. The yeast therefore manufactures something which splits the sugar. This something belongs to the group of **Enzymes** or **Zymins** which play so important a part in physiology generally. These enzymes all act by hastening reactions which go on slowly without their presence, but they do not themselves take any direct part in the reaction. Hence a very small quantity may bring about an extensive change in the substance acted upon. For the manifestation of their activity they require the presence of water and a suitable temperature—in the case of the yeast enzyme about 36° C. is the best. At lower temperatures the reaction becomes slower and is finally stopped, and at a higher temperature it is delayed and finally arrested by the destruction of the enzyme. Sometimes these enzymes lead to a complete decomposition of the substance upon which they act, but this is often prevented by a checking influence exerted by the accumulation of the products of their action, *e.g.* by the alcohol developed from the sugar. With certain enzymes at least, the action may actually be reversed if the enzyme is brought in contact with the final products of decomposition. Thus the enzyme which splits esters into their components may cause a linking of those components to form esters. In this respect they simply aid the establishment of an equilibrium between the component substances in the reaction.

The general action of the enzymes has been termed **katalytic.** It may be compared to the action of an acid in the inversion of cane sugar—

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

Here the acid merely hastens a reaction which would go on slowly in the presence of water alone.

The precise way in which such katalytic actions are brought about is still not quite clear, but there is evidence that the agent acts as a middle-man between the reacting substances, in the case of H_2O_2 taking up the O and then liberating it—in the case of the decomposition of cane sugar taking up H_2O and handing it on; just as in the oxidation of glucose, which occurs when it is boiled with an alkali, a metallic oxide, such as cuprous oxide, may take oxygen from the air and hand it on to the glucose, thus making the oxidation more rapid.

Living yeast differs from these dead substances simply in the fact that it *uses* the energy liberated from the glucose. In virtue of this, the yeast has the power of repair and of growth.

But **protoplasm is also constantly breaking down,** and if yeast be kept at a suitable temperature in water without any supply of material for construction, it gives off carbon dioxide and decreases in bulk on account of these disintegrative changes. These are as essential a part of the life of living matter as the building-up changes, and it is only when they are in progress that the latter are possible.

Protoplasm (living matter) is living only in virtue of its constant chemical changes, metabolism, and these changes are on the one hand destructive (*katabolic*), on the other constructive (*anabolic*). Living matter thus differs from dead matter simply in this respect, that side by side with destructive changes, constructive changes are always going on, whereby its amount is maintained or increased.

Hence our conception of living matter is not of a definite chemical substance, but of a substance constantly undergoing internal changes. It might be compared to a whirlpool constantly dragging things into its vortex, and constantly throwing them out more or less changed, but itself continuing apparently unchanged throughout. Hoppe-Seyler expresses this by saying: "The life of all organisms depends upon, or, one can almost say, is identical with, a chain of chemical changes." Foster puts the same idea in more fanciful language: "We may speak of protoplasm as a complex substance, but we must strive to realise that what we mean by that is a complex whirl, an intricate dance, of which, what we call chemical composition, histological structure, and gross configuration are, so to speak, the figures.".

The rate of these chemical processes may be quickened or slowed by changes in the surroundings, and such changes are called **stimuli**. If the stimulus increases the rate of change, it is said to *excite*; if it diminishes the rate of change, it is said to *depress*. Thus the activity of the changes in yeast may be accelerated by a slight increase of the temperature of the surrounding medium, or it may be depressed by the addition of such a substance as chloroform water.

While the continuance of these chemical changes in protoplasm is **life**, their stoppage is **death**. For the continuance of life the building-up changes must be in excess of or equal to the breaking-down. The evolution of energy must be sufficient for growth and maintenance. It is only the surplus over this which is available for external work. In youth the surplus energy is largely used for growth, in manhood for work. When failure in the supply or in the utilisation of the energy-yielding material occurs, the protoplasm dwindles and disintegrates. Death is sudden when the chemical changes are abruptly stopped, slow when the anabolic changes are interfered with. The series of changes which occur between the infliction of an incurable injury and complete disintegration of the tissue constitute the processes of **Necrobiosis,** and their study is of importance in pathology.

III. Chemistry.—It is impossible to analyse such an ever-changing substance as protoplasm, and although what is left when these chemical changes are stopped can be examined, such analyses give little insight into the essential nature of the living matter.

That substances of great complexity take part in the constant whirl is shown by the analyses of what is left after death. Five or six elements—carbon, hydrogen, oxygen, nitrogen, sulphur, and phosphorus—are present, and these are linked together to form molecules of enormous size.

Water is the most abundant constituent of protoplasm, amounting, as it does, to about 75 per cent.

The **Solids**, constituting the remaining 25 per cent., consist chiefly of a series of bodies closely allied to one another and called "chief substances" or **Proteins**. In addition to these, certain inorganic salts are found in the ash when protoplasm is burned, indicating the presence of POTASSIUM and CALCIUM along with PHOSPHORUS and SULPHUR. The inorganic salts, and especially their kations, appear to be of considerable importance in maintaining the activity of protoplasm, and their possible mode of action will be considered later. Small and varying quantities of FATS, and of CARBOHYDRATES, with traces of a number of other organic substances which need not here be enumerated, are also usually present.

Of these substances the Proteins alone have to be considered here, since they constitute the really important part of the material.

PROTEINS

White of egg or the juice of meat may be taken as examples of such proteins dissolved in water with some salts. If the salts be separated, and the water carefully driven off at a low temperature, a pure protein is left.

(A) **Physical Characters.**—The proteins from the residue of living matter—the Native Proteins, as they may be called—have a white, yellow, or brownish colour. In structure they are usually amorphous, but many have been prepared in a crystalline condition, and it is probable that all may take a crystalline form. The crystals vary in shape, being usually small and needle-like, but sometimes forming larger rhombic plates. Some proteins form apparent solutions in water, others require the presence of neutral inorganic salts, others of an acid or alkali, while some are completely insoluble without a change in their constitution. All are insoluble in alcohol and ether.

When in solution, or apparent solution, the native proteins do not dialyse through an animal membrane. They are **colloids.** Other colloidal bodies reacting much like the proteins have been prepared synthetically by chemists—*e.g.* by heating together amido-benzoic acid and phosphoric anhydride. Like other colloids proteins tend to coagulate, forming a clot just as, for instance, silicic acid may clot when carbon dioxide is passed through its solution. The native proteins are coagulated by simply heating their solution.

All proteins rotate the plane of polarised light to the left.

(B) **Chemistry.**—Proteins contain the following **chemical elements**: carbon, hydrogen, oxygen, nitrogen, and sulphur, in about the following percentage amounts:—

C.	H.	N.	S.	O.
52	7	**16**	1	24

It is important to remember the amounts of nitrogen and carbon, since proteins are the sole source of the former element in the food and an important source of the latter.

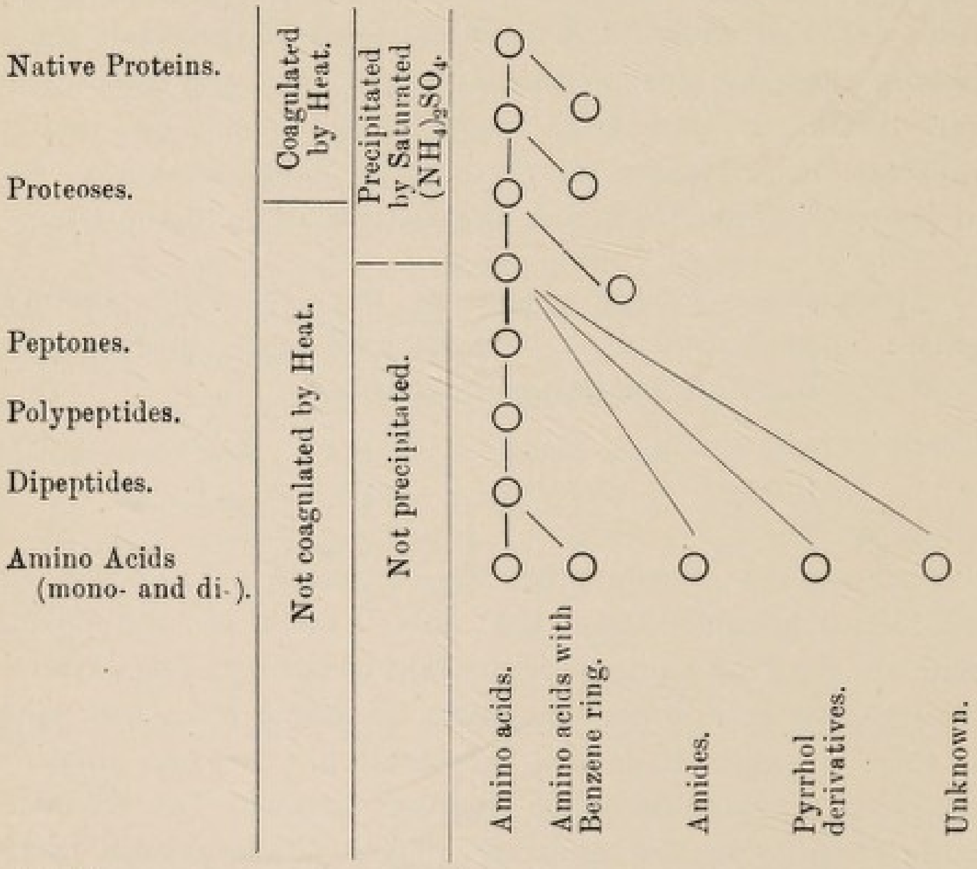
As regards the number of atoms of these elements which go to form a single molecule, information has been obtained by studying compounds with various metals. The following probable formula of the molecule of the chief protein of the white of egg is given simply to show how complex these substances are: $C_{204}H_{322}N_{52}O_{66}S_2$.

The **constitution** of the protein molecule has been investigated first by studying the products of the decomposition of the molecule by various agents, and second by attempting to build up the molecule by the synthesis of the products of disintegration.

1. Products of Decomposition

The native proteins in solution tend to break down into a series of simpler bodies, and this decomposition is greatly hastened by the action of acids or alkalies or of certain enzymes. A series of more and more simple molecules are thus produced which, as they decrease in complexity, give solutions which are less and less colloidal and less and less easily precipitated by alcohol or by neutral salts, till, finally, products are yielded which no longer give the protein tests, which are freely soluble in alcohol, and which have the characteristics of amino acids. Along with these, certain by-products are also given off.

The different stages of the disintegration of the native protein molecule may be arranged as follows[1] :—



Of the **mon-amino acids** thus formed, Leucin—amino-caproic acid—is generally the most abundant.

Of the mon-amino acids linked to the benzene nucleus, Tyrosin—in which amino-proprionic acid is linked to a benzene ring with one H replaced by OH—is the most important.

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[1] For a short account of the chemistry of these products of disintegration, see Appendix.

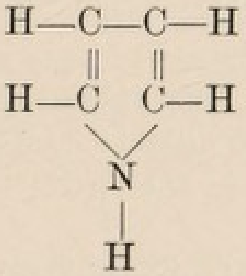
It is these acids with the benzene ring which give the xanthoproteic test—an orange colour when ammonia is added to a protein heated with nitric acid.

In most proteins the **di-amino acids** are less abundant than the mon-amino, and in some they are absent. But in a simple form of protein, discovered by Kossel, linked with nucleic acid in the heads of spermatozoa and called by him Protamine, these diamino acids constitute about 80 per cent. of the molecule.

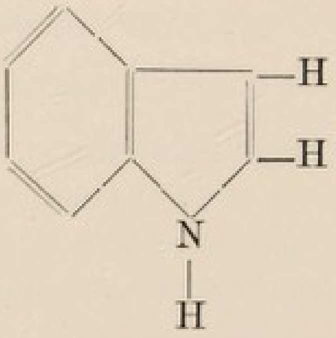
While these amino acids are normally converted to urea before being excreted, in certain states of the metabolism they appear in the urine.

The **amides** are always present in small amount, linked together as in biuret $H_2N—CO—NH—CO—NH_2$, and it is these which give the biuret test—the pink or violet when sodic hydrate is added to the protein with which a trace of cupric sulphate has been mixed.

The **pyrrhol derivatives** are ring formations of four carbons linked by an amidogen,



They are seen in indol and its derivatives, where a phyrrhol ring is attached to the benzene ring, thus

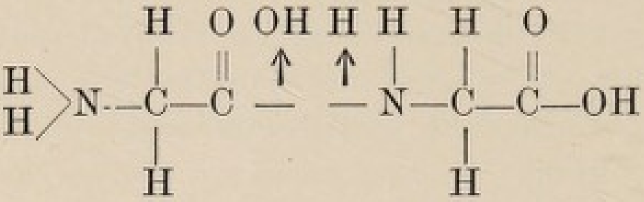


They are apt to split off from the protein still linked to aminoacetic acid (see p. 381).

The presence of indol in the protein molecule explains the purple reaction when a protein is treated with glyoxylic acid and sulphuric acid—Adamkiewicz's reaction.

2. Synthesis of the Products of Disintegration

Emil Fischer and his co-workers have succeeded in building up from the amino acids a series of bodies containing two, four, and as many as ten of the amino acid molecules, linked to one another in series, the OH of the hydroxyl of one being linked on to the amidogen of the other with the giving off of H_2O, thus:—



$$\begin{array}{ccccccccccccc} & & \mathrm{H} & & \mathrm{O} & \mathrm{OH} & \mathrm{H} & \mathrm{H} & & \mathrm{H} & & \mathrm{O} & \\ & & | & & \| & \uparrow & \uparrow & | & & | & & \| & \\ \begin{matrix}\mathrm{H}\\ \mathrm{H}\end{matrix}\!\!>\!\mathrm{N} & - & \mathrm{C} & - & \mathrm{C} & - & - & \mathrm{N} & - & \mathrm{C} & - & \mathrm{C} & -\mathrm{OH} \\ & & | & & & & & & & | & & & \\ & & \mathrm{H} & & & & & & & \mathrm{H} & & & \end{array}$$

Amino-acetic acid. Amino-acetic acid.
Glycin. Glycin.
Glycyl-glycin.

This he calls glycyl-glycin,—the amino acids which have lost the OH of the acid being characterised by the terminal *yl*.

Such compounds he calls Peptides, characterising them, according to the number of molecules linked, as Di-, Tri-, Tetra-, and Poly-peptides.

Some of the higher of these give the biuret test for proteins from the presence of the linked $CO.NH_2$ group; and if an acid with the benzene ring is in the chain, they also give the xanthoproteic test.

He has also succeeded in building the pyrrhol derivative, pyrrholidine carbonic acid, or prolin as he calls it, into polypeptides.

(C) Classification of the Proteins [1]

(A) Simple Proteins

1. **Native Proteins.**—These proteins, either alone, or combined with certain other substances, are constant ingredients of dead protoplasm and of the fluid constituents of the body. They are distinguished from all other proteins by being coagulated on heating.

There are two groups—Globulins and Albumins—the former characterised by being insoluble in distilled water, by requiring the presence of a small quantity of a neutral salt to form a

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[1] The general tests for proteins and the methods of separating the different proteins must be studied practically. (*Chemical Physiology.*)

solution, and by being precipitated from solution by half saturating with ammonium sulphate.

2. **Proteoses** (Proteins with a less complex molecule than albumins and globulins).—They may be formed from albumins (albumoses) and globulins (globuloses), by the action of superheated steam and during digestion. Under the influence of these agents, the complex molecule splits into simpler molecules and takes up water.

These proteoses form a series between the original proteins on the one hand, and the peptones or simplest proteins on the other. They may be divided into two classes:—

(*a*) Those nearly allied to the original proteins—**Proto-proteoses**, which are precipitated in a saturated solution of sodium chloride, NaCl.

(*b*) Those more nearly allied to the peptones—**Deutero-proteoses**, which are not precipitated in a saturated solution of NaCl, but are precipitated by a saturated solution of ammonium sulphate.

3. **Peptones.**—These are products of the further splitting of proteoses. Their characteristic reaction is their solubility in hot saturated ammonium sulphate solution. They diffuse very readily through an animal membrane.

(B) Conjugated Proteins

Proteins have a great tendency to link with other substances, and the following compounds are thus produced:—

(1) **Proteates** (Meta-proteins) are formed by linking acids or alkalies to the native proteins.

(2) **Nucleins**, so called because their existence was first demonstrated in the nuclei or central parts of the cells of the body, may readily be split into a protein part and into **nucleic acid**, a phosphorus-containing material of definite composition, having an acid reaction, and containing about 10 per cent. of phosphorus. In certain places the amount of nucleic acid is large in proportion to the protein, in others it is small. The term *nuclein* is usually confined to the former, *nucleo-albumin* to the latter of these. From the pure nucleic acid, which occurs along with protamine in the heads of spermatozoa, to the proteins almost free of phosphorus there is a continuous series.

Nucleic acid, when decomposed, yields phosphoric acid and a series of bodies called the **purin bodies** which belong to the class of diureides, and consist of two more or less modified urea molecules linked together by an oxy-acid with three carbons in series (see p. 427).

(3) **Phospho-proteins.**—Other compounds of proteins with phosphorus-containing molecules occur which do not yield purin bodies when decomposed. Of these vitellin, the protein of the yolk of egg, is an example.

(4) **Histones** are probably proteins linked to protamine. They occur in the globin which may be separated from blood pigment. They have a basic reaction.

(5) **Glyco-proteins.** — Proteins are linked with sugar-like substances to form compounds, the best-known example of which is **Mucin** (see p. 23).

(6) **Chromo-proteins.**—In the pigment of the blood (**Hæmoglobin**) proteins occur linked to an iron-containing molecule (p. 219).

(C) Sclero-Proteins

These are substances produced by protoplasm which are closely allied to the proteins—Keratin, Collagen, and Elastin. Their nature is considered under the tissues in which they are found.

SECTION II

THE CELL

PROTOPLASM occurs in the animal body as small separate masses or CELLS. These vary considerably in size, but, on an average, they are from 7 to 20 micro-millimetres[1] in diameter. The advantage of this subdivision is obvious. It allows nutrient matter to reach every particle of the protoplasm. In all higher animals each CELL has a perfectly definite structure. It consists of a mass of protoplasm, in which is situated a more or less defined body, the nucleus.

(A) Cell Protoplasm

This has the structure already described under protoplasm, and in different cells the reticulum or *cytomitoma* is differently arranged. In some cells there is a condensation of the reticulum, round the periphery, to form a sort of *cell membrane.*

At some point in the protoplasm of many cells, one or two small spherical bodies, the **centrosomes** (fig. 2), are found, from which rays pass out in different directions. For the detection of these bodies special methods of staining and the use of very high magnifying powers are required. They will be again considered when dealing with the reproduction of cells.

The cell protoplasm frequently contains **granules**, either formed in the protoplasm (p. 23), or consisting of material ingested by the cells.

In the protoplasm, **vacuoles** are sometimes found, and from a study of these vacuoles in protozoa, it appears that they are often formed round material which has been taken into the protoplasm, and that they are filled with a fluid which can digest the nutritious part of the ingested particles. In some cells, vacuoles may appear in the process of disintegration.

In certain cells protoplasm undergoes **changes in shape.** This may well be studied in the white cells in the blood of

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[1] The micro-millimetre is the $\frac{1}{1000}$th of a millimetre.

the frog or newt. Processes are pushed out, and these are again withdrawn, or the whole cell may gradually follow the process, and thus change its position. The processes are called pseudopodia (false feet), and the mode of movement, from its resemblance to that seen in the amœba, is called amœboid.

The part played by the network (cytomitoma) and the more fluid part (cytoplasm) in these movements is not clearly understood. The pseudopodia are at first free of network; but whether the fluid is pressed out by contraction of the meshes, or whether it actively flows out, is not known. In some cells among the protozoa movements take place along some definite line, and the reticulum is arranged more or less parallel to the line of movement. Such contractile processes, from their resemblance to muscles, have been termed **myoids**. In other protozoa the pseudopodia manifest a to-and-fro rhythmic waving movement, which may cause the cell to be moved along, or may

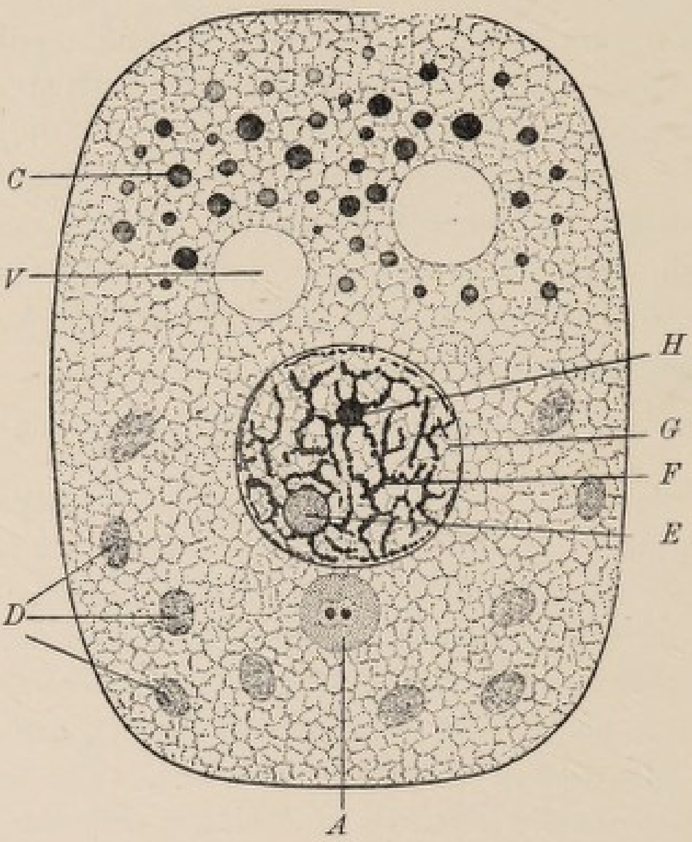


FIG. 2.—Diagram of a Cell to show structure of Protoplasm and Nucleus. In the protoplasm—*A*, attraction sphere enclosing two centrosomes; *V*, vacuole; *C*, included granules; *D*, plastids, present in some cells. In the nucleus—*E*, nucleolus; *F*, chromatin network; *G*, linin network; *H*, karyosome or net-knot (WILSON).

cause the adjacent fluid to move over the cell. Such mobile processes when permanent have been called **cilia**.

These movements are modified by the various STIMULI which modify the activity of the chemical changes in the protoplasm (p. 5). Thus, cooling diminishes, and finally stops them. Gentle heat increases them, but when a certain temperature is reached, they are stopped. Drying and various drugs, such as chloroform, quinine, etc., also arrest the movements.

Changes in the surroundings may cause either contraction or expansion, may repel or attract. When an attracting or a repelling influence, a positive or negative stimulus, acts at one side of the cell—**unilateral stimulation**—it may lead to movement of the cell away from it or towards it. Movements are produced by various chemical substances (**chemiotaxis**), or by light (**phototaxis**), or by electricity (**galvanotaxis**). If the action is towards the stimulus, it is said to be *positive*, if away from it, *negative*.

Chemiotaxis is the attraction or repulsion produced by one-sided application of chemical stimuli. This is well seen in the plasmodial masses of æthalium septicum which grow on tan. Oxygen and water both attract it towards them, and exercise a positive chemiotaxis. It is also seen in the streaming of the white cells of the blood to disintegrating tissues, or to various micro-organisms which have to be destroyed to prevent their poisoning the organism, and in the attraction exercised by the ovum upon the male element in reproduction.

Barotaxis is the effect of unilateral pressure or mechanical stimulation. Many protozoa appear quite unable to leave the solid substance—*e.g.* the microscope slide—with which they are in contact, the unilateral pressure seeming to cause a positive attraction in that direction.

Phototaxis.—Light, which plays so important a part in directing the movements of the higher plants, also acts positively or negatively on many unicellular organisms. Thus the swarm spores of certain algæ are positively attracted by moderate illumination, streaming to the source of light, while they are negatively stimulated by strong light, and stream away from it. Light also plays an important part in directing the movements of certain bacteria.

Thermotaxis.—The unilateral influence of temperature is well seen in the plasmodium of æthalium septicum which streams from cold water towards water at a temperature of about 30° C.

Galvanotaxis.—As would naturally be expected from its stimulating action, a current of electricity has a most powerful effect in directing the movements of many cells. Certain infusoria when brought between the poles of a galvanic battery may be observed to stream towards the negative pole.

The effects of this unilateral stimulation are of great importance in physiology and pathology, since they explain the streaming of leucocytes to attack micro-organisms and other poisons to the animal body, and since they seem to explain many of the apparently volitional acts of unicellular organisms. Many of these organisms appear definitely to select certain foods, but in reality they are simply compelled towards them by this unilateral stimulation.

(B) **Nucleus**

(1) **Structure.**—The nucleus, seen with a moderate magnifying power, appears in most cells as a well-defined circular or oval body situated towards the centre of the cell (figs. 1 (*c*) and 2). Sometimes it is obscured by the surrounding protoplasm. It has a granular appearance, and usually one or more clear refractile bodies—the *nucleoli*—are seen within it. It stains deeply with many reagents of a basic reaction, such as hæmatoxylin, carmine, methylene blue, etc. In some cells the nucleus is irregular in shape, and in some it is broken up into a number of pieces, giving the cell a multi-nucleated character.

It is usually composed of (*a*) fibres arranged in a complicated network (fig. 2). These fibres appear to be of two kinds: (1) forming a network similar to the cytomitoma—the linin network (*G*); and (2) forming generally a coarser network, the fibres of which have a special affinity for basic stains—the chromatin network (*F*). The chromatin substance contains a large amount of nucleic acid, and its richness in phosphorus has been demonstrated by treating the cells with ammonium molybdate and pyrogallol, which colours parts rich in phosphorus of a brown or black tint.

The chromatin fibres vary in their arrangement in different cells. Usually they form a network, but occasionally they are disposed as a continuous skein. In nuclei, with the former arrangement of fibres, swellings may be observed where the fibres unite with one another—the *nodal swellings*, or karyosomes, distinct from the nucleolus. The resting nucleus appears to be surrounded by a distinct *nuclear membrane*, which is, however, probably really a basket-like interlacement of the fibres at the periphery.

Between the fibres is (*b*) a more fluid material which may be called the *nuclear plasma* or karyoplasm. Digestion in the stomach removes the nuclear plasma, but leaves the network unacted upon.

(2) **Functions.**—The part taken by the nucleus in the general life of the cell is not yet fully understood. 1*st.* It exercises an influence on the nutritive processes, since it has been observed in certain of the large cells in lower organisms that a piece of the protoplasm detached from the nucleus ceases to grow, and, after a time, dies. Important interchanges of material go on between the nucleus and the protoplasm. 2*nd.* It is the great reproductive organ of the cell, probably playing an important part in transmitting inherited characters (see p. 194).

Reproduction of Cells

Cells do not go on growing indefinitely. When they reach a certain size they generally either divide, to form two new cells, or they die and undergo degenerative changes. The reason of this is possibly to be found in the well-known physical fact that, as a sphere increases in size, the mass increases more rapidly than the periphery. Hence, as a cell becomes larger and larger, the surface for nourishment becomes smaller and smaller in relationship to the mass of material to be nourished. Probably the altered metabolism so produced sets up the changes which lead to the division of the cell. These changes have now been very carefully studied in a large number of cells, and it has been shown that the nucleus generally takes a most important part in division.

Mitosis.—In a cell about to divide, the first change is a general enlargement of the nucleus. At the same time the centrosome becomes double, and the two portions travel from one another, but remain united by delicate lines to form a spindle-shaped structure (fig. 3, 1). The spindle passes into the centre of the nucleus, and seems to direct the changes in the reticulum. The nuclear membrane disappears, and the nucleus is thus not so sharply marked off from the cell protoplasm. The nucleoli and nodal points also disappear, and with them all the finer fibrils of the network, leaving only the stouter fibres, which are now arranged either in a skein or as loops with their closed extremity to one pole of the nucleus and their open extremity to the other. The nucleus no longer seems to contain a network, but appears to be filled with a convoluted mass of coarse fibres, and hence this stage of nuclear division is called the *convoluted stage*.

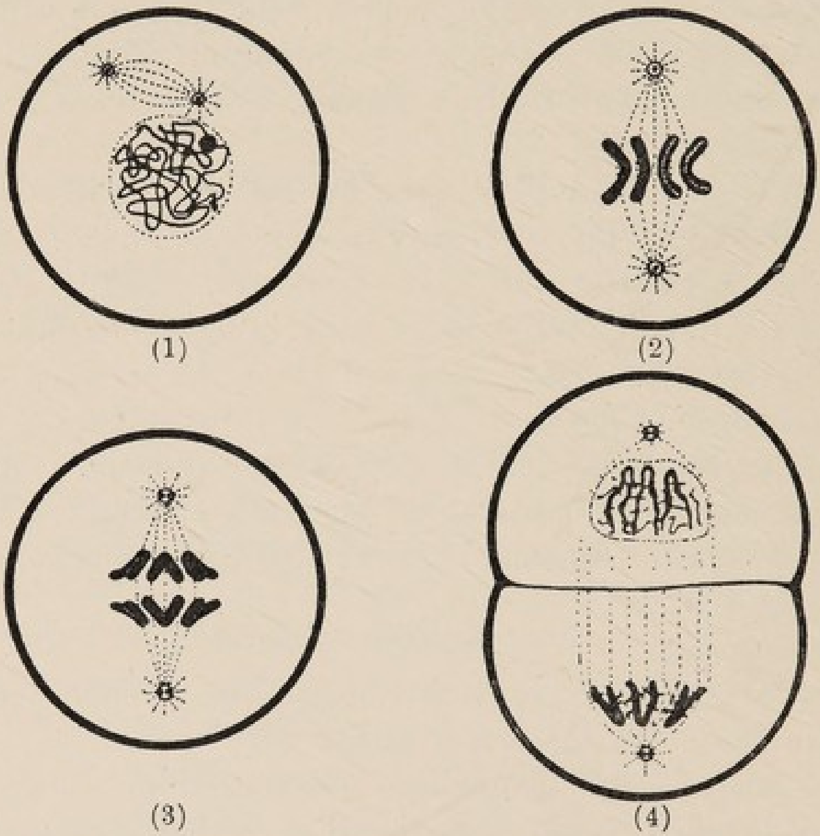


Fig. 3.—Nucleus in Mitosis : (1) Convoluted stage ; (2) Monaster stage ; (3) Dyaster stage ; (4) Complete division.

The spindle continues to grow until it occupies the whole length of the nucleus. The two centrosomes are now very distinct, and from them a series of radiating lines extends out into the protoplasm of the cell.

The nuclear loops of fibres break up into short, thick pieces ; and these become arranged around the equator of the spindle in a radiating manner, so that when the nucleus is viewed from one end it has the appearance of a rosette or a conventional star. This stage of the process is hence often called the single star or *monaster* stage (fig. 3, 2).

Each loop now splits longitudinally into two, the divisions lying side by side (fig. 3, 2).

The next change consists in the separation from one another of the two halves of the split loops—one half of each passing up towards the one polar body, the other half passing towards the other. It is the looped parts which first separate and which lead the way—the open ends of the loops remaining in contact for a longer period, but, finally, also separating. In this way, around each polar body, a series of looped fibres gets arranged in a radiating manner, so that the nucleus now contains two rosettes or stars, and this stage of division is hence called the *dyaster* stage (fig. 3, 3).

The single nucleus is now practically double. Gradually in each half finer fibres develop and produce the reticular appearance. Nuclear nodes, nucleoli, and the nuclear membrane appear, and thus two resting nuclei are formed from a single nucleus. Between these two nuclei a delicate line appears, dividing the cell in two, and the division is accomplished (fig. 3, 4).

The network of the nucleus of actively dividing cells is rich in nucleic acid, but in cells which have ceased to divide, in which the nucleus has ceased to exercise its great reproductive function, the amount of phosphorus—*i.e.* of nucleic acid—diminishes, and may be actually less than the amount in the cell protoplasm.

Amitotic Division.—In some cells the nucleus does not appear to take an active part, the cell dividing without the characteristic changes above discussed.

SECTION III

The Tissues

From the protoplasm of the cells the various tissues of the body—bone, cartilage, muscle, etc.—are formed. The structure of these must be studied practically; all that will be attempted here is to indicate how they are formed from the primitive cell.

The human body is originally a single cell, and from this, by division, a mass of simple cells is produced. In the embryo, these cells get arranged in three layers—an outer, a middle, and an inner—the epiblast, mesoblast, and hypoblast (fig. 176, p. 445).

(*A*) THE VEGETATIVE TISSUES

The Vegetative Tissues are those which support, bind together, protect, and nourish the body. They may be divided into the Epithelial Tissues, formed from the epiblast or hypoblast, and consisting of cells placed upon surfaces, and the Connective Tissues developed from the mesoblast, and consisting chiefly of formed material between cells.

I. EPITHELIUM

1. Squamous Epithelium—

(*a*) **Simple Squamous Epithelium.**—This is seen lining the air vesicles of the lungs. It consists of a single layer of flat, scale-like cells, each with a central nucleus. The outlines of these cells are made manifest by staining with nitrate of silver, which blackens the cement substance between the cells.

(*b*) **Stratified Squamous Epithelium** (fig. 4).—The skin and the lining membrane of the mouth and gullet are covered by several layers of cells. The deeper cells divide, and as the young ones get pushed upwards towards the surface, and away from the nourishing fluids of the body, their nutrition is interfered with, and the protoplasm undergoes a change into a body closely allied in composition to the proteins, *keratin.* This substance is a hard, horny material, which is well seen in the nails and hair, and in the horns and hoofs of certain animals. It first makes its appearance as a number of little masses or granules in the cells, and these run together to fill the cells which from pressure become flattened out into thin scales.

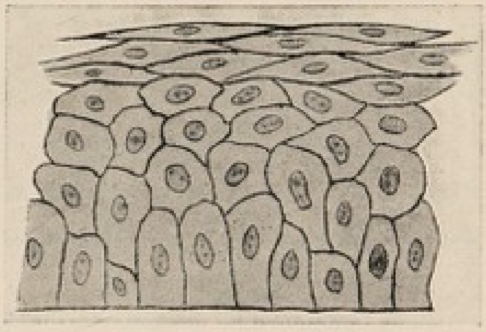


Fig. 4.—Stratified Squamous Epithelium from the cornea.

Keratin forms an admirable protective covering to the body, not only on account of its hardness and toughness, but because poisons cannot readily pass through it, and also because it is not easily acted on by chemicals. Like the proteins, it contains carbon, hydrogen, oxygen, nitrogen, and sulphur; and the first four of these elements are in about the same proportion as in the proteins. But the sulphur is in greater proportion (3 to 5 per cent.), and readily enters into combination with various substances. Hence, lead solutions colour keratin black by forming the black sulphide of lead, and are largely used as hair dyes (see *Chemical Physiology.*)

(*c*) **Transitional Epithelium.**—A slightly modified stratified squamous epithelium lines the urinary passages. It is characterised by the more columnar or pear-like shape of the deeper layers of cells.

2. **Columnar Epithelium** (fig. 5, *a*). — The inmost set of cells in the embryo lining the stomach and intestine, elongate at right angles to their plane of attachment, and become *columnar* in shape. The free border of the cells looks like a hem, an appearance which is due to a series of short rods placed side by side. Probably this is a special development of the reticulum of the protoplasm. The great function of this form of epithelium is to take up the digested matter from the stomach and intestine, and to pass it on to the blood.

Among these columnar cells a certain number of peculiarly modified cells, **chalice cells,** are always found. They are larger than the columnar cells, and somewhat pear-shaped, being attached by their small extremity. Their protoplasm is collected at their point of attachment, while the body of the cell is filled with *mucin*, a clear, transparent material.

3. **Secreting Epithelium.**—A number of cells, having for their function the production of some material which is to be excreted from the cell, are arranged as the lining of depressions, the *glands*.

The simplest form of gland is the *simple tubular*—a test-tube-like depression, lined by secreting cells. Instead of being simple, the tube may be branched, when the gland is said to be *racemose*. In many glands the secreting epithelium is confined to the deeper part of the tube, the *alveolus* or *acinus* (fig. 6), while the more superficial part is lined by cells which do not secrete, forming the *duct*.

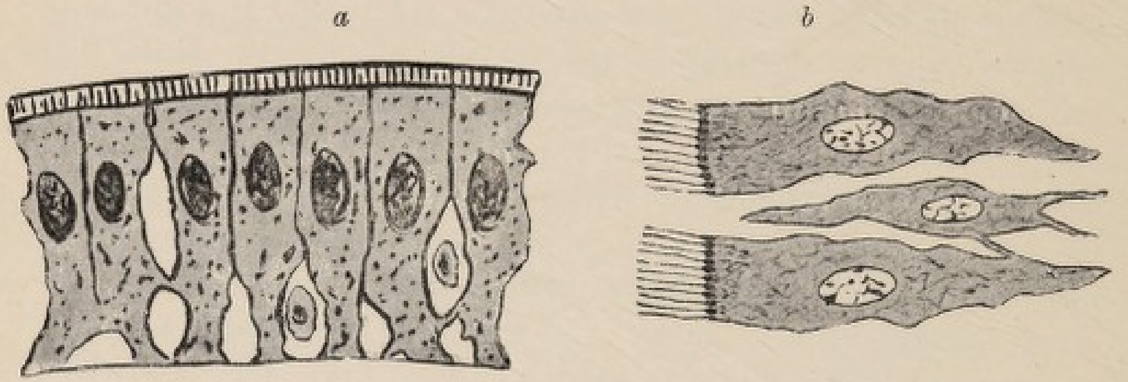


FIG. 5.—(*a*) Columnar Epithelium from the small intestine ; (*b*) Ciliated Epithelium from the trachea.

In many situations several simple glands are grouped together, their ducts opening into one common duct, and a *compound gland* results.

Secreting epithelium varies according to the material it produces.

(A) **Mucin-secreting Epithelium.**—Many glands have for their function the production of mucus, a slimy substance of use in lubricating the mouth, stomach, intestine, etc. The acini containing such cells are usually large. The cells themselves are large, and are placed on a delicate basement membrane, a condensation of the subjacent fibrous tissue, which bounds the acinus. The nuclei are situated near to the attached margin of the cells, which are somewhat irregular in shape, and are packed close together. Their appearance varies according to whether the gland has been at rest or has been actively secreting.

Resting State.—In the former case, in the fresh condition, the cells are large, and pressed closely together. Their protoplasm is filled with large shining granules. After treatment with reagents, each cell becomes distended with clear, transparent mucin formed by the swelling and coalescence of the granules.

After Activity.—After the gland has been actively secreting, the cells are smaller and the granules are much less numerous, being chiefly situated at the free extremity of the cell, and leaving the nucleus much more apparent.

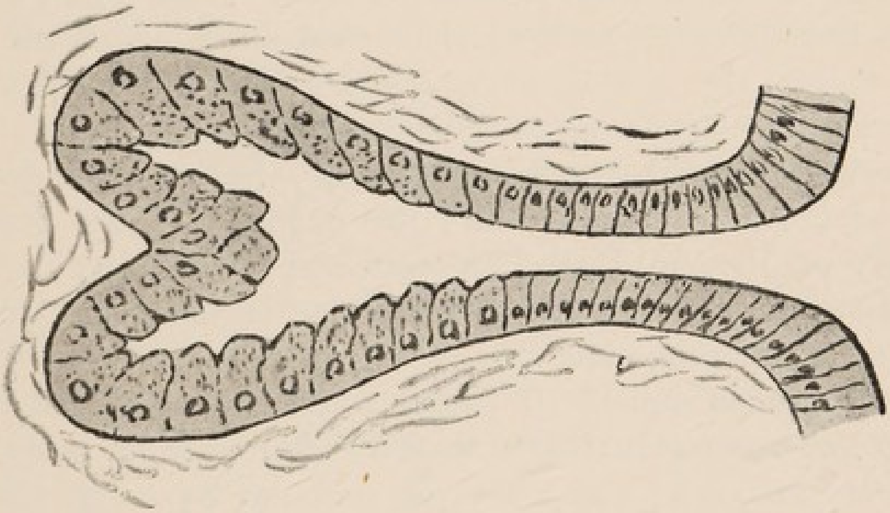


Fig. 6.—A Zymin-secreting Gland, to show an acinus lined by secreting cells containing zymogen granules and the duct.

This form of epithelium, during the resting condition of the gland, takes up nourishing matter and forms this mucin-yielding substance. During the active state of the gland, the mucin-yielder is changed to mucin, and is extruded from the cells into the lumen of the gland.

Mucin is a substance of great importance in the animal economy. When precipitated and freed from water it is white and amorphous. On the addition of water it swells up and forms a glairy mass. In the presence of alkalies it forms a more or less viscous solution, and from this solution it is precipitated by acetic acid. In composition it is a protein linked to a molecule allied to the sugars, glucosamine

$C_6H_{11}NH_2O_5$, and is therefore called a glyco-protein. When boiled with an acid it yields sugar. (See *Chemical Physiology.*)

In adult life the great function of mucin is to give to certain secretions a slimy character which renders them of value as lubricants.

(B) **Zymin-secreting Epithelium.**—Another form of secreting epithelium of great importance is that which forms the various juices which act upon the food to digest it. These juices owe their activity to the presence of enzymes or zymins.

A zymin-forming gland after a prolonged period of rest shows cells closely packed together, so that it is difficult to make out their borders. The protoplasm is loaded with granules which are much smaller than those seen in the mucin-forming cells, and which do not swell up in the same way, under the action of reagents. The nucleus is often obscured by the presence of these granules.

When the gland has been actively secreting, the granules become fewer in number, and are confined to the free extremity of the cell; they are obviously passing out. The cell becomes smaller, and its outline is more distinct and the nucleus more apparent.

The granules which fill the cells are not composed of the active enzyme. If extracts of the living cells be made, they are inert, and it is only after the granules have left the cell, or are in the process of leaving, that they become active. Hence, the granules are said to be composed of zymin-forming substance or zymogen.

The series of changes are parallel to those described in the mucin-forming cells. During the so-called resting state of the gland, the cells are building up zymogen. When the gland is active, the cells throw off the material they have accumulated, and it undergoes a change to zymin.

(C) **Excreting Epithelium** does not manufacture materials of use in the animal economy, but passes substances *out of* the body. Such epithelium is seen in the kidneys, sweat glands, sebaceous glands, mammary glands, and perhaps in the liver. The cells are composed of a granular protoplasm, in which the presence of the material to be excreted either in its fully elaborated condition, or in process of preparation, may frequently be demonstrated—*e.g.* fat globules, iron containing particles. These cells do not merely take up material from the blood and pass it out, but they may profoundly alter it before getting rid of it.

4. **Ciliated Epithelium** (fig. 5, p. 22).—The cells are usually more or less columnar, and the free border is provided with a series of hair-like processes, the *cilia*, which vary in size in different situations.

In the living state the cilia are in constant rhythmic motion, each cilium being suddenly whipped or bent down in one direction, and then again assuming the erect position.

All the cilia on a surface work harmoniously in the same direction, and the movement passes from the cilia of one cell to those of the next in regular order, beginning at one end of the surface and passing to the other.

As a result of this constant harmonious rhythmic movement, any matter lying upon the surface is steadily whipped along it; and since the cilia usually work from the inner parts of the body to the outside, this matter is finally expelled from the body.

The movements of the cilia are dependent on the changes in the protoplasm, and everything which influences the rate of chemical change modifies the rate of ciliary movement, which may thus be taken as an index of the protoplasmic activity.

II. CONNECTIVE TISSUES

1. **Mucoid Tissue.**—The cells of the mesoblast of the embryo, which at first lie in close apposition with one another, become separated, remaining attached by elongated processes. Between the cells, a clear, transparent substance makes its appearance, forming a soft jelly-like tissue. This tissue is widely distributed in the embryo as a precursor of the connective tissues, and after birth it is still to be seen in the pulp of a developing tooth and in the vitreous humour of the eye (fig. 7).

2. **Fibrous Tissue.**—As development advances, the cells of mucoid tissue elongate and become spindle-shaped, and are continued at their ends into fibres (fig. 8). These cells are often called *fibroblasts*.

The connective tissues are thus clearly distinguished from the epithelia by having the formed material *between* and not *in* the cells. They are composed of the following parts :—

I. Formed material.
  (*a*) Fibres.
  (*b*) Matrix.
II. Spaces (Connective Tissue Spaces).
III. Cells.

I. Formed Material.—(A) *Fibres* (fig. 9)—1*st*. Non-elastic (White Fibres). These are delicate, transparent fibrils arranged in bundles, which do not branch, and which have a mucin-like matrix between them. They are composed of a non-elastic substance, *collagen*. This is closely allied to the proteins, and gives the protein reactions faintly, but it does not yield tyrosin when decomposed, while it does yield amino-acetic acid. It is insoluble in cold water, but swells up and becomes transparent

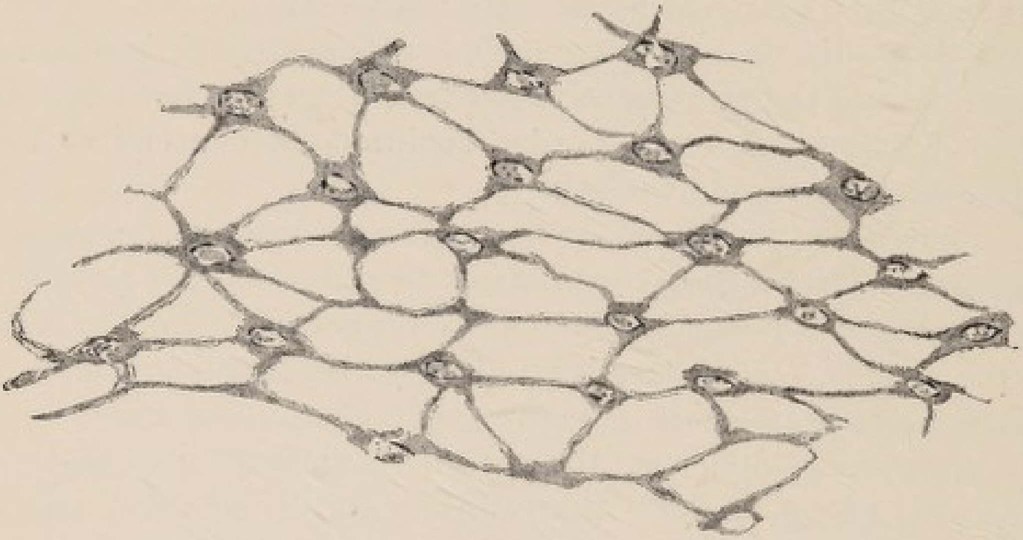


FIG. 7.—Mucoid Tissue from an embryo rabbit.

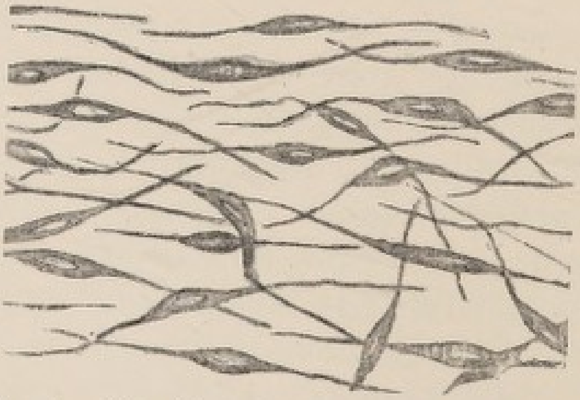


FIG. 8.—Fibroblasts from young fibrous tissue.

in acetic acid. It has a great affinity for carmine, and stains a pink colour with it. When boiled, it takes up water to form a hydrate, *Gelatin*, a substance soluble in hot water, and forming a jelly on cooling. (See *Chemical Physiology.*)

2nd. Elastic Fibres. These are highly refractile elastic fibres, which branch and anastomose with one another. They are composed of *Elastin*, a near ally of the proteins, which is insoluble both in cold and hot water, and is not acted on by acetic acid. It stains yellow with picric acid, and has no affinity for carmine.

(B) *Matrix.*—This is composed of the mucus-like material which is so abundant in the fœtal mucoid tissue.

According to the arrangement of these fibres, and to the preponderance of one or other variety, various types of fibrous tissue are produced.

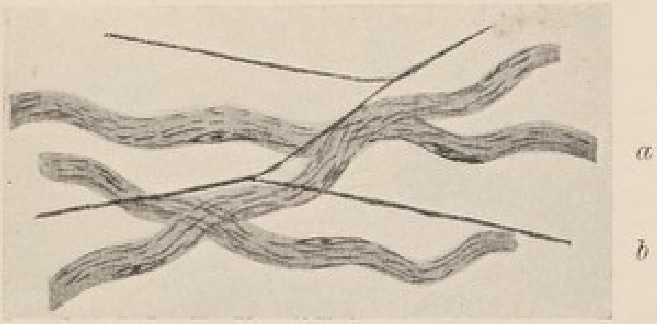


FIG. 9.—Bundles of White Fibres, with Fibroblasts (*a*) and Elastic Fibres anastomosing with one another (*b*).

When a padding is required, as under the skin and under mucous membranes, the fibres are arranged in a loose felt work to constitute *areolar tissue.*

In *fascia*, in *tendon sheaths*, and in *flat tendons*, the fibres are closely packed together to form more or less definite layers. In *tendons* and *ligaments* the fibres run parallel and close together. In ordinary tendons, where no elasticity is required, the fibres are of the white or non-elastic variety. In ligaments where elasticity is desirable the elastic fibres preponderate.

II. The **spaces** of fibrous tissue vary with the arrangement of the fibres. In the loose areolar tissue under the skin they are very large and irregular, in fascia they are flattened, while in tendon, where the fibres are in parallel bundles, they are long channels.

III. The **cells** of fibrous tissue (Fibroblasts) vary greatly in shape. In the young tissue they are elongated spindles, from the ends of which the fibres extend. In some of the loose fibrous tissues they retain this shape, but in the denser tissues they get squeezed upon, and are apt to be flattened and to develop processes thrust out into the spaces.

In certain situations, peculiar modifications of Fibroblasts are to be found—

(A) **Endothelium.**—When these cells line the larger connective tissue spaces they become flattened, and form a covering membrane, called an endothelium. Such a layer lines all the serous cavities of the body, and the lymphatics, blood vessels, and heart, which are all primarily large connective tissue spaces. To demonstrate the outlines of these cells it is necessary to stain with nitrate of silver, which has a special affinity for the interstitial substance, and which thus forms a series of black lines between the cells.

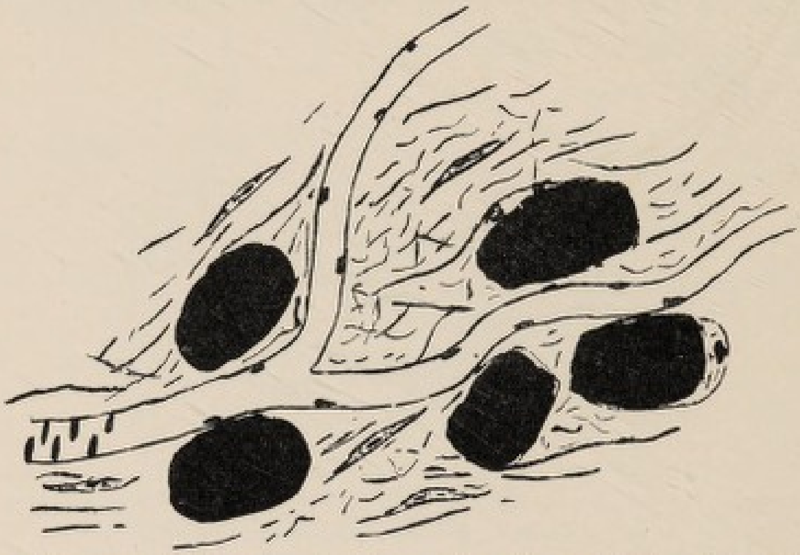


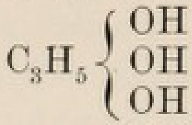
FIG. 10.—Fat Cells stained with osmic acid, and lying alongside a small blood vessel.

(B) **Fat Cells.**—In the areolar tissue of many parts of the body fat makes its appearance in the cells round the smaller blood vessels, and when these cells occur in masses *Adipose Tissue* is produced.

Little droplets of oil first appear, and these become larger, run together, and finally form a large single globule, distending the cell, and pushing to the sides the protoplasm and nucleus as a sort of capsule (fig. 10).

If the animal be starved, the fat gradually disappears out of the cell, and in its place is left a clear albuminous fluid which also disappears, and the cell resumes its former shape.

The **fats** are esters usually of the triatomic alcohol glycerin—



$$C_3H_5\begin{cases}OH\\OH\\OH\end{cases}$$

by the replacement of the hydrogen of the hydroxyl molecules by the radicles of the fatty acids.

The most abundant fatty acids of the body are:—

Palmitic Acid, $C_{16}H_{31}O,OH$
Stearic Acid, $C_{18}H_{35}O,OH$
Oleic Acid, $C_{18}H_{33}O,OH$

and from these the three fats—

Palmitin, $C_3H_5(O,C_{16}H_{31}O)_3 = C_{51}H_{98}O_6$
Stearin, $C_3H_5(O,C_{18}H_{35}O)_3 = C_{57}H_{110}O_6$
Olein, $C_3H_5(O,C_{18}H_{33}O)_3 = C_{57}H_{104}O_6$

are produced.

It will be observed that the molecules of these fats are very rich in carbon and hydrogen, and very poor in oxygen—*i.e.* they contain a large amount of material capable of being oxidised, and thus capable of affording energy in the process of combustion.

The fats resemble one another in being insoluble in water, but soluble in ether and in hot alcohol. As the alcohol cools, they separate out as crystals. They differ from one another in their melting point, palmitin melting at the highest and olein at the lowest temperature. Fat which is rich in palmitin and stearin, as ox fat, is thus hard and solid at the ordinary temperature of the air, while fats rich in olein, as dogs' fats, are semi-fluid at the same temperature. The olein acts as a solvent for the fats of a higher melting point. (For tests, see *Chemical Physiology.*)

The functions of adipose tissue are twofold:—

1*st. Mechanical.*—The mass of adipose tissue under the skin is of importance in protecting the deeper structures from injury. It is a cushion on which external violence expends itself. Further, this layer of subcutaneous fat prevents the loss of heat from the body, being, in fact, an extra garment.

2*nd. Chemical.*—Fat, on account of its great quantity of unoxidised carbon and hydrogen, is the great storehouse of energy in the body (p. 393).

(C) **Pigment Cells.**—In various parts of the eye the connective tissue and other cells contain a black pigment—*Melanin.* The precise mode of origin of this pigment is not known. It contains carbon, hydrogen, nitrogen, oxygen, and it may also contain iron. It may be formed directly in the cells, or it may be produced by the cells from the pigment of the blood. Its function in the eye is to prevent the passage of light through the tissues in which it is contained.

The cells containing the pigment are branched, and in many cases they possess the power of movement. This is specially well seen in such cells in the skin of the frog, where contraction and expansion may be easily studied under the microscope. By these movements the skin, as a whole, is made lighter or darker in colour. The movements of these cells are under the control of the central nervous system.

2. **Lymph Tissue.**—One peculiar modification of fibrous tissue is often described as a special tissue under the name of *Lymph Tissue.* It is composed of a delicate network of white fibres, the interstices of which communicate with lymphatic vessels, and contain masses of simple protoplasmic cells, *lymphocytes*, often in a state of active division. So numerous are these that it is impossible to make out the network under the microscope until they have been removed by washing.

Lymph tissue is very widely distributed throughout the body, and is of great importance in connection with nutrition.

3. **Cartilage.**—While fibrous tissue is the great binding medium of the body, support is afforded in fœtal life and in certain situations in adult life by cartilage.

When cartilage is to be formed, the embryonic cells become more or less oval, and secrete around them a clear pellucid capsule. This may become hard, and persist through life, as in the so-called *parenchymatous cartilage* of the mouse's ear.

(1) *Hyaline Cartilage.*—Development, however, usually goes further, and before the capsule has hardened, the cartilage cells again divide, and each half forms a new capsule which expands the original capsule of the mother cell, and thus increases the amount of the formed material. This formed material has a

homogeneous, translucent appearance, and a tough and elastic consistence, and cuts like cheese with the knife (fig. 11).

The formed material of cartilage is not a special substance, but a mixture of chondroitin-sulphuric acid with collagen in combination with proteins. Chondroitin when decomposed yields glucosamine, a sugar-like substance containing nitrogen, and glycuronic acid, another substance closely related to the sugars (p. 23).

Cartilage is surrounded by a fibrous membrane, the perichondrium, and frequently no hard and fast line of demarcation can be made out between them. The fibrous tissue gradually becomes less fibrillated—the cells become less elongated and more oval, as if the interfibrillar substance increased in amount and became of the same refractive index as the fibres. During old age a fibrillation of the homogeneous-looking cartilage is brought out, especially in costal cartilage, by the deposition of lime salts in the matrix, between the fibres. It was long ago shown that in inflammation of cartilage this fibrillation appears; and by digesting in baryta water, a similar structure may be brought out. The close connection of cartilage with fibrous tissue is thus clearly demonstrated.

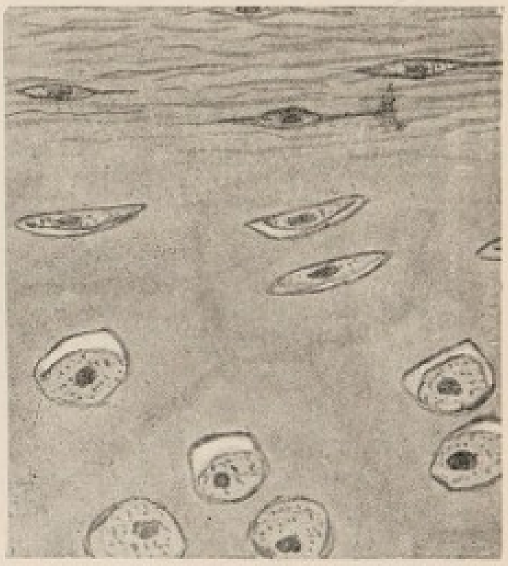


FIG. 11.—Hyaline Cartilage covered by perichondrium.

Such homogeneous or hyaline cartilage precedes most of the bones in the embryo, and covers the ends of the long bones in the adult (articular cartilage), forms the framework of the larynx and trachea, and constitutes the costal cartilages.

(2) *Elastic Fibro-Cartilage.*—In certain situations—*e.g.* in the external ear—a specially elastic form of cartilage is developed, elastic fibres appearing in the cartilaginous matrix, and forming a network through it.

(3) *White Fibro-Cartilage.*—In other situations—*e.g.* the intervertebral discs—a combination of the binding action of fibrous tissue with the padding action of cartilage is required;

and here strands of white fibrous tissue with little islands of hyaline cartilage are found. It is also found when white fibrous tissue, as tendon, is inserted into hyaline cartilage, and is really a mixture of two tissues—white fibrous tissue and cartilage.

4. **Bone.**—The great supporting tissue of the adult is BONE.

(1) DEVELOPMENT AND STRUCTURE.—Bone is formed by a deposition of lime salts in layers or lamellæ of white fibrous tissue; but while some bones, as those of the cranial vault, face, and clavicle, are produced entirely in fibrous tissue, others are preformed in cartilage, which acts as a scaffolding upon which the formation of bone goes on.

FIG. 12.—Intra-membranous Bone Development in the lower jaw of a fœtal cat. Above, the process of ossification is seen shooting out along the fibres, and on the lower surface the process of absorption is going on. Two osteoclasts—large multinucleated cells—are shown to the left.

Intra-membranous Bone Development.—This may be well studied in any of the bones of the cranial vault where cartilage is absent (fig. 12).

At the centre of ossification the matrix between the fibres becomes impregnated with lime salts, chiefly the phosphate and carbonate. How this deposition takes place is not known; and how far it is dependent on the action of cells has not been clearly determined. As a result of this, the connective tissue cells get enclosed in definite spaces, *lacunæ*, and become *bone corpuscles.* Narrow branching channels of communication are left between these lacunæ, the *canaliculi.* This deposition of lime salts spreads out irregularly from the centre into the adjacent fibrous tissue, and this advance is preceded by a line of actively growing cells, sometimes called *osteoblasts.* The fully formed adult bone, however, is not a solid block, but is composed of a compact tissue outside, and of a spongy bony tissue, *cancellous tissue*, inside. This cancellous tissue is formed as a secondary process. Into the block of calcareous matter, formed as above described, processes of the fibrous tissue burrow, carrying in blood vessels, lymphatics, and numerous cells. This burrowing process seems to be carried on by the connective tissue cells, which eat up the bony matter formed. In doing this they frequently change their appearance, becoming large and multi-nucleated (*osteoclasts*). Thus the centre of the bone is eaten out into a series of channels, in which the marrow of the bone is lodged, and between which narrow bridges of bone remain.

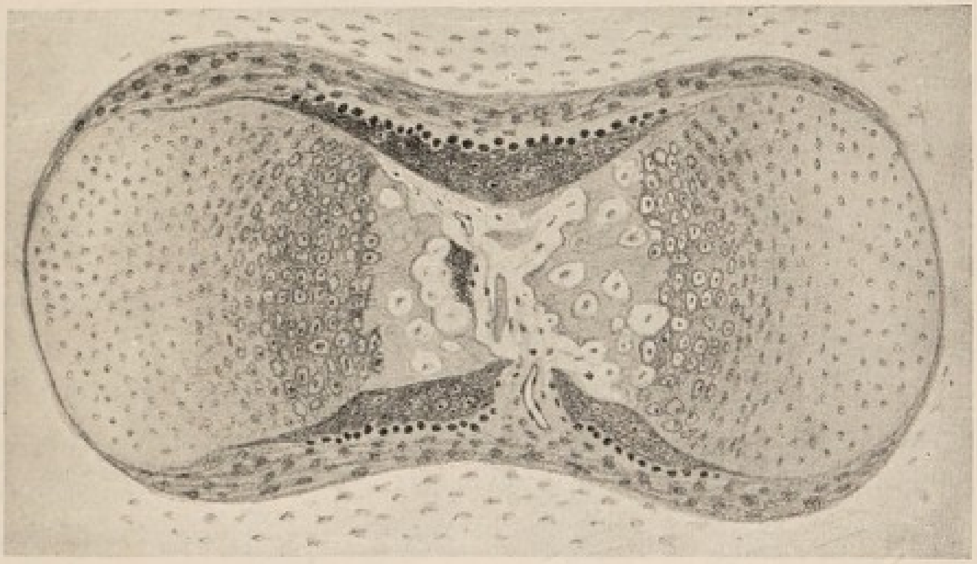


FIG. 13.—Intra-cartilaginous Bone Development. A phalanx of a fœtal finger showing the formation of periosteal bone round the shaft; the opening up of the cartilage at the centre of ossification; the vascularisation of the cartilage by the invasion of periosteum; and the calcification of the cartilage round the spaces.

It is by the extension of the calcifying process outwards, and the burrowing out of the central part of the bone, that the diploë and cancellous tissue are produced.

Intra-cartilaginous Bone Development.—In the bones preformed in cartilage, the process is somewhat more complex, although all the bone is formed in connection with fibrous tissue, the cartilage merely playing the part of a scaffolding and being all removed. Where the adult bone is to be produced, a minute model is formed in hyaline cartilage in the embryo, and this is surrounded by a fibrous covering, the perichondrium. In the deepest layers of this perichondrium the process of calcification takes place, as described above, and spreads outwards, thus encasing the cartilage in an ever-thickening layer of bone (fig. 13). This was demonstrated by inserting a silver plate under the periosteum, and showing that bone was deposited outside of it.

At the same time, in the centre of the cartilage, at what is called the *centre of ossification*, the cells begin to divide actively, and, instead of forming new cartilage, eat away their capsules, and thus open out the cartilage spaces (fig. 13). Into these spaces processes of the perichondrium bore their way, carrying with them blood vessels, and thus rendering the cartilage vascular (fig. 13). The vascularisation of the centre of the cartilage having been effected, the process of absorption extends towards the two ends of the shaft of cartilage, which continues to elongate. The cartilage cells divide and again divide, and, by absorbing the material between them, form long irregular canals running in the long axis of the bone, with trabeculæ of cartilage between them. Into these canals the processes of the periosteum extend, and fill them with its fibrous tissue. A deposition of lime salts takes place upon the trabeculæ, enclosing cells of the invading fibrous tissue, and thus forming a crust of bone, while the cartilage also becomes calcified. If this calcification of the cartilage and deposition of bone were to go on unchecked, the block of cartilage would soon be converted to a solid mass of calcified tissue. But this does not occur. For, as rapidly as the trabeculæ become calcified, they are absorbed, while the active changes extend farther and farther from the centre to the ends of the shaft. The centre is thus reduced to a space filled by fibrous tissue which afterwards becomes the bone marrow.

The process of absorption does not stop at the original block of cartilage; but after all of this has been absorbed, the bone formed round the cartilage (the periosteal bone) is attacked by burrowing processes from inside and outside, which hollow out long channels running in the long axis of the bone. These are the *Haversian spaces* (fig. 14). Round the inside of these, calcification occurs, spreading inwards in layers, and enclosing connective tissue cells, until, at length, only a small canal is left, an *Haversian canal*, containing some connective tissue, blood vessels, lymphatics, and nerves, with layer upon layer of bone concentrically arranged around it. This constitutes an *Haversian system.* In this way the characteristic appearance of the shaft of a long bone is produced (fig. 14), with layers of calcified fibrous tissue, the bone lamellæ, arranged as Haversian, interstitial, peripheral, and medullary lamellæ.

One important function performed by the cartilage is in bringing about the increase in *length* of the bones. In addition to the centre of ossification in the shaft, at each end of the bone one or more similar centres of ossification form. These are the epiphyses. Between these and the central rod of bone—the diaphysis—a zone of cartilage exists until adult life, when the bones stop growing. In this zone, the cells arrange themselves in vertical rows, divide at right angles to the long axis of the bone and form cartilage. This cartilage as it is formed is attacked by the bone-forming changes at the diaphysis and epiphyses, but the amount of new cartilage formed is proportionate to this, and thus a zone of growing cartilage continues to exist until early adult life, when epiphyses and diaphysis join and

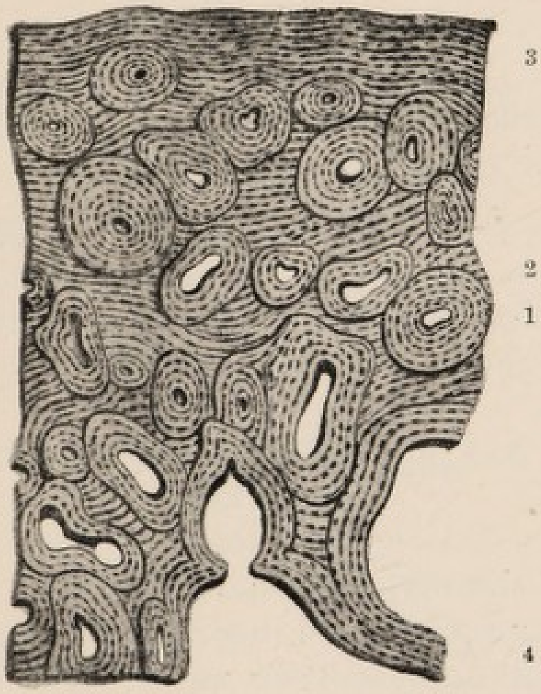


FIG. 14.—Cross section through part of the shaft of an adult long bone to show the arrangement in lamellæ distributed as Haversian (1), interstitial (2), peripheral (3), and medullary (4).

growth in length is stopped. The rate and extent of this growth of the cartilage has an important influence on the growth of the individual.

(2) CHEMISTRY.—The composition of adult bone is roughly as follows:—

- Water, 10 per cent.
- Solids, 90 per cent.
  - Organic, 35 per cent.—chiefly collagen.
  - Inorganic, 65 per cent.
    - Calcium phosphate, 51.
    - „ carbonate, 11.
    - „ fluoride, 0·2.
    - Magnesium phosphate, 1.
    - Sodium salts, 1.

The points to be remembered are the small amount of water, the large amount of inorganic matter, chiefly calcic phosphate, and the nature of the organic matter—collagen.

(*B*) THE MASTER TISSUES OF THE BODY, MUSCLE AND NERVE

By means of the epithelial and connective tissues the body is protected, supported, and nourished. It performs purely vegetative functions, but it is not brought into relationship with its environments. By the development of **nerve** and **muscle** the surroundings are able to act upon the body, and the body can react upon its surroundings.

These tissues may therefore be called the **Master Tissues**, and it is as their servants that all the other tissues functionate.

So far as the chemical changes in the body are concerned, muscle is more important than nerve, for three reasons—First, it is far more bulky, making up something like 42 per cent. of the total weight of the body in man; second, it is constantly active, for even in sleep the muscles of respiration, circulation, and digestion do not rest; and third, the changes going on in it are very extensive, since its great function is to set free energy from the food. *So far as the metabolism of the body is concerned, muscle is the master tissue.* For muscle we take food and breath, and to get rid of the waste of muscle the organs of excretion act. Hence it is in connection with muscle that all the problems of nutrition—digestion, respiration, circulation, and excretion—have to be studied.

I. MUSCLE

The two great functions of muscle are—

To perform mechanical work.
To liberate heat.

1. Muscle at Rest

Structure : Chemistry and Physical Characters

The first trace of the evolution of muscle is found among the infusoria, where, in certain cells, in parts of the protoplasm, the network or cytomitoma is arranged in long parallel threads in the direction of which the cell contracts and expands. Such a development has been termed a *myoid*.

1. Structure of Muscle

Even a cursory examination of mammalian muscle shows that those of the trunk and limbs, **skeletal muscles,** are different from those of such internal organs, as the bladder, uterus and alimentary canal, **visceral muscles.**

The **visceral muscles** appear to be formed from cells similar to ordinary connective tissue cells. These elongate, acquire a covering, and their protoplasm becomes definitely longitudinally fibrillated by the arrangement of the cytomitoma. They thus become spindle-shaped cells, varying in length from about 50 to 200 micro-millimetres. A covering membrane, the *sarcolemma*, develops. This is thin, but tough and elastic, and it adapts itself to the surface of the cell, unless when this is excessively shortened, in which case the sarcolemma may be thrown into folds, which give the cell the appearance of cross-striping. The nucleus is usually long, almost rod-shaped, and is independent of the cytomitoma (fig. 15, *a*).

The **skeletal muscles** develop from a special set of cells, early differentiated as the muscle-plates in the mesoblast down each side of the vertebral column of the embryo. Each cell elongates. The nucleus divides across, but the cell, instead of also dividing, lengthens and continues to elongate as the two daughter nuclei again divide. The cytomitoma becomes arranged longitudinally, and a series of transverse markings appear across the cell. Lastly, a covering, the *sarcolemma*, develops, and the fully-formed fibre is produced (fig. 15, *b*).

This consists of three parts—

1. The **Sarcolemma** is a delicate, tough, elastic membrane closely investing the fibre, and attached to it at Dobie's lines.
2. The **Muscle corpuscles** consist of little masses of protoplasm each with a nucleus, which lie just under the sarcolemma.
3. The **Sarcous substance** is made up of a series of longitudinal fibrils consisting of alternate dim and clear bands—the former staining deeply with eosin. In the middle of the clear band is a narrow dim line, Dobie's line. The fibres and fibrils tend to break across in the region of the clear band, showing that they are weakest at that part. The clear band differs from the dim band, not only in not taking up eosin, but also in the fact that it entirely prevents the passage of polarised light except in one position of the analysing prism, while the dim band allows polarised light to pass, whatever be the position of the prisms.

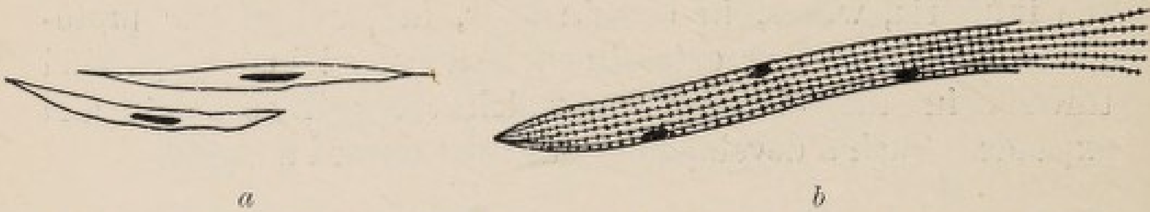


Fig. 15.—(*a*) Fibres of Visceral Muscle ; (*b*) Fibres of Skeletal Muscle to show sarcolemma, muscle corpuscles, and sarcous substance composed of fibrils showing transverse markings.

A probable explanation of these facts is that the sarcous substance is made up, like other protoplasm, of a mitoma and plasma; that the mitoma is arranged in a series of longitudinal fibres, which are broader and stronger in the dim band, and lie closely applied to one another, side by side, while in the clear band they are thinner, and are separated from one another by plasma; and that at Dobie's line there is a swelling on each fibril.

2. Chemistry of Muscle

Like all other living tissues, muscle is largely composed of water. It contains about 75 per cent. The 25 per cent. of solid constituents is made up of a small quantity, about 3 per cent., of ash, and 22 per cent. of organic substances. The ash consists chiefly of potassium and phosphoric acid, with small amounts of sulphuric and hydrochloric acids and of sodium, magnesium, calcium, and iron. The sulphuric acid is derived from the sulphur of the proteins, and a part of the phosphoric acid is derived from the phosphorus of the nucleins of muscle, and probably from other organic combinations.

1. **Proteins.**—Of the organic constituents, by far the greater part is made up of **Proteins.** These may be divided into—

(*a*) Those soluble in neutral salt solutions.
(*b*) Those insoluble in them.

(*a*) The first class of bodies consists entirely of three globulins. Two of these—**Myosinogen** and **Paramyosinogen**—have the peculiar property of clotting under certain conditions, to form what is called **Myosin,** and this process, which occurs after death, is the cause of death stiffening. The *post-mortem* change is supposed to be brought about by the development of an enzyme, since a glycerine extract of dried muscle rapidly causes the formation of myosin. The third globulin, **Myoglobulin,** does not undergo this change. These three proteins are contained in the plasma—the juice which can be expressed from muscles kept near the freezing point. If the plasma is warmed it rapidly clots, just as it does *post-mortem.*

(*b*) The insoluble protein of muscle, **Myostromin,** seems to be of the nature of a nuclein, and probably forms the framework of the fibres. It is always mixed with the collagen of the fibrous tissue of muscle, and it may be separated by dissolving it in carbonate of soda solution, from which it may be again precipitated by weak acetic acid. (*Chemical Physiology.*)

Collagen derived from the fibrous tissue holding the muscle fibres together is also present, and yields gelatin on boiling.

In addition to the proteins, small quantities of other organic substances are found in muscle.

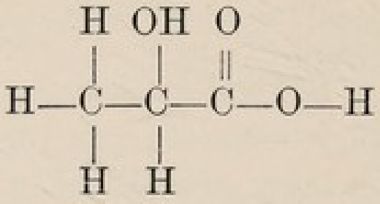
2. **Carbohydrates.—Glucose** ($C_6H_{12}O_6$) is present in muscle, as in all other tissues.

Glycogen $x(C_6H_{10}O_5)$—a substance closely allied to ordinary starch, but giving a brown reaction with iodine—is always present in muscle at rest. If the muscle has been active, the amount of glycogen diminishes, being probably converted to glucose, and used for the nourishment of the tissue. (For the chemistry of the carbohydrates, see p. 344.)

3. **Fat** is present in small quantities in the fibres, and often in very considerable quantities in the fibrous tissue between the fibres.

4. **Inosite**, formerly called muscle sugar, is present in small amounts. It is not a sugar, but a benzene compound.

5. **Sarcolactic Acid.**—Hydroxy-propionic acid—

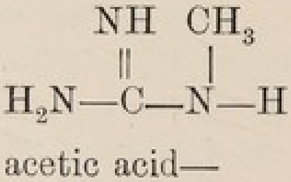


$$\begin{array}{ccccccccc} & & H & & OH & & O & & \\ & & | & & | & & \| & & \\ H & — & C & — & C & — & C & — O — & H \\ & & | & & | & & & & \\ & & H & & H & & & & \end{array}$$

This dextro-rotatory isomere of ordinary lactic acid is increased in muscle during activity and during death stiffening.

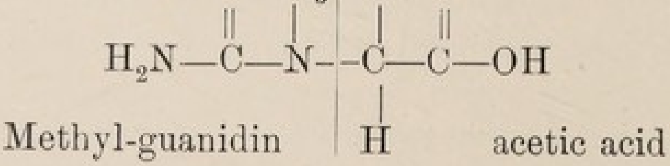
6. **Extractives.**—If dried muscle is treated with alcohol a series of bodies containing nitrogen may be extracted. The chief of these is **Creatin**, or methyl-guanidin-acetic acid. Guanidin $C.NH(NH_2)_2$ is a near ally of urea $CO(NH_2)_2$, being formed by replacing the O with NH.

Methyl-guanidin is produced by replacing an H in guanidin by CH_3—



$$\begin{array}{ccccccc} & & NH & & CH_3 & & \\ & & \| & & | & & \\ H_2N & — & C & — & N & — & H \end{array}$$

If this is linked to acetic acid—



$$\begin{array}{ccccccccc} & & H—N & & CH_3 & & H & & O \\ & & \| & & | & & | & & \| \\ H_2N & — & C & — & N & - - & C & — & C—OH \\ & & & & & & | & & \\ & & & & & & H & & \end{array}$$

is produced.

7. **The Colour of Muscle** varies considerably, some muscles being very pale, almost white in colour—*e.g.* the breast muscles of the fowl; others again being distinctly red, even after all the blood has been removed. This red colour is, in some cases, due to the presence of the pigment of blood, *hæmoglobin*, but in certain muscles it is due to a peculiar set of pigments, Myohæmatins, giving different reactions from the blood pigment.

3. Physical Characters of Muscle

1. Muscle is **translucent** during life, but, as death stiffening sets in, it becomes more opaque.

2. Muscle is markedly **extensile** and **elastic.** A small force is sufficient to change its shape, but when the distorting force is removed it returns completely to its original shape, provided always that the distortion has not overstepped the limits of elasticity.

When a distorting force is suddenly applied to muscle—*e.g.* if a weight is suddenly attached—the distortion takes place at first rapidly, and then more slowly, till the full effect is produced. If now the distorting force is removed the elasticity of the muscle brings it back to its original form, at first rapidly, and then more slowly. (*Practical Physiology.*)

The advantages of these properties of muscle are, that every muscle in almost all positions of the parts of the body is stretched between its point of origin and insertion. When it contracts it can therefore act at once to bring about the desired movement, and no time is lost in preliminary tightening. Again, the force of contraction, acting through such an elastic medium, causes the movement to take place more smoothly, and without jerks. Experimentally, too, it has been ascertained that a force acting through such an elastic medium produces more work than when it acts through a rigid medium.

The extensibility of muscle is of value in allowing a group of muscles to act without being strongly opposed by their antagonistic group. For instance, suppose the extensor muscles of the arm were not readily extensile, when the flexors acted, a large amount of their energy would have to be employed in elongating the extensors. Similarly the elasticity of the muscles tends to bring the parts back to their normal position when the muscles have ceased to contract. It must not, however, be imagined that, in all movements of one set of muscles, the antagonistic muscles are relaxed, although they may be elongated. Often they are in a state of activity so as to guide the movements which are being produced (see p. 58).

Tonus of Muscle.—The tense condition of resting muscle between its points of origin and insertion is not merely due to passive elasticity, but is in part caused by a continuous contraction kept up by the action of the nervous system. If the nerve to a group of muscles be cut, the muscles become soft and flabby and lose their tense feeling.

3. **Heat Production.**—Muscle, like all other living protoplasm, is in a state of continued chemical change, constantly undergoing decomposition and reconstruction. As a result of this chemical change, heat is evolved. But the heat evolved during rest of muscle is trivial.

4. **Electrical Conditions.**—Muscle when at rest is iso-electric, but if one part is injured, it acts to the rest like the zinc plate in a galvanic battery—becomes electro-positive; and hence, if a wire passes from the injured to the uninjured part round a galvanometer, a current is found to flow along the wire from the uninjured to the injured part, just as, when the zinc and copper plates in a galvanic cell are connected, a current flows through the wire from copper to zinc. This is the Current of Injury (p. 63). (*Practical Physiology.*)

2. Muscle in Action

A. Skeletal Muscle

1. Methods of making Muscle Contract

Skeletal muscle remains at rest indefinitely until stimulated to contract, usually by **changes in the nerves**. We desire to contract our biceps: certain changes occur in our brain, these set up changes in the nerves passing to the biceps, and the muscle contracts.

Can skeletal muscle be made to contract without the intervention of nerves—can it be **directly stimulated**?

To answer this, some means of throwing the nerves out of action must be had recourse to. If curare, a South American arrow poison, be injected into an animal—*e.g.* into a frog, the brain of which has been destroyed—it soon loses the power of moving. When the nerve to a muscle is stimulated, the muscle no longer contracts. But, if the muscle be directly stimulated by any of the various agents to be afterwards mentioned, it at once contracts.

It might be urged that the curare leaves unpoisoned the endings of the nerve in the muscle, and that it is by the stimulation of *these* that the muscle is made to contract. But that these are poisoned is shown by the fact that if the artery to the leg be tied just as it enters the muscle, so that the poison acts upon the whole length of the nerve except the nerve endings in the muscle, stimulation of the nerve still causes muscular contraction. Only when the curare is allowed to act upon the nerve endings in the muscle does stimulation of the nerve fail to produce any reaction in the muscle, while direct stimulation of the muscle causes it to contract. This clearly shows that it is the *nerve endings which are poisoned by curare,* and that therefore the application of stimuli to the muscle must act directly upon the muscular fibres (fig. 16). (*Practical Physiology.*)

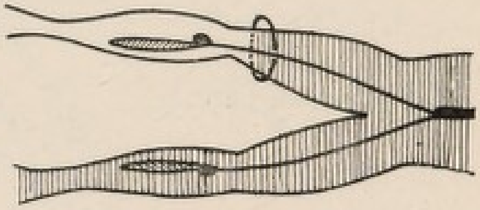


FIG. 16.—Curare Experiment to show sciatic nerves exposed to curare, but nerve endings protected on the left side; while on the right side the curare is allowed to reach the nerve endings in the muscle.

Muscle, however, is more *readily* stimulated through its nerves, and a knowledge of the points of entrance of the nerves into muscles, the *motor points,* is of importance in medicine in indicating the best points at which to apply electrical stimulation (fig. 17).

Various means may be used **to make the muscle contract.**

1*st.* Various chemical substances when applied to a muscle make it contract before killing it, while others kill it at once. Among the former may be mentioned dilute mineral acids and metallic salts. (*Practical Physiology.*)

2*nd.* A sudden mechanical change such as may be produced by pinching, tearing, or striking the muscle will cause it to contract. (*Practical Physiology.*)

3rd. Any sudden change of temperature, either heating or cooling, stimulates muscle. A slow change of temperature has little or no effect. Every muscle, however, passes into a state of contraction, heat stiffening, when a sufficiently high temperature to coagulate its protein constituents is reached. This, however, is not a true living contraction. (*Practical Physiology.*)

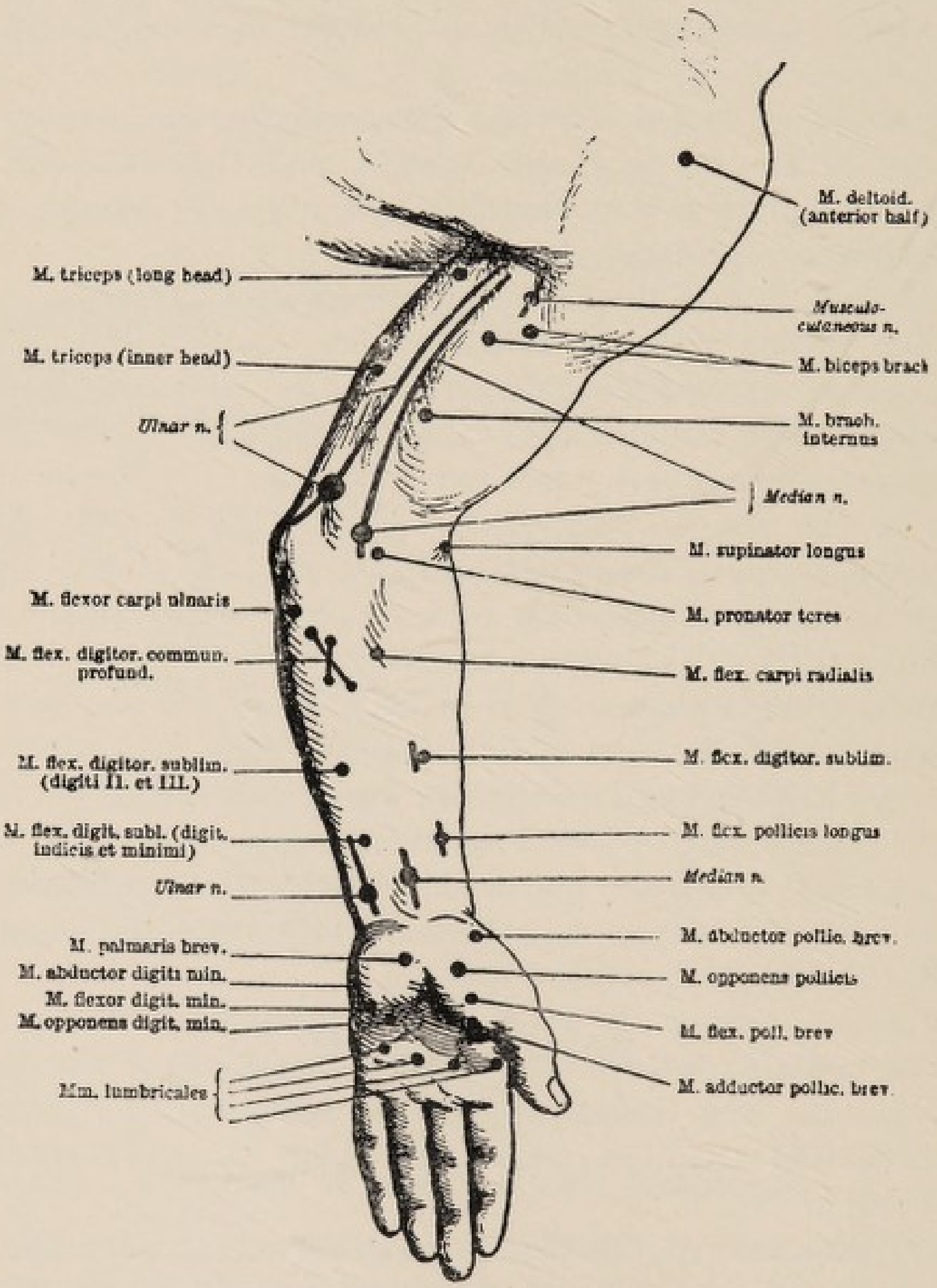


Fig. 17.—Motor Points of Arm.

4th. Muscle may also be made to contract by any sudden change in an electric current passed through it, whether the current be suddenly allowed to pass into it or suddenly cut out of it, or whether it is suddenly made stronger or weaker. (*Practical Physiology.*)

This method of stimulating muscle is constantly used in medicine. It is a matter of no importance how the electricity is procured, but most usually it is obtained either—

1*st.* Directly from a galvanic battery or electric main; or
2*nd.* From an induction coil.

If a galvanic battery or current from the main be used—(1) On making (closing) the current, and upon breaking (opening) the current, a contraction results. While the current is flowing through the muscle, the muscle *usually* remains at rest; but if the current is suddenly increased in strength or suddenly diminished in strength, the muscle at once contracts. With strong currents a sustained contraction—galvanotonus—may persist while the current flows. (*Practical Physiology.*)

It is the suddenness in the variation of the strength of the current rather than its absolute strength which is the factor in stimulating, as may be shown by inserting some form of rheonome into the circuit by which the current may be either slowly or rapidly varied.

(2) If a current be made weaker and weaker, breaking ceases to cause a contraction, while making still produces it. That is, the stimulus on making is stronger than that on breaking.

(3) The two poles do not produce the same effect. The negative pole or kathode—that coming from the zinc plate of the battery—causes contraction of the muscle on closing; while the positive pole or anode causes contraction at opening. This may be summarised as follows:—

1. Contraction on closing; contraction on opening.
2. Closing contraction stronger than opening contraction.
3. Contraction at kathode on closing, at anode on opening.

1. C.C · C.O
2. CC > CO
3. CKC CAO

How can these facts be explained?

Electrotonus

A study of the influence of the current on the muscle while it is passing through it throws important light on this point. (*Practical Physiology.*)

While the current simply flows through the muscle no contraction is produced, but the excitability is profoundly modified.

Round the kathode it becomes more easily stimulated, while round the anode or positive pole it becomes less easily stimulated. This may be expressed by saying that the part of the muscle under the influence of the kathode is in a state of *katelectrotonus*, of increased excitability or of more unstable equilibrium, while the part of the muscle under the influence of the anode is in a state of *anelectrotonus*, of decreased excitability or of more stable equilibrium. Now it is well known that any sudden disturbance of the equilibrium or balance of a series of bodies is apt to cause them to fall asunder. For instance, if from a house of cards one card is suddenly drawn out, the whole structure passes into a condition of unstable equilibrium and is apt to fall to pieces. So with a muscle, if it be suddenly made unstable, as at the kathode on closing, a breaking down occurs and a contraction results. On the other hand, suppose a house of cards is built and made extra stable by introducing some additional cards at the foundation, then if these cards are suddenly withdrawn the chances are that the house falls to bits. So with a muscle. When the current is opened the removal of the state of increased stability at the positive pole may cause a breaking down and produce the anodal opening contraction.

The study of electrotonus thus explains why any sudden change in the flow of electricity through a muscle stimulates it. It further explains why the stimulation and contraction start from the kathode on closing and from the anode on opening; and why the closing contraction is stronger than the opening, since the sudden production of a condition of actual instability must act more powerfully than the simple sudden removal of a condition of increased stability.

This law of Polar Excitation, while it applies to muscle and nerve, does not apply to all protoplasm. Thus amœba shows contraction at the anode and expansion at the kathode when a galvanic current is passed through it.

When the **galvanic current is used to stimulate muscles through the skin** in man or in other living animals, the different action of the two poles is not so marked as in the excised muscle of the frog, because the current, passing through the skin above the muscle to enter the body, flows not along but rather across the muscle, and thus, under each pole applied to the skin there is on one side of the muscle the effect of an entering current—*anode*—and on the other, of a leaving current—*kathode* (fig. 18). Thus the same bit of muscle or nerve is subjected to anelectrotonus on one side and katelectrotonus on the other, and the effects of the two poles, and therefore of closing and of opening, tend to be combined, although the influence of the pole placed immediately above the muscle predominates. Hence with a strong current contraction occurs both on closing and on opening at both poles. As the current is weakened, the contraction at the kathode on opening first disappears, because the anode is not predominant. Next, contraction at the anode on opening disappears because the anodal stimulation is so much weaker than the kathodal. Then, the contraction at the anode on closing goes because the kathode is not predominating; and, finally, the contraction at the kathode on closing also disappears. When the muscle is in

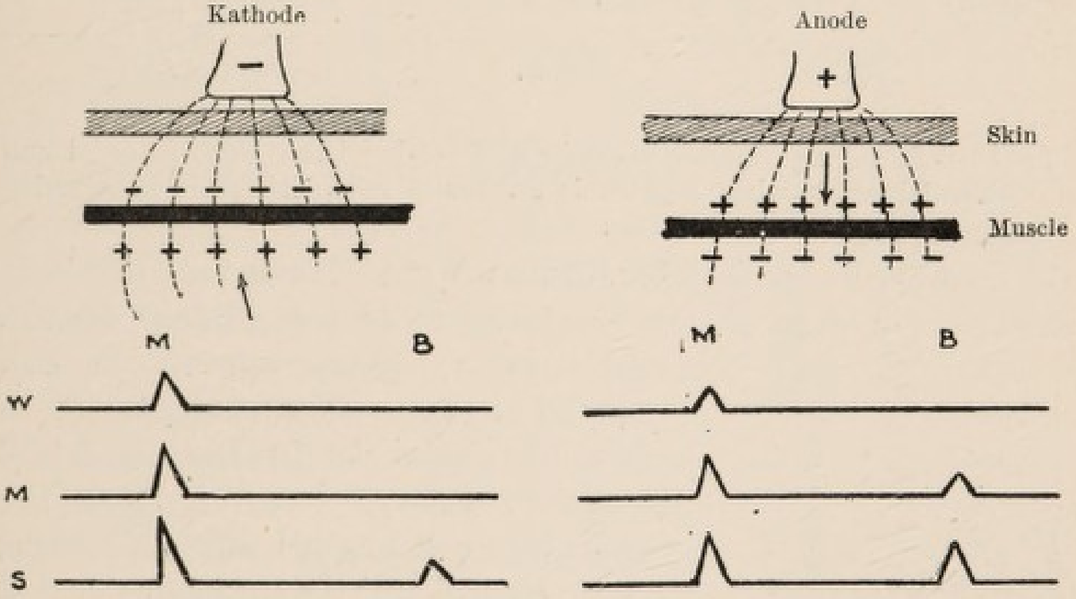


Fig. 18.—Electrical Stimulation of human muscle or nerve to show the passage of the current *across* the structure, and the consequent combination of effects under each pole. *M*, making or closing the current ; *B*, opening or breaking the current. *W*, weak ; *M*, medium ; *S*, strong current.

one stage of the degeneration which follows separation from its nerve, the anodal closing contraction (fig. 18, Anode *M*) becomes much exaggerated. This is called the **reaction of degeneration**.

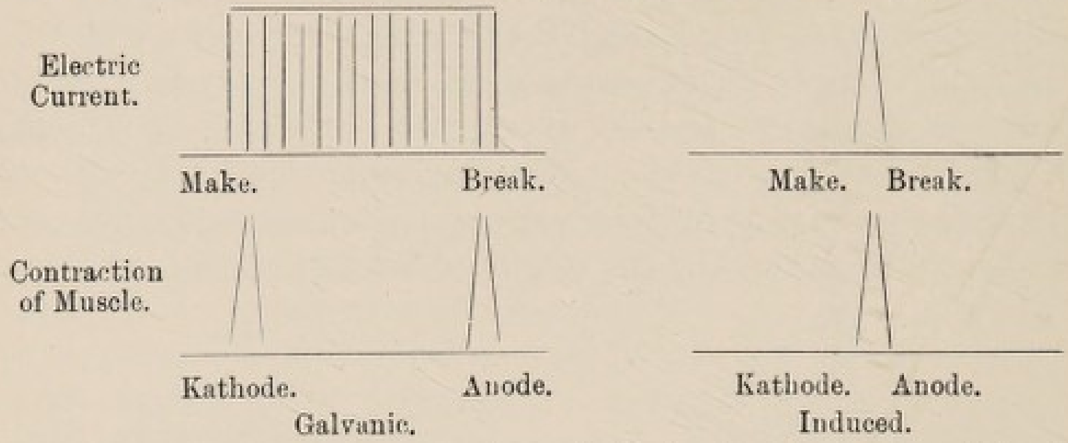


FIG. 19.—To show separation of make and break stimuli and of anodal and kathodal effects when a galvanic current is used, and their combination when the induction coil is used.

When muscle is stimulated by **induced electricity** (fig. 20) the question is much easier, for, with each make and break or each sudden alteration in the strength of the primary circuit, there is a sudden appearance and equally sudden disappearance of a flow of electricity in the secondary coil. If, therefore, wires from the secondary coil are led off to a muscle, each change in the primary circuit causes the sudden and practically simultaneous appearance and disappearance of an electric current in the muscle, and this of course causes a contraction. But here the effects of closing and opening the current are practically fused, and hence the influence of the anode and kathode, and of closing and opening, need not be considered (fig. 20). (*Practical Physiology.*)

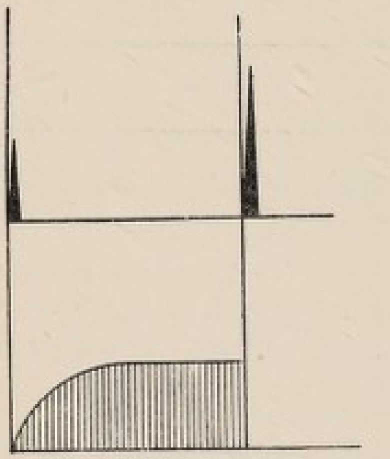


FIG. 20.—Course of Electric Current in primary circuit (lower line), and in secondary circuit (upper line) of an induction coil. Observe that in the secondary the make (upstroke) and break (downstroke) are combined, and that a stronger current is developed in the secondary circuit upon breaking than upon making the primary circuit.

It must, of course, be remembered, that in an induction coil the opening of the primary circuit produces a more powerful current in the secondary coil than the closure of the primary circuit, and therefore a more powerful stimulation of the muscle (fig. 20).

2. The Changes in Muscle during Contraction

I. Change in Shape

The most manifest change is an alteration in the shape of the muscle. It becomes *shorter and thicker*. This anyone can see by studying their own biceps muscle. Contraction of muscle, however, is not a necessary result of excitation. Thus, a part of a muscle when dipped in water may fail to contract when stimulated, but may manifest its excitation by conducting the impulse to the part of the muscle not in the water and thus making it contract.

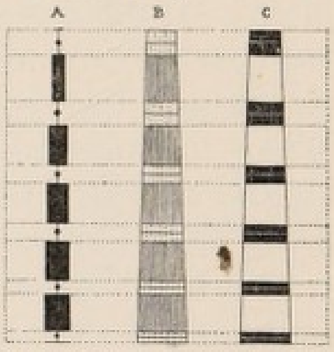


Fig. 21.—Contraction of Skeletal Muscle — relaxed above, contracted below. *A* is a diagram of the change in a fibril; *B* shows the shading of the clear band; and *C* shows the absence of any alteration in the influence of the two bands on polarised light.

In skeletal muscle the shortening and thickening of the muscle as a whole is due to the **shortening and thickening of the individual fibres and their fibrils.**

In these fibrils the shortening and thickening is most marked in the dim band. The clear band also shortens, and at the same time it becomes darker till, in the fully contracted muscle, it may be as dark as the dim band (fig. 21).

These appearances may best be explained on the assumption that the fibrils are the part of the fibre which shorten and thicken, and that these fibrils chiefly shorten where they are thickest—in the dim band. At the same time, by the contraction of the fibrils in the clear band, adjacent dim bands may be supposed to be pulled nearer to one another, and to cast a shadow over the clear band. That no actual chemical change takes place in either band seems to be indicated by the facts that they retain their reaction to polarised light and staining reagents.

Usually the contraction of a muscle occurs **simultaneously in all the fibres.** This is because a nerve fibre passes to every muscular fibre, and sets all in action together. When, as sometimes occurs in disease, the nervous mechanism acts abnormally, the muscular fibres may not all act at once, and a peculiar fibrillar twitching of the muscle may be produced.

If the muscle be *directly* stimulated at any point, the contraction starts from that point and passes as a **wave of contraction** outwards along the fibres. This may be seen by sharply percussing the fibres of the pectoralis major in the chest of an emaciated individual. The rate at which the wave of contraction travels is ascertained by finding how long it takes to pass between any two points at a known distance from one another. Its velocity is found to vary much according to the kind of muscle and the condition of the muscle. In the striped muscular fibres of a frog in good condition it travels at something over *three metres* per second. When the muscle is in bad condition the wave passes more slowly, and in an exhausted muscle it may remain at the point of stimulation. (*Practical Physiology.*)

The cause of the propagation of this wave is simply the continuity of the muscle fibres. The fibres stimulated are set in action, and the evolution of energy in these stimulates the adjacent fibres, and so the contraction passes along the muscle as a flame passes down a trail of gunpowder.

Contraction of Muscle as a whole may best be studied under the following heads:—

1st. The course of contraction.
2nd. The extent of contraction.
3rd. The force of contraction.

1st. **Course of Contraction** (fig. 22).

By attaching the muscle (*M*) to a lever (*L*), and allowing the point of the lever to mark upon some moving surface, a magnified record of the shortening of the muscle when stimulated may be obtained.

A revolving cylinder covered with a smoke-blackened, glazed paper is frequently used for this purpose, and to stimulate and mark the moment of stimulation an induction coil (*p.c.*, *s.c.*), with an electro-magnetic marker (*T.M.*), introduced in the primary circuit, may be employed.

To find the duration of the contraction, a tuning fork, vibrating 100 times per second, may be made to record its vibrations on the surface. (*Practical Physiology.*)

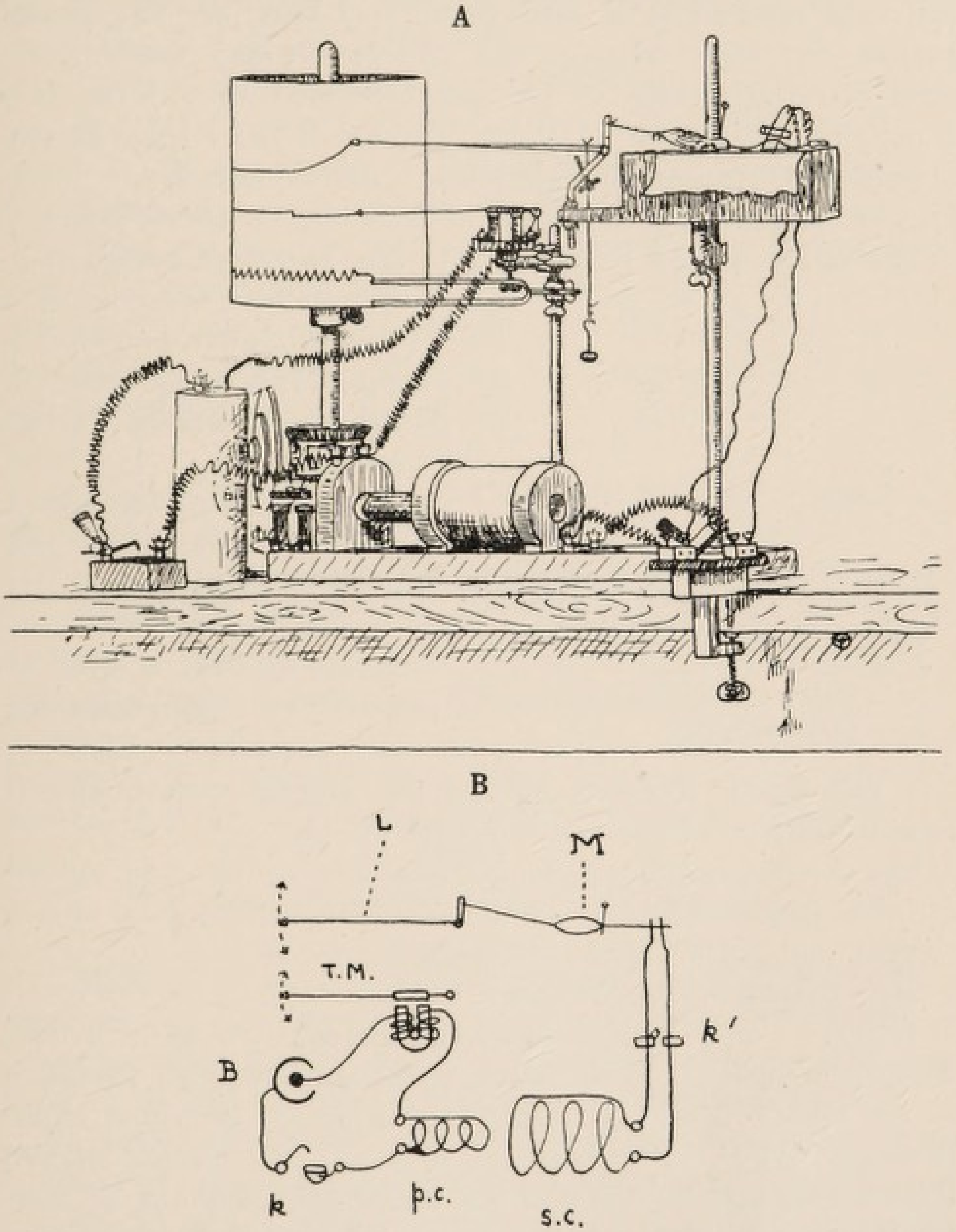


Fig. 22.—A, Method of Recording Muscular Contraction. B, Key to Parts of Apparatus. *M*, Muscle attached to crank lever *L*. *p.c.*, Primary circuit, and, *s.c.*, secondary circuit of an induction coil with short circuiting key, *k′*, in secondary circuit. *B*, Galvanic cell, and, *k*, a mercury key for closing and opening the primary circuit. *T.M.*, A lever moved by an electro-magnet placed in the primary circuit and marking the moment of stimulation. In A, a tuning fork beating 100 times per second is shown recording its vibration on the drum.

In this way such a tracing as is shown in fig. 23 is produced.

From this it is evident that the muscle does not contract the very moment it is stimulated, but that a short **latent period** supervenes between the stimulation and the contraction. In the muscle of the frog attached to a lever this usually occupies about $\frac{1}{100}$th second; but if the change in the muscle is directly photographed without any lever being attached to it, this period is found to be very much shorter.

The latent period is followed by the **period of contraction.** At first it is sudden, but it becomes slower, and finally stops. Its average duration in the frog's muscle is about $\frac{4}{100}$th second.

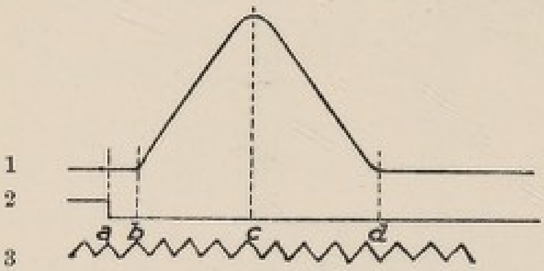


FIG. 23.—Trace of Simple Muscle Twitch (1) showing periods of latency, contraction, and relaxation; record of moment of stimulation (2); and a time record made with a tuning fork vibrating 100 times per second (3).

The **period of relaxation** follows that of contraction, and it depends essentially on the elasticity of the muscle, whereby it tends to recover its shape when the distorting force is removed. The recovery is therefore at first fast and then slow, and it lasts in the frog's muscle about $\frac{5}{100}$th second.

The whole contraction thus lasts only about $\frac{1}{10}$th second in the frog's muscle. In mammalian muscle it is much shorter, and in the muscle of insects shorter still.

2nd. **Extent of Contraction.**

While, as will be afterwards considered, the extent of contraction is modified by the strength of stimulus and the state of the muscle, the total *extent* of contraction is primarily determined by the length of the muscle. If a muscle of two inches contracts to one-half its length, the amount of contraction is one inch, but if a muscle of four inches contracts to the same amount, it shortens by two inches.

3rd. **Force of Contraction** is measured by finding what weight the muscle can lift, and the **absolute force** of a muscle may be expressed by the weight which is just too great to be lifted. The lifting power of a muscle depends primarily upon its thickness or *sectional area*. The absolute force of a muscle may therefore be expressed per unit of sectional area. In man the absolute force per 1 sq. cm. is from 5000 to 10,000 grams. The force of contraction is, however, modified by so many other conditions that no definite figure can be given.

The force of contraction during different parts of the contraction period may be recorded by making the muscle pull upon a strong spring, so that it can barely shorten. The slight bending of the spring may be magnified and recorded by a long lever, and in this way it is found that the ordinary curve of contraction gives a fair representation of the variations in the force. This method of recording the force of contraction is sometimes called the **isometric** method, in distinction to the **isotonic** method of letting the muscle act on a light lever.

In clinical medicine the DYNAMOMETER is used for measuring the force of muscular contraction. (*Practical Physiology.*)

The contraction of muscles in the body of the mammal may be studied by recording their thickening by Marey's muscle forceps, in which a tambour placed between the limbs of a pair of forceps is pressed upon by the contraction of a muscle or group of muscles lying between the opposite limbs, and transmits the pressure to another tambour which carries a recording lever. (*Practical Physiology.*)

II. The Factors modifying the Contraction

1. **Kind of Fibre.**—In skeletal muscles the pale fibres contract more rapidly and completely than the red fibres, which contain more sarcoplasm and nuclei. The peculiarities of the contraction of visceral muscles will be considered later (p. 70).

2. **Species of Animal.**—In vetebrates the contraction of the muscles of warm-blooded animals is more rapid than the contraction in cold-blooded animals. The most rapidly contracting muscles are met with in insects.

3. **State of the Muscle.**—(1) *Continued Exercise.*—If a muscle is made to contract repeatedly, the contractions take place more and more sluggishly. At first each contraction is greater in extent, but, as the contractions go on, the extent diminishes as **fatigue** becomes manifest, and stimulation finally fails to call

forth any response. This condition is probably caused by the accumulation of the products of activity in the muscle acting as poisons upon its protoplasm, for the same phenomena may be induced by the application of dilute acids and certain other drugs, and may be removed for a time by washing out the muscle with salt solutions (fig. 24). (*Practical Physiology.*)

(2) *Temperature.*—If a muscle be warmed above the normal temperature of the animal from which it is taken, all the phases of contraction become more rapid, and the contraction is at first increased in extent, but subsequently decreased in force. If, on the other hand, a muscle be cooled, the various periods are prolonged. At first the contraction becomes greater and more powerful, but as the cooling process goes on it becomes less and less, until finally the most powerful stimuli produce no effect. Cooling has thus practically the same effect as fatigue (fig. 24). (*Practical Physiology.*)

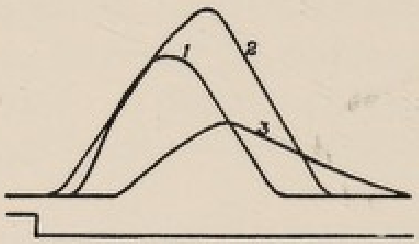


FIG. 24.—Influence of continued Exercise on Skeletal Muscle—(1) the first trace; (2) a trace after moderate exercise; (3) a trace when fatigue has been induced.

(3) Many drugs modify muscular contractions, *e.g.* veratrin enormously prolongs the relaxation period. (*Practical Physiology.*)

5. **Strength of Stimulus.**—A stimulus must have a certain intensity to cause a contraction. The precise strength of this *minimum stimulus* depends upon the condition of the muscle. The application of stronger and stronger stimuli causes the muscular contraction to become more and more rapid, more and more complete, and more and more powerful. But increase in the contraction is not proportionate to the increase in the stimulus. If the stimulus is steadily increased, the increase in contraction becomes less and less. This may be represented diagrammatically in the accompanying figure, where the continuous lines represent the strength of the stimuli and the dotted lines the extent of the contractions (fig. 25).

After a certain strength of stimulus has been reached, further increase of the stimulus does not cause any increase in the muscular contraction. This smallest stimulus which causes the maximum muscular contraction is called the *optimum stimulus.*

Increasing the strength of the stimulus shortens the latent period, but lengthens the periods of contraction and relaxation.

6. **Resistance to Contraction—Weight to be Lifted.**—Starting from the extent of muscular contraction without any load it is found that small weights attached to the muscle actually increase the extent of contraction, but that greater weights diminish it, until finally, when a sufficient weight is applied, the muscle no longer contracts at all, but may actually slightly lengthen, because its extensibility is increased during contraction (fig. 26, *a*).

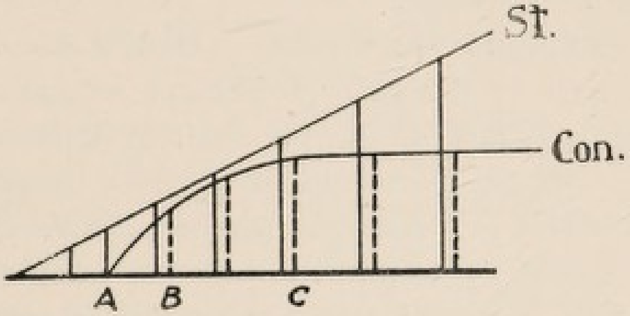


FIG. 25.—Influence of increasing the Strength of the Stimulus upon the contraction of Skeletal Muscle. *St.*, the stimulus ; *Con.*, the resulting contraction. *A*, a subminimal stimulus ; *B*, the minimum adequate stimulus ; *C*, the optimum stimulus.

The application of weights to a muscle causes the latent period and period of contraction to be delayed, while it renders the period of relaxation more rapid, and an over-extension may be produced followed by a recovery resembling a small after-contraction (fig. 26, *b*). (*Practical Physiology.*)

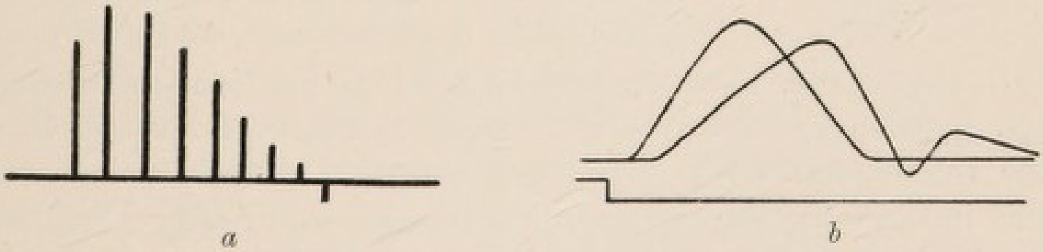


FIG. 26.—Influence of Load on a Muscular Contraction. (*a*) The effect of increasing the load on the extent of contraction ; (*b*) the effect of load on the course of contraction.

7. **Electrotonus.**—As already explained, the passage of a galvanic current through a muscle decreases its contractility at the anode and increases it at the kathode.

8. **Successive Stimuli.**—So far, we have considered the influence of a single stimulus on the shape of muscle. But in nearly every muscular action the contraction of the muscles must last much longer than $\frac{1}{10}$th of a second.

How is this continued contraction of muscles produced? To understand this it is necessary to study the influence of a series of stimuli on muscle.

If, to a frog's muscle which takes $\frac{1}{10}$th of a second to contract and relax, stimuli at the rate of five per second are applied, it is found that a series of simple contractions, each with an interval of $\frac{1}{10}$th of a second between them, is produced (fig. 27, 1). If the stimuli follow one another at the rate of ten per second, a series of simple contractions is still produced, but now with no interval between them.

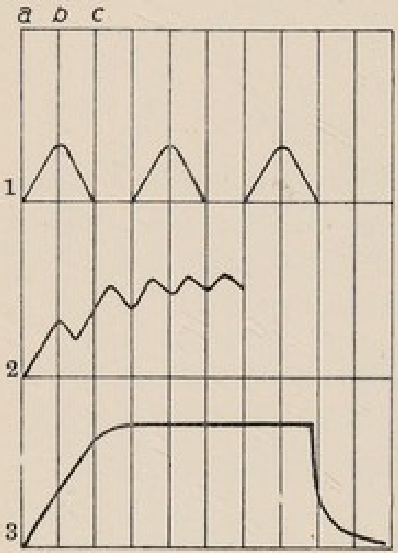


Fig. 27.—Effect of a series of Stimuli on Skeletal Muscle. (See text.)

If stimuli be sent more rapidly to the muscle, say at the rate of twelve per second, the second stimulus will cause a contraction before the contraction due to the first stimulus has entirely passed off (fig. 27, 2). The second contraction will thus be superimposed on the first, and it is found that the second contraction is more complete than the first, and the third than the second. But while the second contraction is markedly greater than the first, the third is not so markedly greater than the second, and each succeeding stimulus causes a less and less increase in the degree of contraction until, after a certain number, no further increase takes place, and the degree of contraction is simply maintained.

When the contractions follow one another at such a rate that the relaxation period of the first contraction has begun, but is not completed, before the second contraction takes place, a lever attached to the muscle, and made to write on a moving surface, produces a toothed line. The contraction is not uniform, but is made up of alternate shortenings and lengthenings of the muscle. This constitutes "*incomplete tetanus.*"

If the second stimulus follows the first so rapidly that the contraction period has not given place to relaxation, then the second contraction will be superimposed on the first, the third on the second, and so on continuously and smoothly without any slight relaxations, and thus the lever will describe a smooth line, rising at first rapidly, then more slowly, till a maximum is reached, and being maintained at this till the series of stimuli causing the contraction is removed, or until fatigue causes relaxation of the muscle. This is the condition of "*complete tetanus*" (fig. 27, 3). (*Practical Physiology.*)

The rate at which stimuli must follow one another in order to produce a tetanus depends on a large number of factors. Anything which increases the duration of a single contraction renders a smaller number of stimuli per second sufficient to produce a tetanus, and thus all the various factors modifying a single muscular contraction, modify the number of stimuli necessary to produce a tetanus (see p. 53). D'Arsonval has shown that an alternating current with very frequent interruptions of about 1,000,000 per second causes no contraction.

Every **voluntary contraction** of any group of the muscles is probably of the nature of a tetanus; and the question thus arises, at what rate do the stimuli which cause such a tetanus pass from the spinal cord to the muscles?

In a tracing of a continued voluntary contraction, indications of about ten variations per second are to be seen, while the rate of the clonic tremor of the leg which may be produced during fatigue by supporting the weight of the leg on the toes is about ten, backward and forward movement, per second, and in various morbid muscular spasms the rate is about the same.

All this would seem to indicate that the number of stimuli which pass to human muscle from the central nervous system is probably about ten per second.

It has, however, been found that passing a strong galvanic current into a muscle may lead to rhythmic contraction, and hence it is possible that the contractions of muscle induced by the central nervous system may be caused by a continued discharge from the nerve centres.

III. Mode of Action of Muscles

The skeletal muscles act to produce movements of the body from place to place, or movements of one part of the body on another. This they do by pulling on the bony framework to cause definite movements of the various joints.

The muscles are arranged in opposing sets in relationship to each joint—one causing movement in one direction, another in the opposite direction—and named according to their mode of action, flexors, extensors, adductors, abductors, etc. But in the production of any particular movement—say flexion of the forearm at the elbow—not only are the muscles manifestly causing the movement in contraction, but the opposing group, the extensors, are also in action to guide and direct the force and extent of the movement. This **Co-operative Antagonism** of groups of muscles is of very great importance, since it explains many of the results observed in paralysis. Thus, if the extensors of the hand be paralysed, as in lead palsy, it is found impossible to clench the hand although the flexors are intact. Again, if part of the brain which causes flexion of the hand of the monkey be stimulated, and the nerve to the flexors divided, the co-operative action of the extensors brings about an extension of the hand. In many movements some of the antagonistic muscles are relaxed under the action of their nerves (see p. 41).

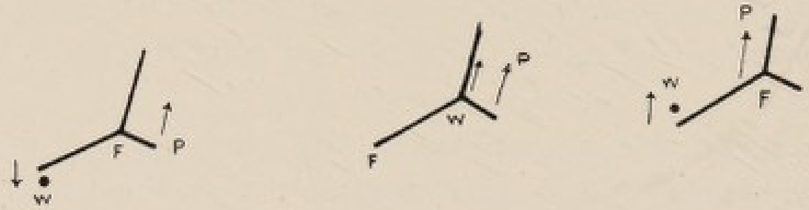


FIG. 28.—The three types of lever illustrated by the movements at the ankle joint.

The muscles round the various joints act on the bones, arranged as a **series of levers,** of the three classes (fig. 28).

1st Class.—Fulcrum between power and weight. In the ankle this is seen when, by a contraction of the gastrocnemius, we push upon some object with the toes.

2nd Class.—Weight between fulcrum and power. In rising on the toes the base of the metatarsals is the fulcrum, the weight comes at the ankle, and the power on the os calcis.

3rd Class.—Power between fulcrum and weight. In raising a weight placed on the dorsal aspect of the toes by the contraction of the extensors of the foot, we have the weight at the toes, the power at the tarsus, and the fulcrum at the ankle.

In the other joints, actions involving the principle of each of these levers may be found.

IV. Work of Muscle

As a result of the changes in shape, muscle performs its great function of doing mechanical work; and the most important question which has to be considered in regard to muscle, as in regard to other machines, is the amount of *work* it can do.

Since the work done depends upon the weight moved and the distance through which it is moved, the work-doing power of muscle is governed by the force of contraction, which determines the weight which can be lifted, and by the amount to which the muscle can shorten, for this will govern the distance through which the weight may be moved.

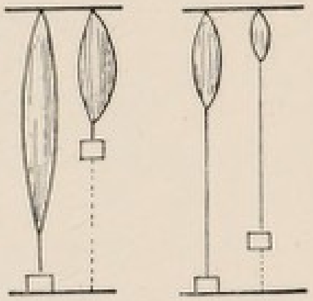


Fig. 29.—Influence of the length of a Muscle upon the work done.

It has been already shown that the force of contraction depends chiefly upon the sectional area of a muscle. A thick muscle is stronger than a thinner one. But, on the other hand, the amount of contraction depends upon the length of the muscle, since each muscle can contract only to a fixed proportion of its original length. A glance at the diagram will at once make this plain (fig. 29).

The *size of the muscle* is thus the first great factor which governs its work-doing power. But the many factors influencing the force of muscular contraction also influence the work-doing power of the muscle (see p. 53).

One factor requires special consideration, namely, the *Load*.

We have already seen that as the load is increased the extent of contraction is diminished.

The following experiment will illustrate the influence of increasing the load on the work-doing power of a muscle—

Load in Grams.		Space through which lifted in mm.		Work in Gram. mm.
0	×	4·5	=	0·0
20	×	3·0	=	60·0
40	×	2·37	=	94·8
60	×	2·00	=	120·0
80	×	1·75	=	140·0
100	×	1·2	=	120·0

It will be seen that increasing the load at first increases the amount of work done, but that after a certain weight is reached, it diminishes it. There is, therefore, for every muscle, so far as its working power is concerned, an **optimum load**.

In studying the amount of work a muscle or set of muscles can do, the element of *time* must always be considered. Obviously contracting muscles will do more work in an hour than in a minute. Hence in trying to form any idea of the amount of work a muscle can do, this must be expressed in work units per unit of bulk and per unit of time. The work unit generally employed is the kilogram-metre—the work required to raise one kilogram to the height of one metre against the force of gravity.

Various instruments—Ergometers—have been devised for measuring the amount of work done by various groups of muscles under different conditions.

The *average* working capacity of skeletal muscle may be estimated as follows:—A labourer who raises 130,000 kilos through one metre during his eight hours of work does a good average day's work. His muscles weigh about 25 kilos, and thus each gram of his muscle will do 5 kilogram-metres per diem, or 0·06 gram metres per second.

When required, much larger amounts of work can be done for short periods. It has been calculated that in the sprint of a 100 yards race, work is done at something like 2 gram metres per second, about thirty times the rate at which a labourer's muscles work. But to increase the rate at which work is done requires an increase in the expenditure of the energy-yielding materials in greater proportion than the increased work—just as to increase the speed of a ship or an engine requires an increase of coal consumption in a proportion roughly corresponding to the square of the increased speed.

V. Heat Production in Muscle

In muscle, as in other machines, by no means the whole of the energy rendered kinetic is used for the production of mechanical work. In a steam-engine much of the energy is dissipated as heat, and the same loss occurs in muscle.

If heat is given off when a muscle contracts, either the muscle itself, or the blood coming from it, will become warmer. Hence to detect such a charge some delicate method of measuring changes of temperature must be employed. The mercurial thermometer is hardly sufficiently sensitive, and, therefore, the thermo-electrical method is most generally employed. Various forms of thermopile may be used.

The rise of temperature in a muscle after a single contraction is extremely small, but after a tetanic contraction, lasting for two or three minutes, it is very much greater.

The amount of heat produced may be calculated if (*a*) the weight of the muscle; (*b*) its temperature before and after contraction; and (*c*) the specific heat of muscle, are known.

The specific heat of muscle is slightly greater than that of water, but the difference is so slight that it may be disregarded. If, then, a muscle of ten grams had a temperature of 15° C. before it was made to contract, and a temperature of 15·05° C. after a period of contraction, then 0·5 gram-degrees of heat have been produced; *i.e.* heat sufficient to raise the temperature of 0·5 gramme of water through 1° C. The heat units employed are the small and large calorie—the small calorie the heat required to raise one gram of water through one degree Centigrade, and the large Calorie—written with a large C—the heat required to raise a kilogram of water through one degree Centigrade.

The amount of heat produced by muscle in different conditions varies so greatly that it is unnecessary to consider it further.

Relationship of Heat Production to Work Production.—Since it is possible to measure both the mechanical work done by a muscle and the amount of energy dissipated as heat, it is possible to determine the relationship of these to one another, and thus to compare muscle with other machines as to proportion of energy which is utilised to produce work. To make this comparison it is necessary to be able to convert "work units" into "heat units," and *vice versa*. It has been found that 0·45 gram-degrees or small calories are equivalent to 1 kilogram-metre.

The proportion of work to heat is not constant. By gradually increasing the stimulus both work production and heat production are increased, but the latter is increased more rapidly, and reaches its maximum sooner. Again, as muscle becomes exhausted, its heat production declines more rapidly than its work production. Exhausted muscle, therefore, works more economically. If an unloaded muscle is made to contract no work is done and all the energy is given off as heat, and the same thing happens where a muscle is so loaded that it cannot contract when stimulated.

But the point of practical importance to determine is—How much of the energy liberated by muscle in normal conditions is usually used for mechanical work, and how much is lost as heat? It will afterwards (p. 339) be shown that all the energy of the body comes from the food, and the amount of energy yielded by any food may be determined by burning it in a calorimeter (see p. 341). To determine the energy used in mechanical work some form of work measurer or ergometer may be used—*e.g.* a wheel turned against a measured resistance. By converting the work units of the work thus done into heat units, and subtracting this from the total energy of the food, the energy lost as heat may be determined, and thus the relationship between work production and heat production may be found. By experiments on men, horses, and dogs, Zuntz has found that about one-third of the energy liberated may, under favourable conditions, be available for mechanical work, while two-thirds is lost as heat. The proportion of energy evolved in mechanical work and heat in normal men has been also studied by Atwater by means of the Respiratory Calorimeter (see p. 408). In these experiments only about six per cent. of the energy was used for mechanical work and the rest was lost as heat. Compared with other machines, such as steam-engines, muscle must be regarded as an economical worker, and it has the advantage that the heat liberated is necessary to maintain the temperature at which the chemical changes which are the basis of life can go on.

VI. Electrical Changes in Muscle

When a muscle contracts certain electrical changes occur. These may be best studied in the heart, which is a muscle which can be exposed without injury. With other muscles the injury inflicted in isolating them sets up electrical *currents of injury* (p. 42).

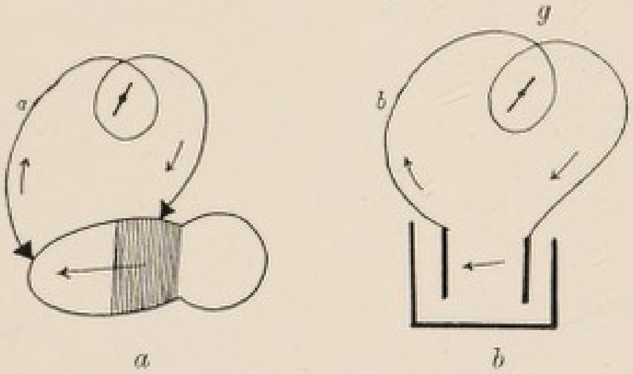


Fig. 30.—To show electric current of action in a muscle (*a*) compared with that in a galvanic cell (*b*). The contracting part of the muscle is shaded. (*g*) Galvanometer.

If one end of a wire be brought in contact with the base of the ventricle by means of a non-polarisable electrode (in which some material which does not act upon the muscle and is not acted upon by the muscle is in contact with it), and another wire be similarly connected with the apex, and if these wires are led off round a galvanometer, it will be found that with each contraction of the heart an electric current is set up, the one part of the heart becoming first positive and then negative to the other part.

This means that, when the contraction occurs, the part which first contracts becomes of a higher electric potential than the rest of the muscle, so that electricity flows from it to the uncontracted part in the organ, and from the uncontracting part to the contracting part in the wire round the galvanometer. The contracting part is thus similar to the positive element of a battery, the zinc; the uncontracting part to the negative element, and the wire coming from the contracting part will, therefore, correspond to the negative *pole*—that from the uncontracting part to the positive *pole*.

It has now been shown that this current of action occurs along with, and does not precede, the period of contraction. The electric change in contracting muscle may be demonstrated by laying the nerve of one muscle-nerve preparation over the muscle of another muscle-nerve preparation or over the beating heart, when it will be found that the first muscle contracts with each contraction of the second, being stimulated by the current of action. (*Practical Physiology.*)

VII. Extensibility of Muscle

The extensibility of muscle is increased during contraction so that the application of a weight causes a greater lengthening than when the muscle is at rest.

3. The Chemical Changes in Muscle and the Source of the Energy evolved

Chemical changes are constantly going on in muscle and the study of these chemical changes in resting muscle and in the contracting muscle explains the source of the energy of muscle. Disintegration leads to the liberation of energy and construction leads to the repair of the muscles and to the storage of energy.

No part of physiology is of more importance; for it is the chemical changes in muscle which give rise to the great waste products of the body, and it is to make good these losses that fresh nourishment has to be supplied. The chemical changes in muscle therefore govern both the intake and output of matter from the body.

By studying the question from a number of different standpoints, and by comparing the results so obtained, a fairly clear conception of the chemical changes and the source of muscular energy has been obtained.

1. **Composition of Muscle before and after Contraction.**— The method which most naturally presents itself is to take

two muscles or groups of muscles corresponding to one another, and to examine the chemistry of one before it has been made to contract, and of the other after it has been contracting for some time.

Resting muscle is alkaline; but if an excised muscle, outside the body, be kept contracting for some time, it becomes acid, and this acidity is due to the appearance of *carbon dioxide* and *sarcolactic acid.* Muscle in the body does not become acid, because the alkaline lymph at once neutralises the acid which is produced.

Again, after contraction, the *glycogen* of the muscle is found to be diminished. But the most important change is that the amount of *carbon dioxide,* CO_2, which can be extracted from muscle is very greatly increased.

As yet the changes, if any, in the *proteins* of muscle during contraction have not been fully investigated, and the results of the work accomplished on the *nitrogenous extractives,* which are formed by the decomposition of the proteins, are not trustworthy. They seem to indicate that these bodies are increased during muscular contraction *in the excised muscle.* These changes in a muscle may be diagrammatically represented as follows:—

+ Carbon dioxide.
+ Sarcolactic acid.
+ Nitrogenous extractives?
− Glycogen.

The results obtained by this method of investigation are thus of considerable value, but alone they give us no clear idea of the nature of the chemical changes.

2. **Respiration of Excised Muscle.**—By enclosing the excised muscle in a closed space containing air of known composition, and by investigating the changes in the components of the air after the muscle has either been kept at rest for some time or made to contract, important light has also been thrown on these chemical changes.

It has been found that the resting muscle constantly takes up oxygen from the air round about it, and constantly gives off carbon dioxide. In contracting, more carbon dioxide is given off, and *usually* the amount of oxygen taken up is also increased (fig. 31).

Here we have at once evidence that muscle breathes, and that this process of respiration is increased during muscular activity. The affinity of muscle for oxygen is very great, so great that it can actually take oxygen out of chemical combinations. If alizarin blue be injected into the vein of an animal, the blood becomes blue, but the muscles remain colourless, having reduced the pigment to a colourless condition. When freely exposed to air after death, the blue colour returns.

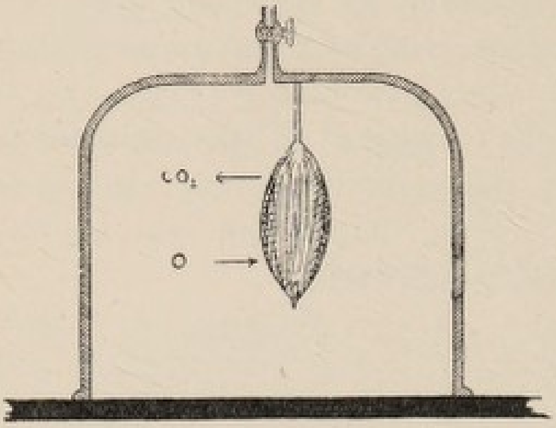


FIG. 31.—Respiration of muscle in a closed chamber.

3. **Changes in the Blood passing through Muscle.**—For the investigation of this the hind legs of a dog have been used. The blood going to one leg, and the blood coming from the other, are collected at the same time. It is found that the blood in passing through the muscles has *gained carbon dioxide* and *lost oxygen.* If the muscles be kept contracted, it is further ascertained that the amount of carbon dioxide gained is increased, while *usually* the amount of oxygen taken up is also increased. This observation confirms the investigations on the changes in the air surrounding a muscle.

But the solid constituents of the blood are also changed. If the muscles have been contracting, the blood is found to contain *sarcolactic acid* probably combined with ammonia.

We shall afterwards find that blood contains small quantities of *glucose*, $C_6H_{12}O_6$. As it passes through muscle it loses some of this, even when the muscle is at rest, and a much larger amount when the muscle has been active.

The changes in the *proteins* of the blood going to and coming from muscle have not been properly investigated.

Some observers have obtained results which seem to indicate that the amount of *fat* which is found in the blood is diminished as the blood passes through the muscles, but whether this diminution is greater during muscular activity has not been studied.

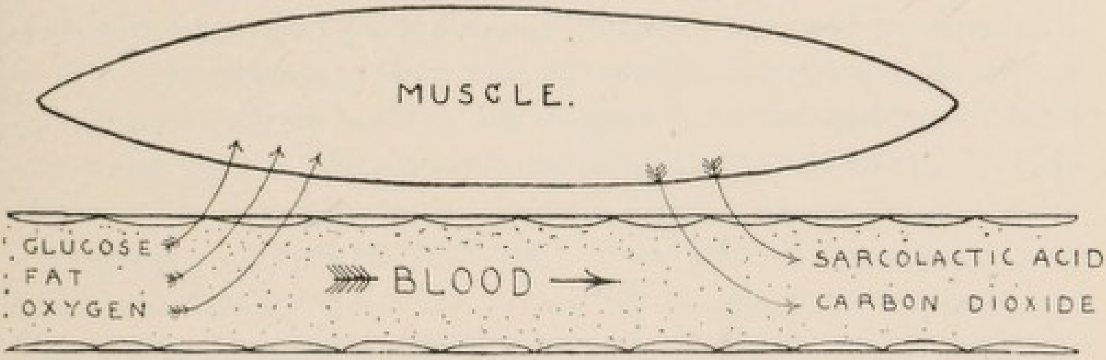


FIG. 32.—Exchanges between muscle and blood.

Such direct observations on muscle and the blood nourishing it indicate that constant chemical changes are going on when the muscle is at rest. It is constantly giving off carbon dioxide and constantly consuming oxygen, glucose, and possibly fats and proteins. When doing work these chemical changes become more active. We may compare resting muscle in its chemical changes to an engine with its fires banked down. Active muscle is comparable to the engine with its fires in full blast.

4. **Effects of Muscular Work upon the Excreta.**—Another method of study has yielded results of very great value—the investigation of the effects of muscular work upon the excreta.

Not only is muscle the most bulky and most constantly active tissue, but it is the tissue in which the most extensive chemical changes occur in the liberation of the energy for work and heat production; and hence, the waste products of the body are chiefly derived from muscle, and their amount and character must afford an indication of the changes in that tissue.

This was long ago recognised, but the older experimenters did not sufficiently realise that the excretions are modified by the amount and character of the food taken, and hence their results are of little value. In studying the influence of muscular work on the excreta, food must be withheld or must be unvarying during the experiment.

If this precaution is taken, it is found that the excretion of the various elements composing muscle is modified by muscular work.

Attention has chiefly been directed to the variations in the output of **carbon** and **nitrogen,** the two most important elements in muscle, the former mainly appearing as carbon dioxide in the expired air, the latter as urea in the urine. It has been found that if a **fasting** or **underfed** animal is made to do work the excretion of both these elements is increased, the carbon proportionately to the work done, the nitrogen in quantities not strictly proportionate to the work, being greater the more underfed the animal is and the harder the work done, and being less the better nourished the animal is or the less the work that is done (fig. 33, 1).

If a lean animal be fed on an exclusively **protein diet,** the excretion of carbon and nitrogen is increased, practically proportionately to the work done (fig. 33, 2).

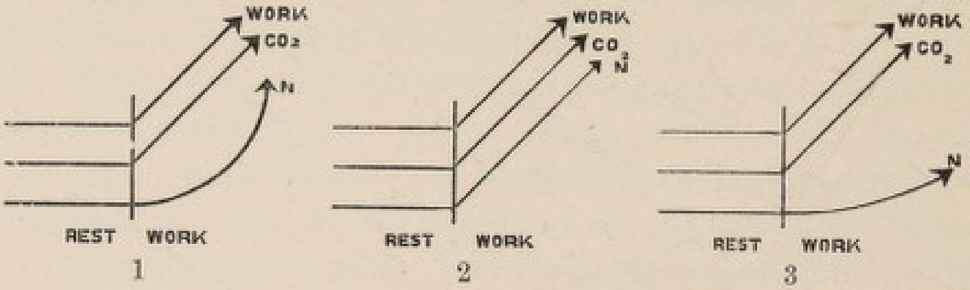


FIG. 33.—To illustrate the influence of Muscular Work upon the Excretion of Carbon and of Nitrogen—(1) in a fasting or underfed animal ; (2) in an animal fed on proteins ; (3) in an animal on a normal diet.

But if the animal be well fed on an **ordinary diet,** containing proteins, carbohydrates, and fats, the performance of muscular work increases the excretion of carbon proportionately to the work done, but may cause only a very slight increase in the excretion of nitrogen (fig. 33, 3).

From the increased excretion of nitrogen and carbon the consumption of proteins may be calculated, since proteins contain 16 per cent. of nitrogen and 52 per cent. of carbon—*i.e.* 3·4 times more carbon than nitrogen. Each gram of nitrogen excreted thus represents the breaking down of 6·25 grams of protein, and it is accompanied by 3·4 grams of carbon. If more carbon is excreted, it must come from carbohydrates or fat.

Proceeding in this way, it is found that **in the fasting animal and in the animal fed on proteins, the muscles get their energy chiefly from proteins, but that in an animal on an ordinary diet the muscles get it chiefly from the carbohydrates and fats of the food.**

An example of such an investigation may be given. Suppose that an animal during a period of rest excretes daily 10 grams of nitrogen, and that it then does 100,000 kgms. of work, and during the next three days the excretion of nitrogen is raised 2 grams above the 10 per diem. This means that $2 \times 6{\cdot}25 = 12{\cdot}5$ grams of protein has been decomposed. Now the amount of energy which can be liberated from 1 gram of protein has been found to be equivalent to 1738 kgms. (kilogrammetres), and therefore the 12·5 grams decomposed in the experiment is sufficient to yield 21,635 kgms. of energy, about 20 per cent. of the total energy expended in the work. The rest of the energy must be derived from fats and carbohydrates.

5. **A study of the ordinary diet** of animals doing muscular work corroborates the conclusions arrived at by an examination of the excreta. The diet of a horse on hard muscular work consists of something like the following proportions of food constituents per 1000 kilos. of body weight :—

	Amount.	Yielding Calories.
Proteins	2,300	9,500
Fats	800	7,500
Carbohydrates . . .	12,500	50,000
		67,000

The energy is here expressed in heat units, *Calories*—the amount of heat required to raise 1 kilogram of water through 1 degree centigrade. Of the total 67,000 Calories of energy daily taken in the food, only 14 per cent. is derived from proteins, the rest comes from the carbohydrates and fats.

Thus during muscular work the three great constituents of the body and of the food—proteins, fats, and carbohydrates —are broken down to liberate their energy, and apparently the muscle tends to use the non-nitrogenous fats and carbohydrates in preference to the proteins. Only when forced to do so does it take a large proportion of its energy from these substances.

It may be urged that in athletic training proteins must be a source of energy, since experience has taught that they are of such value. But their great value is as material from which the energy-liberating machine, the muscles, can be built up and increased, so that it can dispose of larger and larger quantities of food.

Muscle then is a machine which has the power of liberating energy from proteins, fats, and carbohydrates, but it uses proteins more especially in construction and repair.

The muscles liberate energy from these substances by breaking them down into simpler molecules, just as a blow causes the disintegration of nitro-glycerine and liberates its stored energy. There is not such a direct oxidation as occurs in the coals in the furnace of an engine, for, if this were so, the consumption of oxygen would always be equivalent to the elimination of carbon dioxide and the other products of disintegration. It has, however, been shown that a frog, deprived of all free oxygen by placing it in the receiver of an air pump and then transferred through mercury to an atmosphere of nitrogen, still continues to produce carbon dioxide. This means that its **oxygen must be intramolecular**, must be in the muscle molecule, like the oxygen of nitro-glycerine. Probably the presence of this oxygen is one of the causes of the instability of the molecule.

The muscle then takes these substances into itself—makes them part of its molecule—**assimilates** them before breaking them down. It is not necessary to suppose that all the substances are equally intimately associated with the muscle protoplasm. In all probability the protein becomes much more truly a part of the muscle than the carbohydrates and fats, but with each one of them it is essential that it should come into the domain of the muscle and not simply remain in the blood and lymph, in which it cannot be used.

B. Visceral Muscles

In several important respects the visceral muscles differ in their mode of action from the skeletal muscles.

1. Their connection with nerves is by no means so definite and precise, for, instead of each nerve-fibre ending in a muscle-fibre, the nerves to non-striped muscle form an irregular network upon them, and the muscle-fibre appears to be capable of action, possibly before these nerves have developed in the embryo and when the influence of these nerves has been cut off in the adult. In the intestine the mode of action of the muscles is largely dominated by the plexus of nerves (see p. 385).

2. The great features of the action of visceral muscle are —1st, its tendency to sustained tonic contraction; and 2nd, its spontaneous regular rhythmic contraction and relaxation.

1*st*. The continuous slight tonic contraction is seen in all the visceral muscles; and, while it may be increased or diminished by the intervention of nerves, it appears to be chiefly an expression of the continuous metabolism of the muscle protoplasm.

2*nd*. The rhythmic contractions and relaxations are not equally manifest in all situations, nor are they so continuous; but they are well marked in the muscles around such hollow viscera as the intestines, bladder, and uterus. Like the tonic contractions, they are to a certain extent independent of nerve action, but are influenced by it.

These contractions recur at regular intervals of varying duration. Each contraction lasts for a considerable period—sometimes over a minute—and the relaxation is correspondingly long. Everything which increases the rate of chemical change increases the rapidity of the rhythm. Thus warming the muscle and the action of a galvanic current have this action.

3. When the muscle is at rest, a contraction may be produced by any of the modes of stimulation which will cause the skeletal muscles to contract; and it may thus be demonstrated that the latent period is very long.

4. Unlike skeletal muscles, the extent of contraction is not increased by increasing the strength of the stimulus. The smallest available stimulus causes the maximum contraction; but if the same stimulus is repeated at regular intervals the resulting contractions become greater and greater during the application of the first four or five stimuli,

so that the record of a series of contractions has a somewhat stair-like appearance.

5. A series of stimuli do not cause a tetanus, but simply increase the rapidity and force of the individual contractions.

Cardiac Muscle physiologically resembles other visceral muscles, but its period of contraction is shorter and its rhythm generally more rapid.

4. Death of Muscle

The death of the muscle is not simultaneous with the death of the individual. For some time after somatic death the muscles remain alive and are capable of contraction under stimulation. Gradually, however, their irritability diminishes and finally disappears. They are then dead, and **necrobiotic changes** begin. The first of these—**Rigor Mortis**—is a disintegrative chemical change whereby carbon dioxide and sarcolactic acid are set free, and, at the same time, the soluble myosinogen changes to the insoluble myosin and the muscle becomes contracted, less extensile, less elastic, and more opaque. The contraction is a feeble one, and since it affects flexors and extensors equally, it does not generally alter the position of the limbs, although it may sometimes do so. As these changes occur, heat is evolved and the muscles become warmer.

The time of onset of rigor varies with the condition of the muscles. If they have been very active just before death stiffening tends to appear rapidly.

It lasts for a period which varies with the species of animal and with the condition of the muscles, and as it disappears the muscles again become soft, and the body becomes limp. In all probability this latter change is due to a solution of the myosin by an enzyme like that of the stomach—pepsin—which seems to exist in all the tissues. This can act only in the presence of an acid, and the appearance of sarcolactic acid, therefore, allows it to come into play.

II. NERVE

It is through the nerves that our surroundings act upon us, and through nerves that our muscles are made to respond appropriately to the surrounding conditions.

1. Structure and Development

In unicellular organisms changes in the surroundings act directly on the cell protoplasm, *e.g.* an amœba, when touched, draws itself together. But, even in these simplest organisms, certain kinds of external conditions will produce one kind of change, while others will produce a different one, as has been shown in considering unilateral stimulation (p. 15). Even among unicellular organisms—*e.g.* among the infusoria—animals are found in which the cell is differentiated into a receiving and reacting part. Poteriodendron, a little infusorian sitting in a cup-like frame, consists of a long process or cilium extending up from a cell while a contractile myoid attaches the cell to the floor of the cup. When the cilium is touched the myoid contracts, and draws the creature into the protection of its covering.

In more complex multicellular organism, *e.g.* in medusa, the different parts are connected to one another by a network of protoplasmic strands, which bring each part into relationship with the others, and thus secure co-ordinate reaction to any stimulus. A similar network exists and performs important functions in the wall of the alimentary canal of vertebrates.

Fig. 34. — Poteriodendron to illustrate the first stage in the evolution of a neuro - muscular system.

In more highly organised animals, where the reaction has to be more definitely appropriate to the surrounding conditions, and where the complexity of the mechanism involved is greater, there is a development by which *special conditions* at *special parts* of the surface each lead to *special reactions*. This is brought about by the establishment of a **nervous system**—a mechanism which may be compared to a series of shunting stations between the *receptive* mechanism on the surface and the *reacting* mechanism—the muscles, glands, etc. To form this, a part of the epithelial covering of the embryo sinks inwards as a canal composed of the surface cells, and these cells form functional connections with the surface on the one hand and with the reacting structures on the other. At first the cells composing this tube are undifferentiated and alike, but later some of them throw out processes towards the surface and others towards the reacting structures, and these are connected, not by actual continuity, but by coming in close relationship to one another in a series of branching processes, forming a **synapsis** (fig. 35).

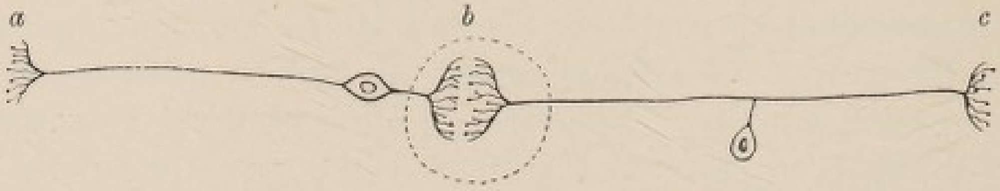


FIG. 35.—To show a *receiving* (*c*) and a *reacting* Neuron (*a*), each with dendrites at its extremities, and their connection to one another through a Synapsis (*b*).

Each of the units so formed has been called a **neuron**; and a neuron may be defined as one of the cells with all its processes which build up the nervous system. These neurons may be divided into the *receiving* and *reacting* series, but in structure they are alike.

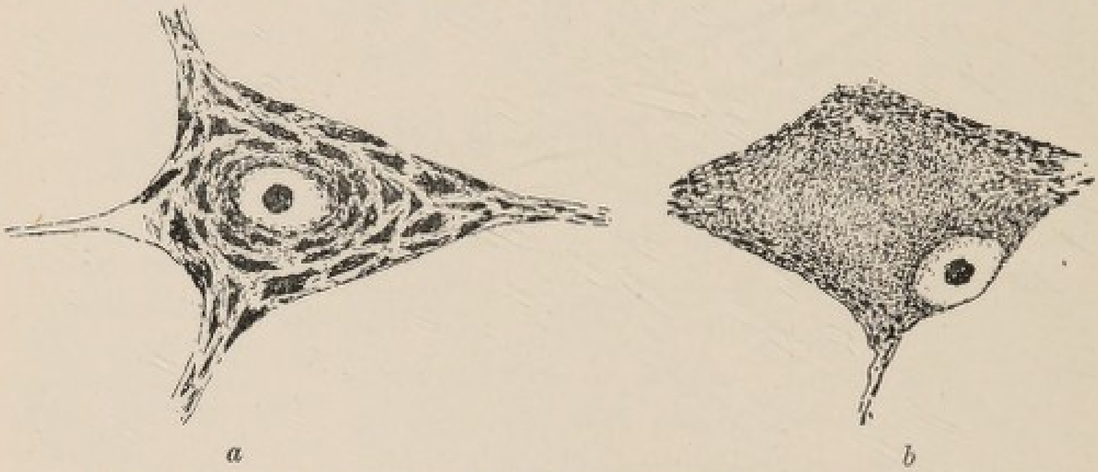


FIG. 36.—(*a*) A Nerve Cell with Nissl's granules; (*b*) a similar cell showing changes on section of its axon.

The shape and characters of the **cells**, and their position upon the processes of the neuron—the fibres—vary greatly, but they have all the following characters in common:—They are nucleated protoplasts, the protoplasm of which shows a well-marked network, in the meshes of which a material which stains deeply with basic stains, and which seems to be used up during the activity of the neuron, may accumulate in granules. The granules formed of this material are generally known as **Nissl's granules** (fig. 36).

These cells give off at least one process, which continues for some distance, as the **axon**. Frequently other processes are given off, which may either pass away as fibres, or may, while still in close proximity to the cell, form a branching system of **dendrites**. The axons end in much the same manner, so that all the processes are essentially the same. These processes are fibrillated, and the fibrillæ may be traced through the protoplasm of the cells (fig. 37). In many cases the dendrites show little buds or **gemmules** upon their course, and, according to some observers, it is through these that one neuron is brought into definite relationship at one time with one set of neurons, and at another with other adjacent neurons. There is also some evidence that the dendrites as a whole may expand and contract, and thus become connected with those of adjacent neurons.

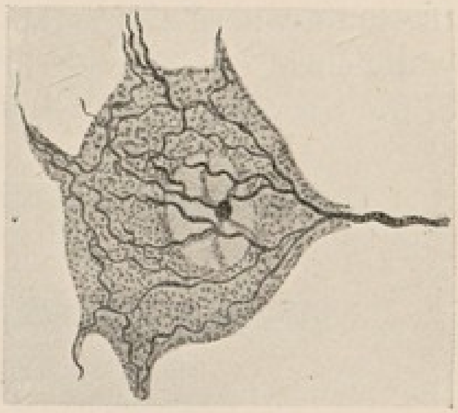


Fig. 37.—A Nerve Cell highly magnified to show passage of processes through the protoplasm.

Axon.—The axon process, as it passes away from the cell, becomes a **Nerve Fibre**, and acquires one or two coverings.

1. A thin transparent membrane, the **primitive sheath** or **neurilemma**, is present in all peripheral nerves. Between it and the axis cylinder there are a number of nuclei surrounded by a small quantity of protoplasm, the **nerve corpuscles**. The mode of origin of these is unknown. Fibres with only this sheath have a grey colour, and may be called *non-medullated fibres*. They are abundant in the visceral nerves.

2. A thick white sheath—the **medullary sheath** or white sheath of Schwann—which gives the white colour to most of the nerves of the body, appears somewhat late in the development of many nerve fibres. It lies between the primitive sheath with the nerve corpuscles and the axon. It is not continuous, but is interrupted at regular intervals by con-

strictions of the neurilemma at the nodes of Ranvier (fig. 38). It is composed of a sponge-work or felt-work of a horn-like material—*neuro-keratin*—the meshes of which are filled with a peculiar fatty material.

The nerve fibres run together in bundles to constitute the **nerves** of the body, and each bundle is surrounded by a dense fibrous sheath, the perineurium. When a bundle divides, each branch has a sheath of perineurium, and in many nerves this sheath is continued, as the sheath of Henle, on to the single fibres which are ultimately branched off from the nerve.

2. Chemistry of Nerve

The chemistry of neuron cells and their processes has been deduced from a study of the chemistry of the grey matter of the brain where they preponderate, while the chemistry of the white sheath is indicated by the analyses of the white substance of the brain, which consists chiefly of medullated fibres.

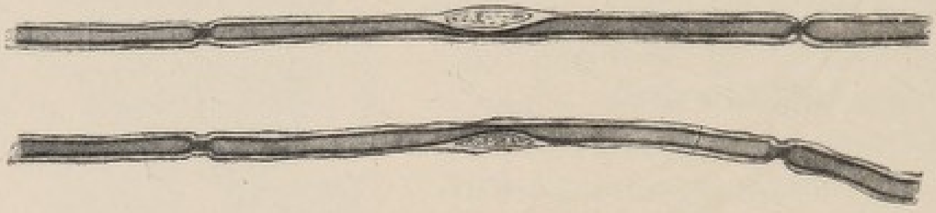


Fig. 38.—Pieces of two white Nerve Fibres.

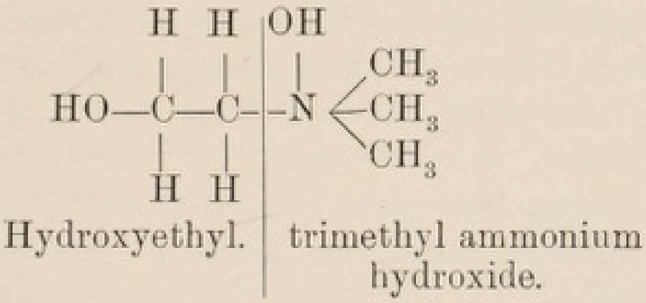
The **grey matter** contains over 80 per cent. of water. The solids consist of rather less than 10 per cent. of proteins. Two globulins, one coagulating at 47° C. and the other at 73° to 75° C., and a nucleo-proteid coagulating at 56° to 60° C., have been isolated. Lecithin and cholesterin, each to about 3 per cent., are the other important constituents.

The **white matter** contains only about 70 per cent. of water. The proteins, similar to those in the grey matter, constitute between 7 and 8 per cent. Lecithin occurs in about the same amount as in the grey matter, but cholesterin constitutes no less than 15 or 16 per cent.

From the fatty material of the white sheaths various complex substances have been isolated. The most abundant of these has been called **protagon**. It yields stearic acid; hence it is allied to the fats, and it contains nitrogen and phosphorus. Its constitution is not known. Along with protagon, or as a result of its decomposition, **lecithin** occurs.

This is a fat in which one of the acid radicles is replaced by phosphoric acid linked to cholin.

$$\text{Glycerol}\begin{cases}\text{Fatty acid.}\\ \text{Fatty acid.}\\ \text{Phosphoric acid.}\\ \qquad\qquad\;\;| \\ \qquad\qquad\text{Cholin.}\end{cases}$$



The chief interest of cholin is that it is toxic, and some of the symptoms occurring in degenerative changes of the nervous system may be due to its presence. It is closely allied to muscarin, a very powerful vegetable poison.

Cholesterin, like the glycerine of ordinary fats, is an alcohol, but it is monatomic—$C_{27}H_{45}HO$—and it is capable of linking with fatty acids. It is very soluble in hot alcohol, and crystallises out on cooling in characteristic square plates, with a notch out of one corner.

3. Physiology of Nerve

The neurons form a most intricate labyrinth throughout all parts of the body, and more especially throughout the central nervous system. Each is brought into relationship with many others by its dendritic terminations, and there is a continued interaction between them, the activity of any one influencing the activity of many others. In this way the constant activity of the nervous system, which goes on from birth to death, during consciousness and in the absence of consciousness, is kept up.

It is unnecessary and gratuitous to invoke the conception of automatic action on the part of any portion of the nervous system. Throughout life these neurons are constantly being acted upon from without, and activity once started by any stimulus sets up a stream of action which may be co-existent with life.

1. **Stimulation of Neurons.**—Neurons, like all other protoplasm, react to changes in external conditions; they are capable of stimulation. A neuron is usually stimulated from one or other of its terminal dendritic endings, either by changes in the tissues round these or by changes in other neurons. Thus (fig. 35) a neuron may be thrown into action by changes in the tissue at its extremity, and a second may be stimulated by the activity of the former. They may also be stimulated at any part of their course, as may be demonstrated by pinching the ulnar nerve behind the internal condyle of the humerus.

Means of Stimulation.—Just as with muscle, so with neurons; any *sudden* change excites to activity—be this change a mechanical one, as in pinching a nerve, or a change in the temperature, or in the electric conditions in its neighbourhood, or in the chemical surroundings of the neuron—agents which withdraw water, like glycerine, stimulating most strongly. All that has been said of the stimulation of muscle applies to the stimulation of nerve (see p. 42 *et seq.*). (*Practical Physiology.*)

The **condition of the neuron modifies the effect of the stimulus**, and the condition of other neurons modifies the ultimate result of the stimulus on the body.

The excitability of a neuron is modified by many factors. It may be increased by a slight cooling, but is decreased at lower *temperatures.* It is increased by warming up to a certain point. *Drying* at first increases excitability, then abolishes it. During the flow of an *electric current* it is increased in the neighbourhood of the negative pole, decreased around the positive pole, in the same way as in muscle (see p. 42). It is influenced by many *chemical substances*, some of which increase its excitability in small doses, and diminish it in larger doses; some again even in the smallest dose depress its activity, *e.g.* potassium salts. *Continued activity* has no effect on the excitability of axons, and the phenomena of fatigue are not manifested in them.

2. **Manifestations of the Activity of Neurons.**—So far as is at present known, the activity of neurous is not accompanied by any obvious change in them, although it is possible that

movements of the dendrites or of the gemmules upon them may occur. The activity of neurons is made evident—

(*a*) By their action upon other structures, *e.g.* muscles, glands, etc., either (α) directly or (β) indirectly through other neurons.

(*b*) By changes in the consciousness.

(*c*) By electric changes in the neurons.

(*a*) and (*b*) **Action on other Structures.**—The activity of the **outgoing neurons**—neurons conducting impulses from the central nervous system to muscles, glands, etc.—is manifested by changes in the muscles or other structures to which they go: while the activity of **ingoing neurons** is made evident by their action on outgoing neurons to muscles, etc., and sometimes by modifications in the state of consciousness, which may be of the nature of a simple brief sensation, or, by the implication of a number of other neurons, may develop into a series of changes accompanied by a corresponding series of sensations.

Very interesting results follow from this fact that the activity of neurons is made manifest by changes in the structures to which they pass. Langley has demonstrated that if the vagus, which conducts downwards to the abdominal viscera, be cut, and the cervical sympathetic, which conducts upwards to the head, be also cut, and the central end of the vagus united to the peripheral end of the sympathetic, fibres grow outwards from the vagus into the sympathetic, and when the vagus is stimulated, the results which naturally follow stimulation of the sympathetic occur. Kennedy has shown that, if the nerves to the flexors and the nerves to the extensors of a dog's forelimb be cut, and the central end of the former united to the peripheral end of the latter, and *vice versâ*, co-ordinate movements occur, and that if that part of the brain which naturally causes extension be stimulated, flexion occurs. He has applied the information thus gained to the treatment of abnormal conditions in the human subject. In a woman who suffered from spasmodic action of the muscles of the face supplied by the seventh cranial nerve, he divided this nerve and connected its peripheral end with the central end of the spinal accessory and thus secured a complete recovery.

(*c*) **Electrical Changes.**—The part of the neuron in action is electro-positive to the rest of the neuron, just as the contracting part of a muscle is electro-positive to the rest (p. 63).

3. **Conduction in Neurons.**—When a neuron is stimulated at any point, some time elapses before the result of the stimulation is made manifest, and the farther the point stimulated is from the structure acted upon, the longer is this latent period. This of course indicates that the change, whatever it is, does not develop simultaneously throughout the neuron, but, starting from one point, be it at one end or in the middle, travels or is conducted along. The **rate of conduction** may be determined by stimulating a nerve going to a muscle at two points at known distances from one another, and measuring the difference of time which elapses between the contraction resulting from stimulation at each (fig. 39). (*Practical Physiology.*)

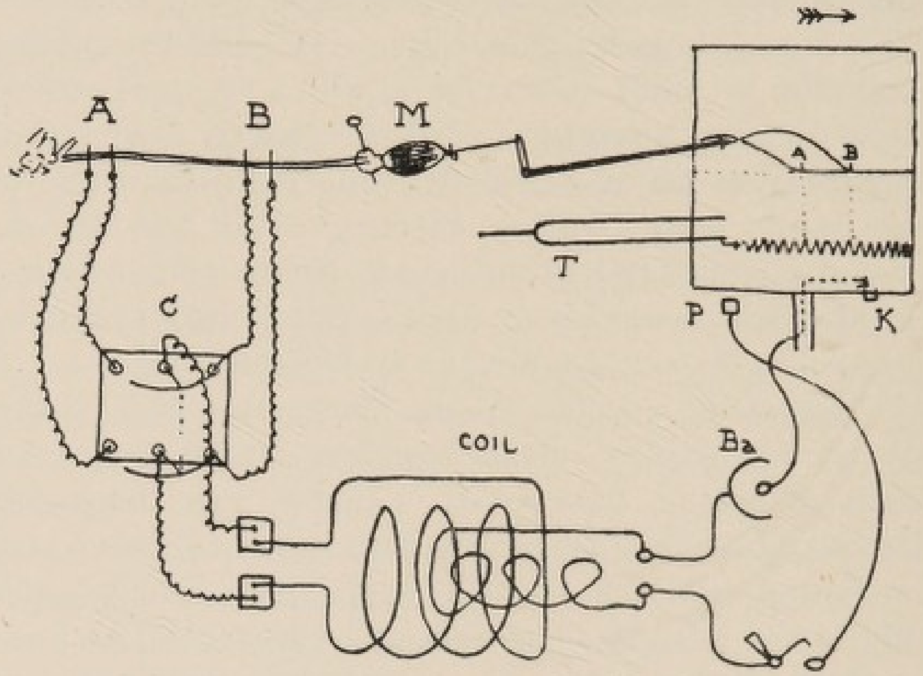


Fig. 39.—*M*, Muscle attached to crank lever marking on revolving drum. The secondary circuit of an induction coil is connected with a commutator, with the crossed wires removed so that the current may be sent either through the wires going to the nerve at *A* far from the muscle, or at *B*, a point at a measured distance nearer the muscle. On the drum, *A* represents the onset of contraction on stimulating at *A*, and *B* the onset on stimulating at *B*. To secure stimulation in each case with the drum in the same position, the make and break of the primary circuit is caused by the point *K* touching and quitting the point *P*.

The **rate of conduction** varies considerably; everything stimulating protoplasmic activity accelerating, and everything depressing protoplasmic activity diminishing it. Under normal conditions in the fresh nerve of the frog, the nerve change travels about 33 metres per second.

Factors modifying Conduction.—Conduction is modified by the *temperature*. Cooling a nerve lowers its power of conduction, gently heating it increases it. Various *drugs* which diminish protoplasmic activity—*e.g.* chloroform—diminish conduction. The *electric current* acts differently on conduction and on excitability. While a weak current has little or no effect, a strong current markedly decreases conductivity round the positive pole, and to a less extent decreases it at the negative pole, so that the general effect of a strong current is to decrease conductivity.

From this influence of the electric current upon *excitability* and *conductivity* certain differences are to be observed in the effects of stimulating an exposed nerve with currents of various strengths and different directions downwards *to* the muscle or upwards *from* the muscle. These have been formulated as Pflüger's Law; but since they have no bearing upon the stimulation of unexposed nerves in the living body they need not here be considered.

By using the electric changes as an index of nerve action, it has been found that when a neuron is stimulated in the middle, the **change travels in both directions**, although its result is made manifest only by the action of the structure at one end on which it normally acts. This two-way conduction may also be demonstrated by the experiment of paradoxical contraction, in which, by stimulating the branch of the sciatic nerve of the frog going to the muscles of the thigh, the nerve fibres to the gastrocnemius lying alongside of them are also stimulated, and cause that muscle to contract. That this does not occur when impulses from the central nervous system pass along the nerve is because the strength of these impulses, as indicated by the electrical change, are very much weaker than those caused by direct stimulation. (*Practical Physiology.*)

Classification of Neurons by the direction of Conduction.—Since a nerve is normally stimulated from one or other end, and hence conducts in one direction, and since the passage of impulses along it are made manifest by changes in the structure to which it goes, it is possible to classify nerve fibres according to whether they conduct to or from the central nervous system, and according to the structure upon which they act.

To find out the direction of conduction and the special mode of action of any nerve, two methods of investigation are employed—

1*st*. The nerve may be cut, and the results of section studied.

2*nd*. The nerve may be stimulated, and the result of stimulation noted.

Usually these methods are used in conjunction; first, the nerve is cut, and when the changes thus produced have been noted, the upper end and the lower end of the cut nerve are stimulated.

It is, of course, only if a nerve is constantly transmitting impulses that section reveals any change. If the nerve is not constantly active, stimulation alone will teach anything of its functions.

Outgoing or Efferent Nerves.—Section of certain nerves produces a change of action in muscles, glands, etc., or, if the nerve is not constantly acting, stimulation of the peripheral end of the cut nerve causes some change in the activity of these structures. Stimulation of the central end of such nerves produces no effect. These nerves therefore conduct impulses from the central nervous system outward.

Many of these nerves produce an increase on the activity of the parts to which they go, but others diminish or inhibit activity. The former class may be called **augmentor** nerves, the latter **inhibitory** nerves.

The augmentor nerves may further be divided into groups according to the structures upon which they act. Those acting on muscle may be called *motor nerves*; those acting to cause secretion from a gland, *secretory nerves*; those acting to constrict blood vessels, *vaso-constrictor nerves.*

The inhibitory nerves may be similarly subdivided into *musculo-inhibitory, secreto-inhibitory, and vaso-inhibitory nerves.*

Ingoing or Afferent Nerves.—Section of another set of nerves may produce loss of sensation in some part of the body. When the peripheral end of the cut nerve is stimulated no result is obtained. When the central end is stimulated, sensations or some kind of action results. Such nerves obviously conduct to the central nervous system. Those which, when stimulated, give rise to sensations may be called *sensory*; those which give rise to some action are called *excito-reflex*, because the action which results is produced by what is called reflex action. But these are not distinct from one another, and a nerve which at one time when stimulated will cause a sensation, may at another time cause a reflex action without sensation. As an example of such a nerve we may take the branches of the fifth cranial nerve which pass to the conjunctiva of the eye. When the conjunctiva is touched—*i.e.* when this nerve is stimulated—the orbicularis palpebrarum is brought into action through the seventh cranial nerve, and the eye is closed. The conjunctival branch of the fifth cranial nerve is thus an *excito-motor nerve.*

When the terminations of the lingual branch of the fifth nerve in the tongue are stimulated the result is a free flow of saliva, through the action of the seventh nerve and the secretory branches of the glosso-pharyngeal. The lingual nerve is thus *excito-secretory.*

Stimulation of the nerves from any part—*e.g.* by a mustard blister—causes relaxation of the blood vessels of the part, and such afferent nerves may be called *excito-vaso-inhibitory.*

Many nerves of the body contain both afferent and efferent nerve fibres, and are called **mixed nerves.**

The **passage of excitation from one neuron to others in such actions** occupies a very appreciable **time.**

In the case of reflex closure of the eye, about ·06 second elapses between the touching of the eye and the resulting "wink."

Knowing the rate at which nerve changes pass along nerves, and knowing the length of the ingoing and of the outgoing neurons, the time taken in the passage of the change along these is readily calculated. In a reflex wink it is about ·01 second.

Hence only one-sixth of the total "**latent time**" of the reflex action is occupied in the passage of the change along the neurons, and ·05 second, or five-sixths of the whole is taken up in the passage of the change from one neuron to another. Obviously the synapsis between the dendrites of the neurons offers a resistance, and this resistance varies with the condition of the neurons involved, possibly with the condition of the dendrites which form the synapses.

If the toe of a frog deprived of its brain is pinched, the leg is drawn up; but if a dose of strychnine is first administered, even touching the toes causes a violent spasm of every muscle in the body. The resistance is decreased. If, on the other hand, a dose of bromide of potassium has been administered, or if ice be put on the back of the animal, much more powerful stimulation is required to produce any reaction. The resistance is increased. The activity of the central synapses may be increased or diminished in various ways, and hence it is never easy to predicate the ultimate result of any stimulation of the nervous system. But, other things being equal, the strength of stimulus applied to the first neuron—that is, the extent of excitation—directly affects the extent of the resulting action. (*Practical Physiology.*)

The **nature of the "impulse"** which passes along a nerve is due to changes in the axis cylinder, since this, without its sheath, can conduct. Further, it is dependent on the vitality of the nerve. Death of the nerve, as when it is heated to 47° C., at once stops the transmission of an impulse.

We may at once dismiss the idea that the impulse is due to a flow of electricity. Electricity travels along a nerve at about 300 million metres per second, a velocity much higher than that of the nerve impulse.

Two possibilities remain. The impulse may be of the nature of a molecular vibration, such as occurs in a stethoscope which conducts sound vibration, or it may consist of a series of chemical changes such as cause the activity of protoplasm generally.

In considering this matter it must be remembered that the amount of energy evolved in a nerve impulse need not be great. All it has to do is to *start* the activity of the part to which it goes. Hence if chemical changes are the basis of the impulse, these may be extremely small in amount and difficult to detect, while at the same time recuperation may be extremely active.

As a matter of fact, the evidence of chemical changes in nerve fibres is entirely wanting. No change in reaction, no heat production, and no phenomena of fatigue can be demonstrated.

4. **The function of the cell** is to preside over the nutrition of the neuron. If any part of the neuron is cut off from its connection with the cell, it dies and degenerates (see p. 173).

In the cat, excitability disappears after three days, and the white sheath shows degeneration changes in eight days. The fatty matter runs into globules and stains black with osmic acid even after treatment with chrome salts (Marchi's method). This seems to be due to the fact that osmic acid acts upon the unsaturated oleic acid, and that in the normal nerve this is oxidised by the chrome salt, whereas in the degenerated nerve so much is set free that it cannot all be oxidised, and therefore stains with osmic acid. The white substances gradually disappear. At the end of a month the phosphorus has all gone, and by the end of about forty-four days the fat can no longer be detected. At this stage Marchi's method is useless, and the degenerated fibres may be demonstrated by the fact that they do not stain with osmic acid or with Weigert's hæmatoxylin method, which stains the white sheaths of normal fibres. As the degeneration advances, the axis cylinder breaks down and the nerve corpuscles proliferate and absorb the remains of the white sheath, so that nothing is left but the primitive sheath filled by nucleated protoplasm. Into this, axons may grow downwards from the central end of the nerve, and *regeneration* may occur. This generally begins after forty-four days and is well marked after about one hundred days.

Some investigators have maintained that regeneration occurs by the development of new fibrils in the degenerated nerve itself, but the mass of evidence indicates that when an apparent peripheral regeneration has occurred it has been due to the ingrowth of axons from adjacent cut nerves.

The cell of the neuron appears to have the power of accumulating a reserve of material as Nissl's granules, for it has been found that after continued action these granules diminish in amount. The nucleus, too, would seem to have the power of giving off material for the nourishment of the neuron, since in conditions of excessive activity it has been found shrunken and distorted.

But the cell is also dependent for its proper nutrition upon the condition of the rest of the neuron. When the axon is cut, the chromatin of the cell nucleus decreases, and the nucleus becomes displaced to one side, and ultimately the whole cell degenerates. This is sometimes called Nissl's Degeneration (see fig. 36).

SECTION IV

The Neuro-Muscular Mechanism

The study of the physiology of **muscle** and **nerve** leads to the consideration of how the **neuro-muscular mechanism** acts, so that (1st) the various visceral muscles respond appropriately to the conditions in which they are placed, and (2nd) so that the co-relationship of the animal with its surroundings may be maintained.

We shall at present deal with the second of these, leaving the former for consideration when studying the physiology of the viscera.

1. THE NEURAL ARCS

The neuro-muscular mechanism is controlled by three chains or arcs of neurons, consisting of ingoing neurons on the one side and outgoing neurons on the other.

1. **Spinal or Peripheral Arc—A. Ingoing** (fig. 40, *A*).—These neurons start in dendritic expansions at the periphery, and enter the cord by the superior or dorsal roots of the spinal nerves. In these roots they are connected with cells by lateral branches (see p. 158). When they enter the cord they either pass to the dorsal portion, and divide into (*a*) branches running for a short distance down the cord; (*b*) branches running right up to the top of the spinal cord to end in synapses round masses of cells—the nuclei of the dorsal columns, or, (*c*) either directly or by collaterals, they form synapses with other neurons. The most important of these in the spinal arc are the neurons in the ventral part from which the outgoing fibres spring. The other neurons with which synapses are formed send fibres either up the same side of the cord or across to the opposite side. These may be considered as part of the next two arcs (see p. 170).

B. Outgoing (fig. 40, *B*).—From the neurons in the ventral part of the cord, fibres are given off which pass out in the ventral roots of the spinal nerves to muscles, glands, and other reacting structures.

The fibres entering and leaving the base of the brain by the cranial nerves belong to this arc.

The action of these neurons is controlled and modified by the two other series of central neurons.

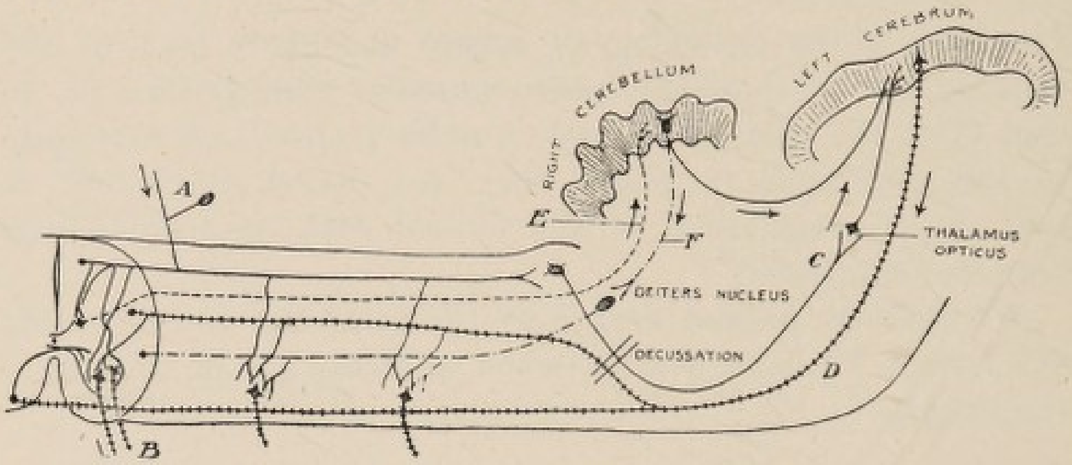


Fig. 40.—To show the three Arcs in the Central Nervous System. *A*, Peripheral ingoing neuron giving off collaterals in the cord and some terminating above in the nuclei of the dorsal columns ; *B*, peripheral outgoing neurons ; *C*, ingoing cerebral neurons ; *D*, outgoing cerebral neurons, crossing to the opposite side at // ; *E*, ingoing cerebellar neurons ; *F*, outgoing cerebellar neurons.

2. **Cerebral Arc—A. Ingoing** (fig. 40, *C*)—(*a*) *Lower Neurons.*—These are the ingoing neurons of the spinal arc, described above.

(*b*) *Intermediate Neurons.*—These start (i.) from the cells in the nuclei of the dorsal columns, and, crossing the middle line, run up to the base of the great brain, where they end in synapses round other cells in the thalamus opticus (fig. 40, *C*); (ii.) from the cells in the spinal cord with which the spinal ingoing neurons have made synapses. The fibres to the cerebrum cross in the cord and run up to end in synapses in the thalamus; (iii.) from the synapses in the base of the brain, formed by the incoming fibres of the head sense organs. These fibres also pass up to end in the thalamus.

(*c*) *Upper Neurons.*—From cells in the thalamus, processes pass up to the cortex of the great brain, to end in synapses with the neurons situated there.

B. Outgoing (fig. 40, *D*).—The outgoing neurons start in the cells of the cortex cerebri, and pass down to the upper part of the spinal cord, where most of them cross and run down the lateral column of the spinal cord, giving off collaterals which end in synapses round the cells in the ventral horn of grey matter, from which the spinal outgoing neurons pass to the muscles, etc. Those which do not cross run down the ventral column of the cord for some distance, and end by crossing and becoming associated with the cells in the ventral horn.

3. **Cerebellar Arc—A. Ingoing** (fig. 40, *E*).—Some of the collaterals of the spinal ingoing neurons end in synapses round a mass of nerve cells at the side of the grey matter of the spinal cord—the cells of Lockhart-Clarke. From these cells, fibres extend up at the margin of the cord to the lesser brain or cerebellum to form, directly or indirectly, synapses round the cells in this organ. From the same group of cells other fibres cross to the opposite side and run up to the cerebellum. Fibres from the synapses, formed by the incoming fibres from the labyrinth of the ear and probably from the eye, also course to the cerebellum.

B. Outgoing (fig. 40, *F*).—From neurons near the surface of the cerebellum and in the central nuclei axons extend (*a*) to the medulla oblongata, where they end in synapses round a mass of cells—the nucleus of Deiters. From these cells, fibres extend down the lateral columns of the same side of the spinal cord, and give off collaterals to the cells of the ventral horn of grey matter. (*b*) To the cerebrum.

The **nervous system may thus be considered as built up of these three arcs.**

1*st*. **The Spinal** arcs consist of the peripheral ingoing neurons and the peripheral outgoing neurons. These arcs exist not only at the level of the cord at which the ingoing neuron enters, but are placed at various levels above and below this point (fig. 40).

2*nd*. **The Cerebral** arcs consist of (1) the peripheral; (2) the intermediate; and (3) the upper ingoing neurons; (4) the central outgoing neurons; and (5) the peripheral outgoing neurons.

3rd. **The Cerebellar** arcs consist of (1) peripheral ingoing neurons; (2) the cerebellar ingoing neurons; (3) the outgoing cerebellar neurons, either direct to the cord or through the cerebrum; and (4) the peripheral outgoing neurons.

2. MODE OF ACTION OF THE NEURAL ARCS

A. Spinal Arcs in Reflex Action

The mode of action of the spinal arcs, uncomplicated by the influence of the two higher arcs which act upon them, may best be studied by dividing the spinal cord high up so as to remove from it their modifying action.

One of the simplest spinal reactions may be studied in a frog in which the brain has been destroyed. If the animal be suspended by the head, and one of the toes gently pinched, the leg is drawn up (*Practical Physiology*). Here an impulse is transmitted up from the ends of the receiving neuron in the skin to the cord, and this leads to changes in outgoing neurons which pass to the muscles of the leg to make them act in a definite manner to withdraw the leg from the source of irritation. This is a **Reflex Action**, an action in which, apart from any necessary implication of consciousness, an external stimulus leads to a definite reaction through the agency of one or more spinal arcs.

The mechanism involved consists in:—

1. The special terminations of the neurons acted upon—the Receptors.
2. The Conductors—the ingoing and outgoing neurons and the synapses between these.
3. The reacting organs or muscles, which may be termed the Effectors.

It is convenient to deal first with the conductors.

The Conductors.—These are (1) the ingoing neurons; (2) the synapses; (3) the outgoing neurons. The mode of action of this chain differs materially in several points from the action of single neuron fibres or groups of these which make up the nerve trunk.

1. Conduction is slower, *i.e.* there is a longer interval, a longer **latent period,** between the application of the stimulus and the resulting action. Thus the time between the appli-

cation of a stimulus to a frog's foot and the drawing up of the leg is many times longer than the time which would be taken in the passage of a nerve impulse up to the cord and down again (*Practical Physiology*). The change takes an appreciable time to pass across the synapse. The duration of this time varies very greatly and is dependent on the strength of the stimulus and on the condition of the synapse.

2. While the latent period varies with the strength of stimulus, there is not the same correspondence between the strength of the stimulus and the extent of reaction in reflex arcs as there is in simple nerve fibres, and the extent of the reaction depends very largely upon the condition of the synapses. Thus, in a decapitated frog poisoned with strychnine the least touch produces very powerful reactions, while if ice be put on the spinal cord, very strong stimulation may call forth no response (*Practical Physiology*).

3. When a nerve is directly stimulated, the effect stops with the stoppage of the stimulus. But with reflex arcs the effect may be continued as an **after-discharge** for some considerable time after the stimulus is stopped. The extent of this after-discharge varies with the strength of the stimulus and with the condition of the synapse (*Practical Physiology*).

4. In a nerve the smallest effective stimulus causes the passage of an impulse and repetition of the stimulus does not increase its effect. But in reflex arcs a subminimal stimulus if repeated again and again breaks down the resistance to its passage across the synapse and leads to a reaction; there is a **summation of stimuli** (*Practical Physiology*).

5. In a nerve rhythmic stimuli lead to results at the same rate. But rhythmic stimulation of the receptors of a reflex arc is apt to set up reflex movements of quite **independent rhythm**. This is well seen in the scratch reflex which may be elicited by stimulating the skin over the shoulder in a dog with the spinal cord cut across high up. At whatever rate the stimuli are applied to the skin, the scratch movement of the hind leg recurs regularly four or five times per second.

6. While a nerve conducts impulses in both directions, a reflex arc allows its passage across the synapse in one direction only *from* the receiving *to* the reacting neuron. There is, as it were, a **valve action**.

7. Nerve fibres do not manifest **fatigue**, but reflex arcs readily do so, apparently through a change in the synapses, and these synapses are also much more susceptible to the influence of poisons—*e.g.* deficiency of oxygen or the action of such drugs as chloroform—than are nerve fibres.

8. A nerve may be stimulated again and again at very short intervals of time. If it loses its excitability after stimulation the **refractory period** is very brief. Reflex arcs manifest much more prolonged refractory periods, during which it is impossible to elicit another response. This is of great importance in preventing confusion of movements. For, since a reflex act takes an appreciable time to be performed, it is of importance that it should be completed before another is started. Sherrington has studied this in "a spinal dog," a dog with the spinal cord cut high up. One of the best examples is to be seen in the result which follows pressing the finger between the toes of the hind leg; the leg is forcibly extended as in forward progression, an act in which the other limbs must take their part before the first leg is again extended. Here a refractory period of very considerable duration supervenes on stimulation to allow of the other legs acting in proper sequence.

The spinal reflexes are **definite and purposive** in character. This may be shown by placing on the thigh of a decerebrated frog a little piece of blotting paper dipped in acetic acid. Definite and purposive movements for the removal of the paper are made by the leg, movements involving the co-ordinated and orderly consecutive action of certain muscles and the relaxation of other muscles (*Practical Physiology*). This implies the co-ordinated action of a number of outgoing neurons in response to a particular stimulation of a few in-going neurons, a co-ordinated action involving *excitation* of certain muscles and *inhibition* of others. This co-ordination in action must owe its origin to a process of evolution by which appropriate lines of conduction have been established in the spinal cord.

The reciprocal **excitation** and **inhibition** of muscles is a feature of very great importance. It has been very fully studied by Sherrington in the "spinal dog." Excitation and inhibition may occur (*a*) at the same time as when the flexors contract and the extensors are inhibited in drawing up the leg, or (*b*) they may follow one another as in the scratch reflex, which may be elicited when the skin over the shoulder of the dog is stimulated. The hind leg then performs rhythmic scratching movements, involving alternate contraction and relaxation of the flexor muscles. The mechanism involved in the ordinary flexion action of scratching is indicated in fig. 41.

That specific channels for excitation and inhibition do not exist is shown by the fact that under the influence of strychnine, the inhibitory effects may be abolished and converted to excitor effects. As a result of this, havoc is played with the co-ordination of the reflexes.

A simple uncomplicated reflex action probably does not exist, for every ingoing impression sets up a series of changes which in turn act upon the reflex arc. Thus an ingoing impulse from the skin sets up reflex contraction of muscles, and this contraction stimulates peripheral structures in the muscles, tendons, and joints, from which impulses pass inwards to act upon the arc. At the same time changes in the viscera may be produced which lead to excitation of ingoing fibres, and these again react upon the central synapses (fig. 42).

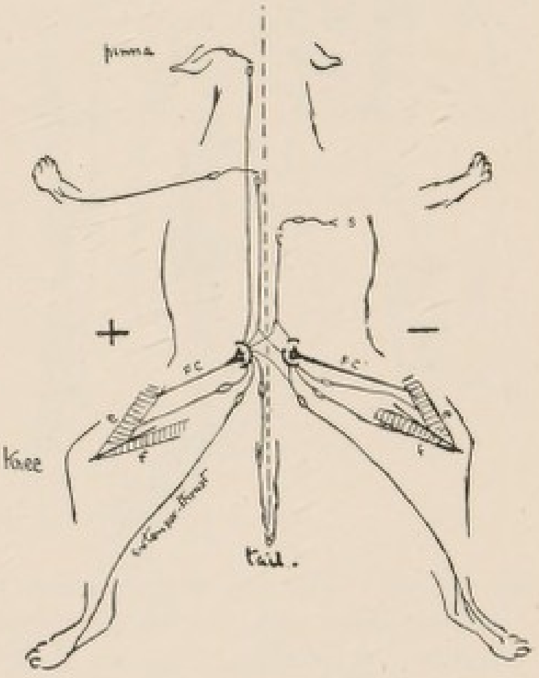


Fig. 41.—To show play of different Reflex Arcs upon a motor neuron *FC* to the vasto-crureus muscle of dog, *e*. Stimulation of the ear, tail, fore foot, and pressure on the pad of the hind foot of the same side, all cause excitation, as also do stimulation of the shoulder of the opposite side and nocuous stimuli of the opposite hind foot. On the other hand, it is inhibited by stimulation of the shoulder of the same side, as in the scratch reflex and by nocuous stimuli of the hind foot of the same side. (Sherrington.)

The activity of every spinal arc is carried on alongside that of many others, and each of these may materially modify its character. Two reflexes induced by similar stimulation from adjacent areas may reinforce one another and increase the general reaction. On the other hand, two stimuli of different kinds from the same area may induce one or other reflex. Thus, while pressing the finger in the pad of the dog's foot causes the extensor thrust, injurious stimuli cause a flexion-withdrawal of the foot. When the two stimuli are applied at once, one or other, but not a combination of the reflex actions, will manifest itself. In the performance of each of these reflexes the same outgoing nerve paths are employed, and in the contest between the two stimuli one of the stimuli overcomes and replaces the other. In this way **inco-ordinate movements by mixtures of reflexes are prevented.**

The ingoing fibres are probably five times as numerous as the outgoing fibres, and each one of them is connected, or may become functionally connected, with many different combinations of outgoing fibres. Hence it is difficult to get a reflex which does not interfere with others, either by increasing or antagonising them. The outgoing paths are merely passive channels in the hands of certain ingoing reflex paths. In illustration of this, Sherrington cites the outgoing motor neuron to the *vasto-crureus* of the dog, and in fig. 41 shows how this is the common path to different reflexes induced by different stimulation of different parts of the body. Some stimuli excite its activity and may be grouped together as "allied"; others inhibit its activity and thus act as "antagonistic" to the former group.

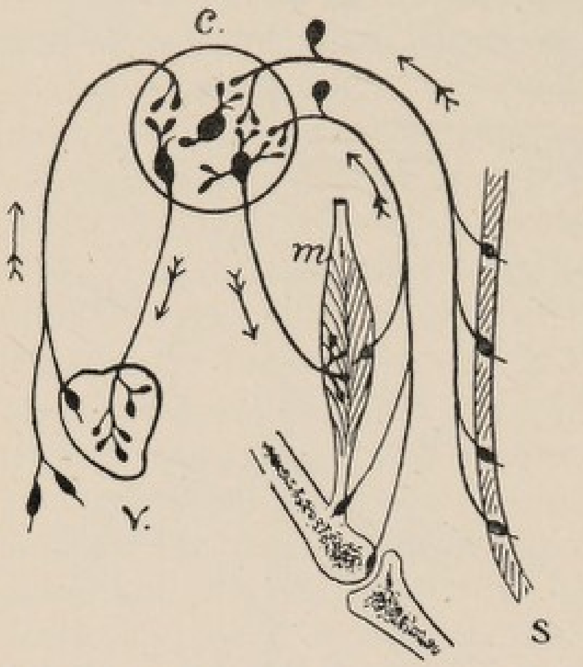


FIG. 42.—To show the way in which the different reflex arcs react on one another. *S*, skin; *M*, muscle; *V*, viscus; *C*, spinal cord with synapses. (M'DOUGALL.)

Spread of Reflexes.—While with gentle stimuli many reflexes tend to manifest themselves in the outgoing neurons of the same region of the cord, other reflexes, such as the scratch reflex of the dog, always involve neurons in widely different regions. But even in reflexes which are localised when gentle stimuli are applied, and which tend to spread under the influence of powerful stimulation, the spreading occurs along definite lines for each type of stimulation. Thus, the ordinary flexion-withdrawal of the foot on stimulation is at first confined to the ham-string muscles, but, as the stimulus is increased in strength, the movement spreads to involve the flexors of the hip and knee, extension of the opposite hind leg, then extension of the fore limb of the same side and flexion at the elbow of the opposite fore limb with some extension of the wrist, turning the head towards the same side, often opening of the mouth and lateral deviation of the tail. Thus a **reflex figure** tends to be struck, and in the striking of this figure the stimuli from the muscles and joints set up by each stage of the movements probably play a very important part (fig. 43). These definite channels of spread of reflex action appear to have been developed by the progress of evolution.

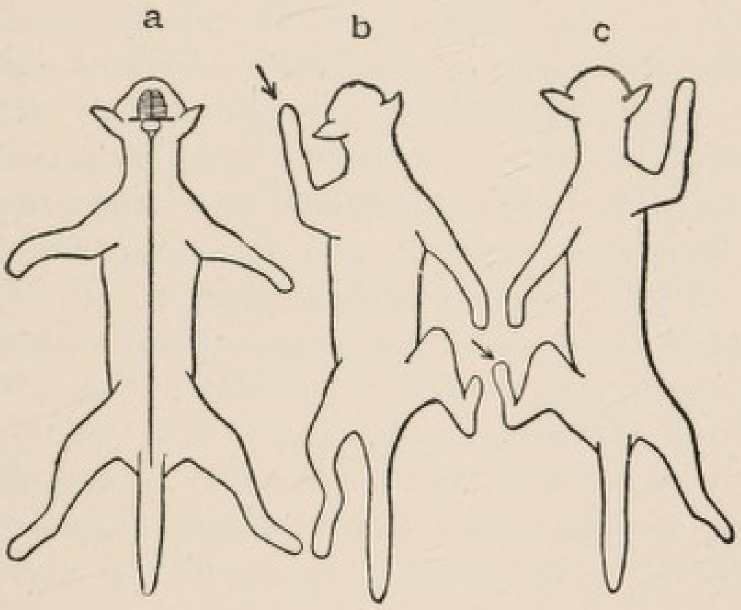


FIG. 43.—Reflex figures struck in decerebrated cat on stimulating a fore and a hind paw. (SHERRINGTON.)

The Receptors.—It is much more easy to elicit reflex action by acting upon the neuron-termination than by acting upon the nerve in its course. This may be demonstrated by observing the relative strengths of the pinch which it is necessary to apply to the skin of the foot of the frog and to the exposed sciatic nerve in order to produce a reflex contraction of the muscles. The receptors have the property of **lowering**

the threshold of effective stimulation. When the mechanisms involved in the special senses are studied (p. 100 *et seq.*) it will be found that special receptors are developed, each variety of which lowers the threshold of excitability of the arc for one kind of stimulus and increases it for all others. It is by this arrangement that different kinds of change each produce their appropriate result.

Classification of Receptors.—It has been already seen that different reflexes of the cord may be evoked by different kinds of stimulation from without. Different stimuli each call forth a distinctive response. Thus, an injurious stimulus to the foot causes a flexion and withdrawal of the leg, while pressure between the toes causes an extension. Various receptors are, as it were, tuned to special kinds of stimulation. Those which respond to stimuli from without may be called **extero-ceptive.**

They may be roughly classified into those responding to injurious stimuli, *noci-ceptive*, and those responding to non-injurious stimuli. Those connected with the cord respond to stimuli resulting from changes in close proximity to the body, such as touch, the addition or withdrawal of heat, the application of chemical substances.

But spinal reflexes are not only evoked by stimulation from the outside of the animal, but also from stimulation of the inside, *e.g.* stimulation of the inside of the stomach. The receptors situated in these viscera may be called **intero-ceptive.**

Yet another set of stimuli come into play in spinal reflex action. The end organs of neurons in the muscles, tendons and joints may be stimulated by the reflex response of the muscles, and may in turn set up reflex action often sustained and tonic in character and of great importance in determining the posture assumed. These receptors, stimulated by the condition of the animal's own tissues, may be termed **proprio-ceptive** (see fig. 42).

Stimulation of the extero-ceptive receptors plays the chief part in *initiating* movements, stimulation of the proprio-ceptive, as a result of these, in *guiding and co-ordinating* the movements. The proprio-ceptive reflex when induced may reinforce the extero-ceptive reflex which started it, or it may evoke compensatory movements, bringing the part back to its former position.

B. Brain Arcs in Reflex Action

It is obviously of importance to an animal that its anterior end, which in progression first comes into relationship with any change in its surroundings, and in which is situated the mouth, by which it feeds and therefore exists, should be well provided with receptors, so that through them appropriate reactions of the whole body to changes in the conditions may be produced.

Hence it is in connection with the head that the most complex development of extero-ceptive receptors (see p. 104) occurs. Some of them, as those in connection with the spinal cord, respond to stimuli in close proximity, *e.g.* the sensitive tactile whiskers of the cat, and the receptors in the mouth, which produce different reactions to nocuous and non-nocuous stimuli. But in addition to these, others are developed which are acted upon by stimuli coming from a distance, *e.g.* light, sound, volatile chemical substances, and these may be called **distance receptors.** Their great importance is that by their action the body is prepared for the more immediate contact with the external condition, and is adjusted either to escape nocuous agencies or to seize nutritive material, *e.g.* in the capture of prey. So important is the action of these distance receptors in the higher animals, that a mass of nerve tissue, the cerebrum, is developed to bring about the reaction of the head and body generally to these stimuli. In order that these reactions to the distance receptors may be properly co-ordinated with the responses to the non-distance receptors, such as the organs of touch, these latter are closely linked to the cerebrum by definite bands of nerve fibres (fig. 40).

Still further to secure the appropriate and co-ordinated action of the head and body to these distance stimuli, a special proprio-ceptive mechanism is developed in the head, a mechanism which is called into play by movements of the head, and which thus assists in adjusting the position of the head and body, just as the action of the proprio-ceptive structures in muscles assist in adjusting the position of the limbs (see p. 102). This mechanism is developed from the internal ear, and may be termed the **labyrinthine receptor mechanism** (see p. 154).

It is the dominant adjusting or balancing mechanism in the body and it exercises a constant control over the proprio-ceptive mechanism connected with the cord. So much is this the case that its destruction leads to inability to co-ordinate the movements of the eyes, head and limbs, and to loss of muscular tone. This is seen in the "knock-out" blow on the jaw, which forces the condyles against the base of the skull, and by deranging the action of the labyrinth leads to a sudden and absolute loss of muscular tone.

Just as the cerebrum is developed in connection with the distance receptors of the head, so the cerebellum is developed in connection with the labyrinthine receptor mechanism. And just as the non-distance receptors of the cord are connected up with the cerebrum, so the proprio-ceptive mechanism of the cord is connected with the cerebellum.

Thus it is that in the higher animals the head receptors and the brain which is developed in connection with them dominate the cord and control the various spinal reflexes.

So far the reactions of the neuro-muscular mechanism have been considered simply as an affair of reflexes. But the activity of the cerebrum is accompanied by changes in consciousness, and it is assumed by some that the state of consciousness is *the* determining factor in the result, and hence such actions have been called **voluntary**. But since in such conditions as sleep-walking and hypnosis the most complex and selective actions are performed without the intervention of consciousness, it must be admitted that this metaphysical phenomenon is not an *integral* part of the response of the nervous system.

On the other hand, we know that the character of the reaction to any stimulus is largely dependent upon the **state of the nervous centres.** Just as a touch produces a different effect in a frog poisoned with strychnine and in one under the influence of bromide of potassium, so a sudden noise may produce a totally different reaction upon a person with a fatigued brain or a brain poisoned by alcohol, and upon one with the brain in a good state of nutrition.

Not only does the temporary state of nutrition thus modify the result of a stimulus, but the **paths of action previously opened** and defined through the centres also have a marked influence. (1) These paths may have been formed in past generations and inherited from the parents. In young fowls, as soon as they are hatched, the acts of walking and of pecking are at once performed, and in many families particular gestures or expressions follow certain modes of stimulation in many different individuals without the consciousness of the person being involved. They are inherited cerebral reflexes. (2) Paths may also have been developed in the individual as the result of previous activities of the nervous mechanism. For, if a given action has once followed a given stimulus, it always tends to follow it again. This, in fact, is the basis of all rational education alike in man and in the horse and dog—to open up paths in the nervous system by which the most suitable response may be made to any given stimulus, and to prevent the formation of paths by which inappropriate reaction may be produced.

3. FATIGUE OF THE NEURO-MUSCULAR MECHANISM

Continued action of the neuro-muscular mechanism leads to fatigue, and this may best be studied by means of some form of **ergograph**, an instrument which enables the response of a muscle to stimuli to be recorded. If a muscle be "voluntarily" or reflexly stimulated again and again it finally ceases to react. But if now the outgoing nerve is stimulated the muscle contracts at once. This shows that fatigue first manifests itself in the central synapses. If the outgoing nerve be repeatedly stimulated, after a time the muscle no longer responds, but if the muscle be directly stimulated it contracts. The muscle therefore is not fatigued. Since the electrical changes which accompany conduction in a nerve still go on, it is obvious that the nerve still acts. It is therefore the nerve ending in the muscle which fatigues after the central synapses.

Fatigue is due to the accumulation of the products of the activity of muscle, and it may be induced in a normal dog by injecting the blood from a dog which has been fatigued.

In studying the neuro-muscular mechanism it is most important to keep clearly in mind the meaning of the terms *stimulus*, *reaction*, and *sensation*. (*a*) Stimulus is the change in the surroundings which produces (*b*) the Reaction, the modification in the action of some part of the body. (*c*) Sensation is the change in the consciousness which may accompany the application of a stimulus and the reaction.

Special Neuro-Muscular Mechanisms of the Horse

1. In **standing** the weight of the body is chiefly slung by the serrati magni on the scapulæ, which are supported by the bony column of the fore limb, the flexors and extensors maintaining the condition of partial flexion at the elbow joint, and the bend at the fetlock being supported by the strong superior sesamoidean ligament. The posterior common ligament of the carpus is upon the stretch and acts as a further stay. The hind limbs are used alternately to support the weight of the posterior part of the body, that not in use being partly flexed and resting on the toe. From the fact that the hind legs are less straight than the fore legs, more muscular work is required in using them as supports.

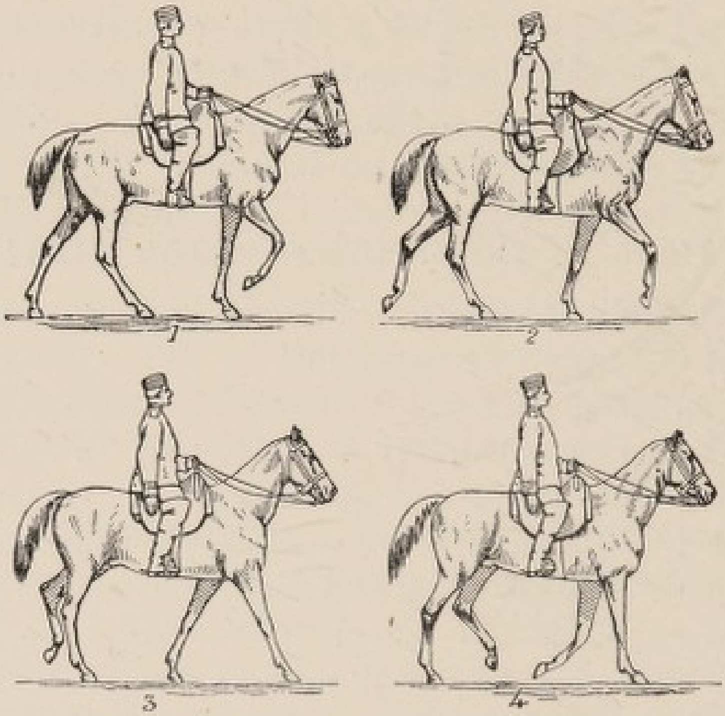


FIG. 44.—The Walk. (ELLENBERGER.)

2. The movements of the horse at the different paces have been analysed by instantaneous photography.

(1) **Walk.**—The body being balanced on three legs, as shown in fig. 44, one fore leg is advanced, the body moves forward on the corresponding hind leg and the opposite hind foot leaves the ground before the fore foot reaches it, so that for a moment

the horse is balanced on diagonal legs (2). The hind foot which has left the ground is now advanced, and before it is planted the corresponding fore foot is lifted (3), and thus, at this stage, the animal is balanced on the fore and hind leg of the same side (4). As the hind foot comes to the ground, the condition described at the starting is again reached and the process is repeated.

(2) **Trot.**—The body is driven forward by the alternate propulsive action of the diagonal fore and hind legs. The near fore and off hind feet leave the ground together, propelling the body upwards and forwards (fig. 45, 1), and are then advanced to again reach the ground, when the off fore and near hind feet repeat the same movements (3).

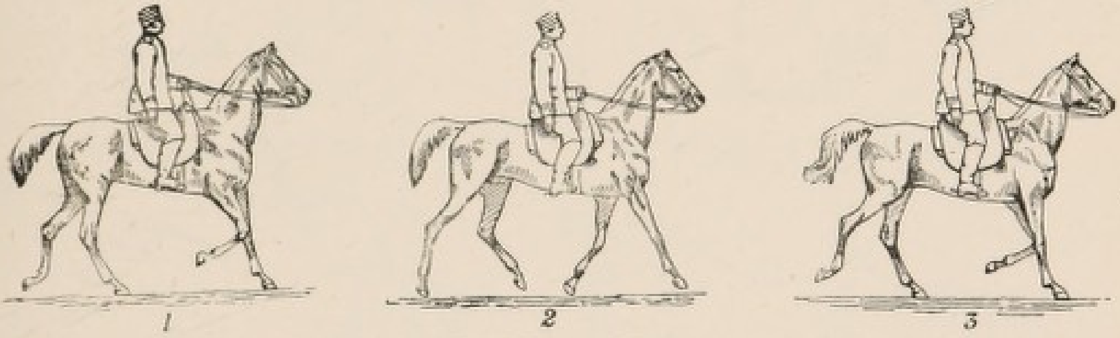


FIG. 45.—The Trot. (ELLENBERGER.)

(3) **Amble.**—Here the two legs of the same side act together as do the diagonal legs in trotting.

(4) **Gallop.**—At one stage of the pace, all the feet are off the ground and well tucked under the body (fig. 46, 1). One hind foot, say the near, first reaches the ground (2), and immediately after the opposite hind foot is planted in advance of it (3). The near fore now comes to the ground, and as it does so the near hind is lifted and the horse rests on diagonal fore and hind legs (4). Then the off hind foot leaves the ground and

	Near Hind.	O Hind.	Near Fore.	Off Fore.
1	off	off	off	off
2	on	off	off	off
3	on	on	off	off
4	off	on	on	off
5	off	off	on	on
6	off	off	off	on

the animal is now on the near fore foot (5). The off fore foot is now planted and the near fore leaves the ground (6), and finally the off fore is also raised and the horse is again in the air.

(5) **Canter.**—The canter is a less energetic gallop. At one moment all the feet are off the ground, and they are planted in the same order as in the gallop—near hind, off hind, near fore. But while in the gallop the near hind has left the ground before the near fore is planted, in the canter all these are on the ground at once, and it is only as the off fore comes to the ground that the near hind followed by the near fore is raised. The off hind and then the off fore next follow, and all the feet are again off the ground.

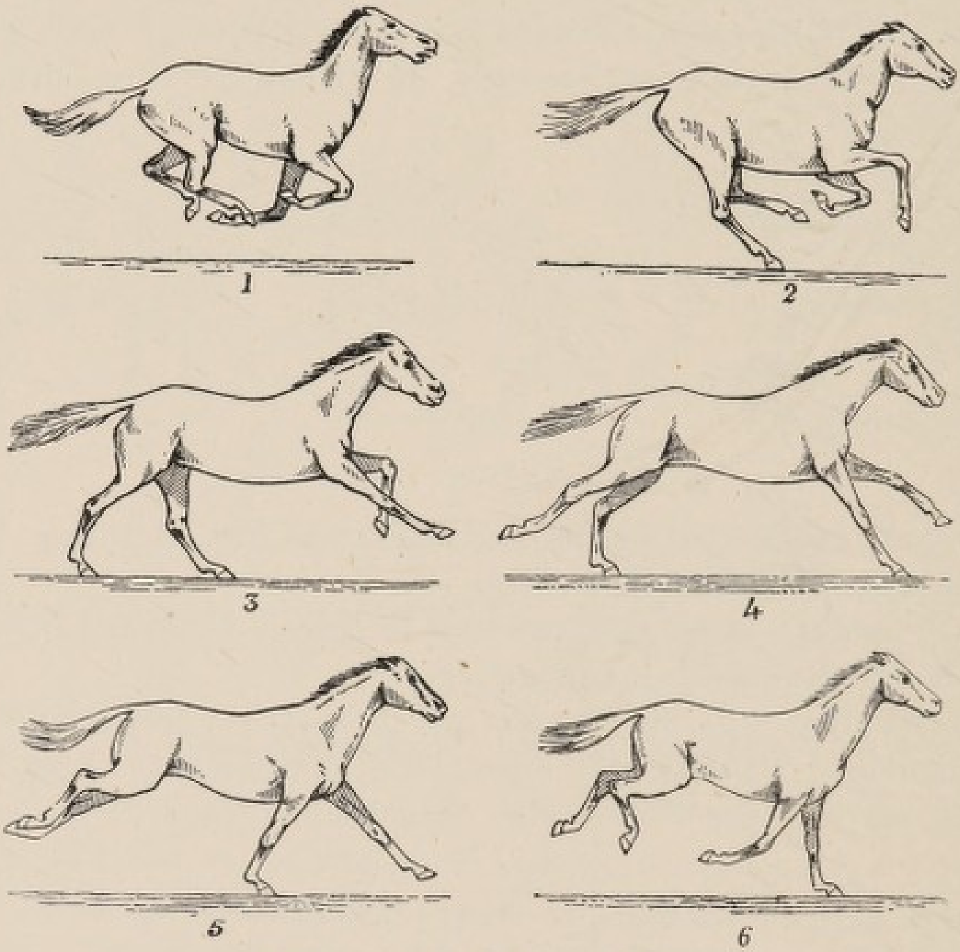


FIG. 46.—The Gallop. (F. SMITH.)

(6) **Jump.**—The fore legs propel the body upwards, and the hind legs give a further forward and upward propulsion and are then fully flexed under the body to clear the obstacle. The animal alights on its fore feet, one reaching the ground before the other.

The Foot

The physiology of the **foot** in the horse in these neuromuscular actions is of great importance (fig. 47).

The anatomical study of the structure has taught that the weight of the body is transmitted through the coronal bone (second phalanx) (*P.*) to the foot, and that the articular surface of the coronal is larger than that of the pedal bone (third phalanx) (*Pe.*), so that it rests at its posterior part upon the navicular bone (*N.*) and perforans tendon (*P.T.*). Further, at each side of the pedal bone posteriorly are the large lateral cartilages with a dense fibrous and fatty mass of tissue between them (*C.*). The periosteum of the pedal bone is covered by a

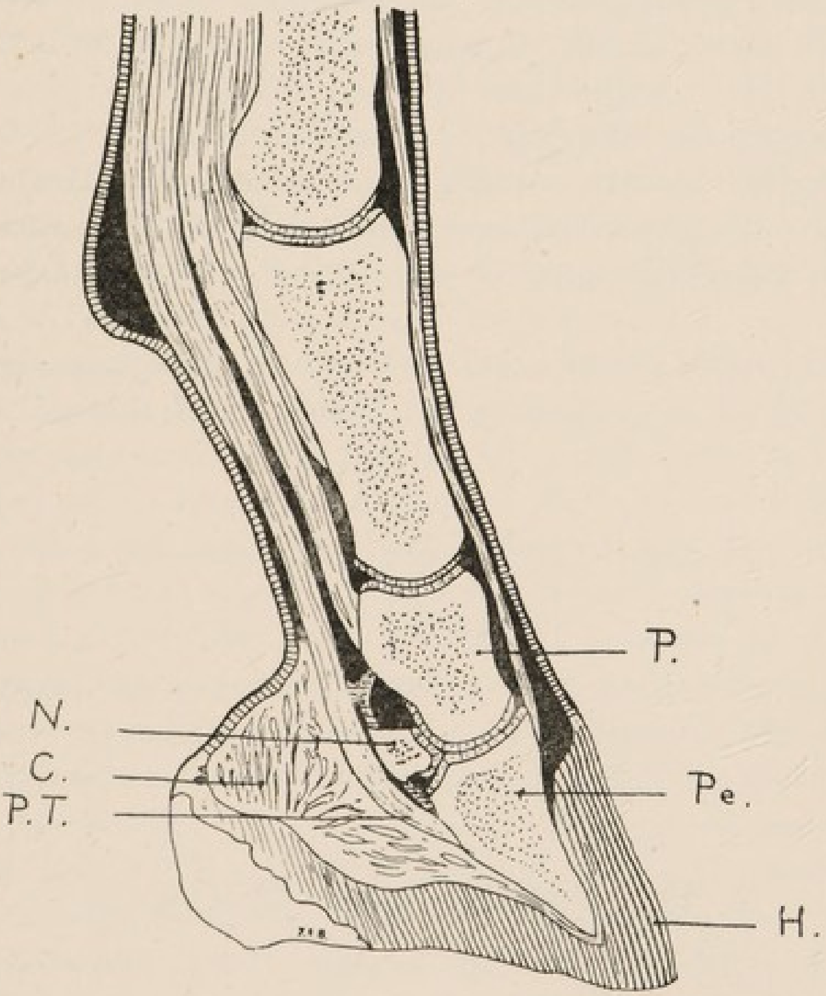


Fig. 47.—Longitudinal Section of Foot of the Horse. *H.*, hoof; *C.*, intercartilaginous pad; *Pe.*, pedal bone; *P.*, coronal bone; *N.*, navicular bone; *P.T.*, perforans tendon.

dense fibrous tissue which on its surface is raised in numerous ridges with side branches—the sensitive lamellæ, vertical in direction in front and oblique posteriorly, and on the surface of these is formed the great epithelial structure, the borny **hoof** (*H.*), comparable to an exaggerated nail. In this the anatomical point of importance is the fact that it is very dense and hard in front and softer and more elastic behind, especially in the region of the prominence on the sole called the frog.

As the foot is brought down the heel first comes to the ground and, in the natural condition, shock is prevented by the elasticity of the posterior part of the foot, due to:—

1. The elastic horn of the frog;
2. The almost transversely disposed lamellæ;
3. The elastic lateral cartilage and intermediate tissue;
4. The pressure being transmitted from the coronal bone through the elastic sling of the navicular bone and perforans tendon.

The alternate compression and expansion of these structures has the effect of massaging the blood out of the veins of the foot and of thus assisting its onward propulsion, a matter of no small importance in such dependent structures as the feet.

As the foot is raised it is the toe which last leaves the ground, driving the body forward and upward, hence the hard resistant character of the hoof in front, its firm and direct connection with the pedal bone, the vertical direction of the lamellæ, and the arrangement by which as the coronopedal joint is flexed the pressure is transmitted directly from one bone to the other.

4. THE CHIEF RECEPTOR MECHANISMS

The Senses

In order that each particular kind of change in the surroundings of the body may produce its appropriate reaction, it is essential that the different kinds of changes should act in different ways—that the contact of gross matter, changes of temperature, vibrations of the air, vibrations of the ether, and various chemical changes should produce their special effects.

To secure this, as we have already seen, special peripheral developments of neurons, special receptors, have been evolved which react more particularly to each of these special kinds of change. With these peripheral neurons particular parts of the central nervous system are connected and associated, so that a special reaction to each of the various kinds of stimuli may occur. These reactions may be accompanied by changes in the consciousness—by sensations; and since our consciousness is our instrument of knowledge—our Ego—these sensations appear to us the chief and most important part of the action of the mechanism, and hence their activities are often considered as **The Senses**. That, in many reactions, sensation is not an essential part, we have already indicated. Most of our knowledge of the senses has necessarily been gained by observation and experiment on the human subject, and it is perhaps unjustifiable to assume that the results obtained can be applied to lower animals. We know that in certain animals certain receiving mechanisms are specially developed, while in others other mechanisms are of chief importance. But how far the activity of these mechanisms affects the consciousness it is impossible to say.

A. INTERO-CEPTIVE MECHANISM

Common Sensibility

Throughout the internal organs are various peripheral terminations of ingoing nerves, some apparently of the nature of simple dendritic expansions, some of dendritic expansions enclosed in definite fibrous capsules (Pacinian Corpuscles), which are called into action by different kinds of stimulation, nocuous and innocuous, to produce reflex adjustments of the bodily mechanism either without or with the involution of consciousness—that is, either without or with the production of sensation (see p. 96). Thus when food is taken into the stomach it stimulates the ends of the different nerves, and these carry the impulse up to the central nervous system to produce a reflex dilatation of the gastric blood vessels.

When the consciousness is involved in the action of these mechanisms the sensations experienced are generally vague and difficult to describe, and have been grouped under the term of Common Sensations. The ordinary sensations of **thirst** and

hunger are examples of these, sensations which, although due to changes in the mouth, throat, or stomach, give us information as to the general needs of the body. Such sensations may be considered as normal and physiological. But when abnormal conditions exist in certain localities they produce sensations such as **tickling**, **tingling**, etc., and generally lead to a reflex endeavour to remove the abnormal stimulus.

When nocuous stimuli act they generally not only evoke some reflex adjustment, as when indigestible matter in the stomach causes vomiting, but they produce changes in the consciousness which are generally classed as unpleasant or painful. All **pain**, since it means a change in consciousness, is metaphysical. There is not such a thing as "physical pain." The fatigue and other sequences to any kind of pain are frequently cited as proofs of the influence of the mind on the body. But we have no right to assume that they are caused by the "pain" rather than by the physical disturbances in the nervous system of which the pain is an accompaniment.

It must be recognised that pain is purely a relative term, and that conditions which in one individual will cause pain will not cause it in another, while stimuli which will produce what are called painful sensations when the nervous system is debilitated may give rise to sensations not considered as painful when the nervous system is normal.

The mechanism of common sensibility is not acted on by the same stimuli in all parts of the body. The *mouth and throat* are the parts to which the sensations are referred in abstinence from fluids, the stomach in the absence of food. The *intestine* appears to give rise to sensation only when abnormally stimulated. In the *skin* the mechanism of common sensibility is so closely associated with the mechanism of the tactile and temperature senses that it is difficult to differentiate them. Abnormal stimulation of the skin produces painful sensations very readily, while similar changes in other tissues—*e.g.* muscles—cause no modification of consciousness.

The nerve channels by which the changes producing common sensibility are transmitted in the central nervous system are distinct from those connected with the tactile and other senses, and common sensibility may persist while the tactile sense is lost (see p. 109).

B. PROPRIO-CEPTIVE SPINAL MECHANISM

Kinæsthetic or Muscle and Joint Sense

The importance of the action of the receptors which are stimulated by the action of muscles has been indicated in the study of reflex action (p. 96). A double mechanism is involved—1st, A mechanism stimulated by the contraction of the muscles; and 2nd, a mechanism acted on by movements at the joints. The receptors are of three kinds:—

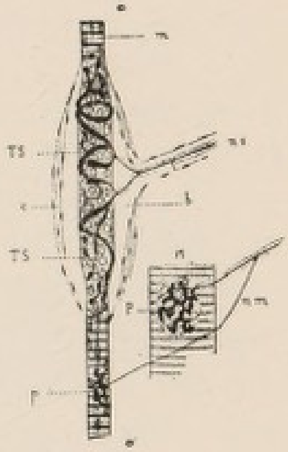


Fig. 48. — Structure of muscle spindle—only one fibre represented. *b*, capsular space; *c*, capsule; *p*, motor termination; *T.S.*, sensory termination on the spindle fibre. (*From* Regaud and Favre.)

(1st) *Muscle Spindles.*—Among the fibres of the muscles are found long fusiform structures containing modified parts of the muscle fibres. Into each spindle a medullated nerve passes and breaks up into a non-medullated plexus round the fibres (fig. 48).

(2nd) *Organs of Golgi* are small fibrous capsules in the tendons near the muscle fibres into which a medullated fibre enters, and losing its white sheath forms a plexus of fibrils with varicosities upon them.

(3rd) Varicose terminations of axons surrounded by fibrous tissues are found in the synovial membranes and round joints.

Through these mechanisms information is transmitted to the central nervous system as to the position and movements of the various parts, and this, as has been already indicated, although not necessarily modifying the consciousness, is of the utmost importance in **guiding the movements.** When the consciousness is affected, valuable information as to the conditions of the surroundings may be gained. In estimating the **weight** of bodies, these sensations are much used. The body to be weighed is taken in the hand, and by determining the amount of muscular contraction required to support or raise it, the weight is estimated. The **shape** and **size** of objects are also determined by this sense in conjunction with the sense of touch by estimating the distance through which the limb touching it may be moved in different directions. In the dark the **distance** of objects is also judged by estimating the extent of movement of the hand and arm necessary to touch them.

The receptors in deeply seated structures may also be stimulated by pressure from without, for Head has found that after the cutaneous nerves to a part have been divided, pressure with the point of a pencil is still felt and well localised.

C. EXTERO-CEPTIVE MECHANISM

The Special Senses

As we have already seen, the outside of the body is richly supplied with a variety of receptors, each one of which has a low threshold of stimulation for one particular kind of stimulus and a very high threshold for all other kinds.

We have further seen that these may be divided into receptors, stimulated by changes set up close to the body, *non-distance receptors* and receptors acted upon by changes which may originate at a distance—*distance receptors.* Among the former may be classed the receptors in the skin and mouth, and among the latter those in the nose, ear, and eye.

NON-DISTANCE RECEPTORS

(*a*) For Contact

Tactile Sense

Even after the nerves from a portion of skin have been cut, contact with the point of a pencil is felt, but a prick with a sharp pin, heat and cold, and such gentle contact as touching a hair are no longer felt, and, if a fold of skin is pinched up, and a pencil pressed on the side of the fold, it is not felt. This means that deeply-placed receptors, the fibres of which travel with motor nerves, can be stimulated by pressure through the skin. This, however, is not the mechanism concerned in true tactile sense.

1. Receptors

Tactile corpuscles consist of a naked branching varicose termination of axons surrounded by sheaths of fibrous tissue, situated in the papillæ of the true skin (fig. 49).

2. Physiology

The study of reflex action in the "spinal dog" (p. 93) has revealed how various may be the reactions to different stimuli of the skin, according to the part stimulated and to the character of the stimulus. Thus harmful stimulation of the foot causes a flexion and drawing up of the leg, pressure of the sole with the finger causes the extensor thrust. Again, gentle stimulation on the shoulder causes the characteristic scratching reflex.

Nocuous stimuli seem to cause a different reflex result from non-nocuous. They are antagonistic, and the nocuous stimulus is generally prepotent, and is able to replace in reflex action the non-nocuous. The sensation which accompanies their stimulation is not that of contact but of pain, and the central neurons which transmit such impulses run independently of those transmitting true touch impulses.

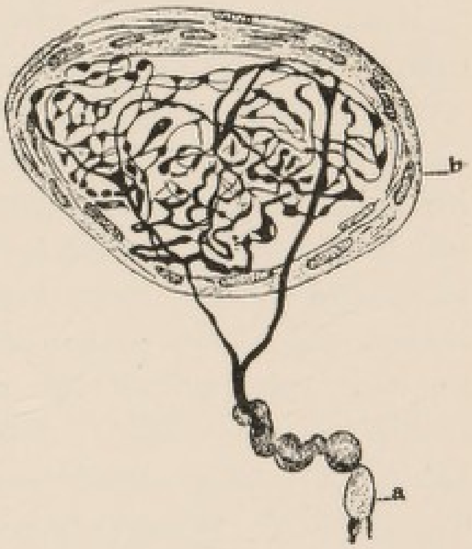


FIG. 49.—Simple form of sensory nerve termination. In the tactile corpuscle the nerve fibre coils round the capsule before entering. (DOGIEL.)

The tactile sense may be best studied under three heads:—

1. **The Power of Distinguishing Differences of Pressure.**—Variations of pressure in time and space are alone distinguished. We live under an atmospheric pressure of 760 mm. of mercury, but this gives rise to no sensation. Any *sudden* increase or diminution of pressure, however, leads to a marked change of sensation, but a slow change causes a lesser modification of consciousness.

2. **The Power of Localising the Place of Contact.**—Where the tactile organs are abundant, as in the lips of the horse, the power of distinguishing accurately the point touched is more acute than in places where these are more scattered.

3. **The Power of Distinguishing Contacts in Time.**—If the finger be brought against a toothed wheel rotated slowly, the contacts of the individual teeth will be separately felt.

But if the wheel is made to rotate more and more rapidly, the separate sensations are no longer felt, but a continuous sense of contact is experienced. (*Practical Physiology.*) This indicates that, if stimuli follow one another sufficiently rapidly, the sensations produced are fused. From this it is obvious that the sensation lasts longer than the stimulus—the contact.

The paths of conduction to and in the central nervous system and the position of the centre in the brain are considered on p. 205.

(*b*) For Addition and Withdrawal of Heat

Thermal Sense

Heat, like light, is physically a form of vibration of the ether. The temperature sense depends upon the fact that when heat is withdrawn from the body we have one kind of sensation which we call *cold*, and when heat is added to our body another sensation which we call *hot*. This depends upon the temperature of our body in relationship to the surroundings, and not merely on the temperature of surrounding bodies. If three basins of water are taken, one very hot, one very cold, and one of medium temperature, and if a hand be placed, one in the very hot and one in the very cold water for a short time, and then transferred to the basin with water at a medium temperature, the water will feel hot upon the hand that has been in the cold water and cold upon the hand that has been in the hot water. (*Practical Physiology.*)

The rate at which heat is abstracted or added is the governing factor in causing the sensation; a sudden change of temperature stimulates far more powerfully than a slow change. For this reason the **thermal conductivity of substances in contact** with the skin has an influence upon the sensation. If a piece of iron and a piece of flannel side by side be touched, the first will feel cold, the second will not, because the former has high thermal conductivity, the latter has not, and thus the former abstracts heat more rapidly than the latter.

Certain parts of the skin are stimulated by the withdrawal of heat, and their stimulation is accompanied by sensations of cold, while others are stimulated by the addition of heat and give rise to a sense of warmth. This may be demonstrated by taking the cold point of a pencil and passing it over the back of the hand, when it will be felt as cold only at certain points ; such points have been called **cold spots,** while similar spots stimulated by the addition of heat are called **hot spots.** (*Practical Physiology.*)

The temperature sense is independent of the tactile sense. The one may be lost and the other retained. It is probable that the nerve endings in the deeper layers of epithelium are connected with the temperature sense.

Much light has been thrown by Head on the nature of the nervous mechanism connected with cutaneous sensibility in man and probably in the lower animals. He had the radial and external cutaneous nerves in his own arm divided below the elbow, and he thus severed all fibres from the skin over an area on the outside of the hand and fore-arm.

(1) Immediately after the operation he found that the pressure sense was not lost, and that a touch with a pencil was felt and well localised. True tactile sense, as tested by touching with a soft substance like cotton wool, and the sense of pain as tested by the prick with a pin, were lost. Ulcers tended to form over the paralysed area.

(2) After seven weeks he found that a prick with a pin could be felt as a painful sensation, not well localised and radiating widely. Differences of temperature between ice-cold water and water at 50° C. could be appreciated, and the cold and hot spots were sharply defined and reacted as cold to water at 24° C. and hot to everything above 38° or 40° C. The sensation radiated widely and was not graduated, the intensity depending upon the number of spots stimulated, large surfaces at 25° C. giving a more marked sensation of cold than small surfaces at 0° C.

By the end of 200 days this condition was completely restored over the whole area, and ulcers no longer tended to form. He considers that the nerve structures involved constitute the great reflex mechanism presiding over the nutrition of the skin. In action it produces qualitative not quantitative changes in the consciousness. He terms it **Protopathic Sensibility**.

(3) For more than a year the area remained insensitive to light touch with cotton wool, then gradually it became sensitive to

such light contact and to slight differences of temperature, giving sensations of *warmth* and *coldness* as opposed to the previous sensations of *hot* and *cold*. This he terms **Epicritic Sensibility.**

He discovered a small area on his hand in which the epicritic sense was not lost but the protopathic sense was lost. Light touch and differences of temperature between 36° and 45° C. were appreciated, but the difference between water at 50° C. and ice was not felt.

He concludes from this and from the different rate of regeneration that the two sets of nerves are independent.

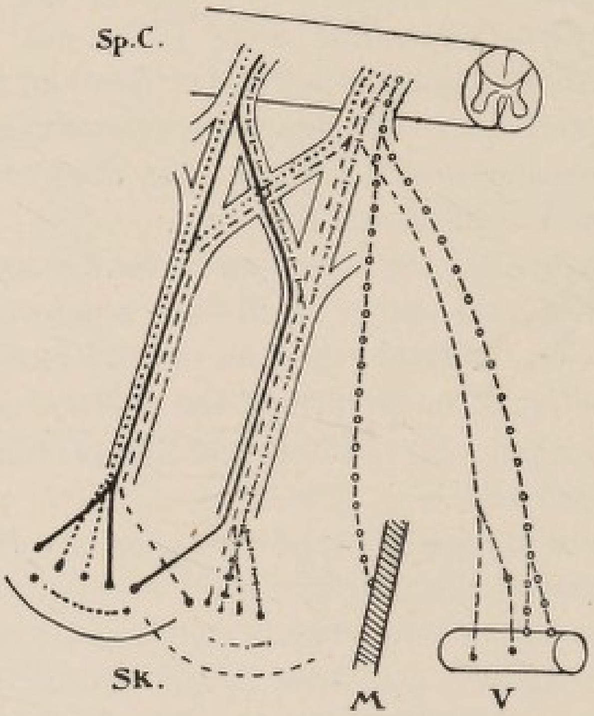


Fig. 50.—To show the arrangement of Epicritic, Protopathic, and Deep-ingoing Fibres in their distribution, and in their course in peripheral nerves and in the plexuses ; -̇|-̇|-̇ Epicritic Fibres ; ═══ Protopathic Fibres ; -o-o-o Deep Fibres. (See text.)

He further finds, from the study of cases of nerve section, that division of a peripheral nerve leaves sharply-defined areas of loss of epicritic sense, but great overlaps in the protopathic sense. On the other hand, when a cord of the brachial plexus is divided, the area showing loss of protopathic sense is more sharply defined. When a series of posterior roots are cut, loss of protopathic and epicritic sensibility correspond. He concludes that the posterior roots are the units for protopathic sense, while the peripheral nerves are the units for epicritic sense (fig. 50).

In the spinal cord there is no indication of separate channels for these two kinds of nerves, but the sensory impulses get shunted into special tracts for heat, cold, touch, etc. (see p. 206).

He also considers visceral sensations. He finds that, when water is applied to the inside of the colon, differences of temperature between 20° and 40° C. are not appreciated, but ice-cold water is felt as cold and water at 50° C. as hot. The sensation is not localised. He argues that the viscera have protopathic but not epicritic sensibility, but he points out that most of the visceral sensations are due to a sense akin to the muscle sense.

He concludes that the body within and without is supplied with protopathic fibres and with fibres associated with sensation of movement and of pressure, but that to the skin alone epicritic fibres pass (fig. 50).

How far epicritic sensibility exists in the lower animals it is not easy to determine. Possibly it has been evolved in the primates in connection with the important part played by the tactile sense of the hand in directing the movements of the animal.

(*c*) FOR CHEMICAL STIMULI

Sense of Taste

1. **Receptors.**—These receptors are developed in the mouth with the object of determining the utilization or rejection of material taken into the mouth according as it is beneficial or nocuous.

The most important receptors consist of groups of spindle-shaped cells with which the dendritic termination of the nerves from the mouth are connected, each group of cells being surrounded by a series of flat epithelial cells like the staves of a barrel to form a taste bulb. These *taste bulbs* are most abundant at the back of the tongue, on the sides of the large circumvallate papillæ which form the prominent V-shaped line on the posterior part of the dorsum.

2. **Connections with the Central Nervous System.** — The posterior third of the tongue is supplied by the glosso-

pharyngeal nerve. The anterior two-thirds are supplied by the lingual of the fifth and the chorda tympani of the seventh. It has been maintained that all these fibres enter the medulla by way of the Gasserian ganglions and the root of the fifth nerve; but the study of cases in which the ganglion has been removed does not support this view, and the evidence seems to indicate that the fibres enter the medulla by the roots of the nerve in which they run.

The position of the receiving centre in the brain is considered on p. 205.

3. **Physiology.**—As to the way in which this mechanism is stimulated our knowledge is very imperfect. In order to act, the substance must be in solution. The strength of the sensation depends on the concentration of the solution, upon the extent of the surface of the tongue acted upon, upon the duration of the action, and upon the temperature of the solution. If the temperature is very high or very low the taste sensation is impaired by the feelings of cold or heat.

It is most difficult to classify the many various taste sensations which may be experienced, but they may roughly be divided into four main groups:—

1. Sweet.
2. Bitter.
3. Acid.
4. Saline.

Whether different sets of terminations react specially to each of these is not known, but it has been found that substances giving rise to the sensation which we call bitter act best on the back of the tongue, while substances producing sweet or acid sensations act on the sides and front. Again, chewing the leaves of *gymnema sylvestre* abolishes sensations of sweet and bitter, but does not interfere with those of acid and saline, and leaves the tactile sense unimpaired. On the other hand, cocaine paralyses the tactile sense before it interferes with the sense of taste.

The sense of taste is very closely connected with the sense of smell, and, when the latter is interfered with, many substances seem tasteless which under normal conditions have a marked flavour.

DISTANCE RECEPTORS

(*a*) For Chemical Stimuli

Sense of Smell

Smell, as Sherrington puts it, is taste at a distance. Just as the taste organs are stimulated by substances taken into the mouth, so the olfactory organs are stimulated by volatile substances inhaled through the nose.

The olfactory organs are the most fundamental of all distance receptors, and they play a most important part in the life of the lower animals in guiding them to their food and repelling them from danger, in causing positive and negative chemiotaxis. In such animals the mechanism is very highly developed.

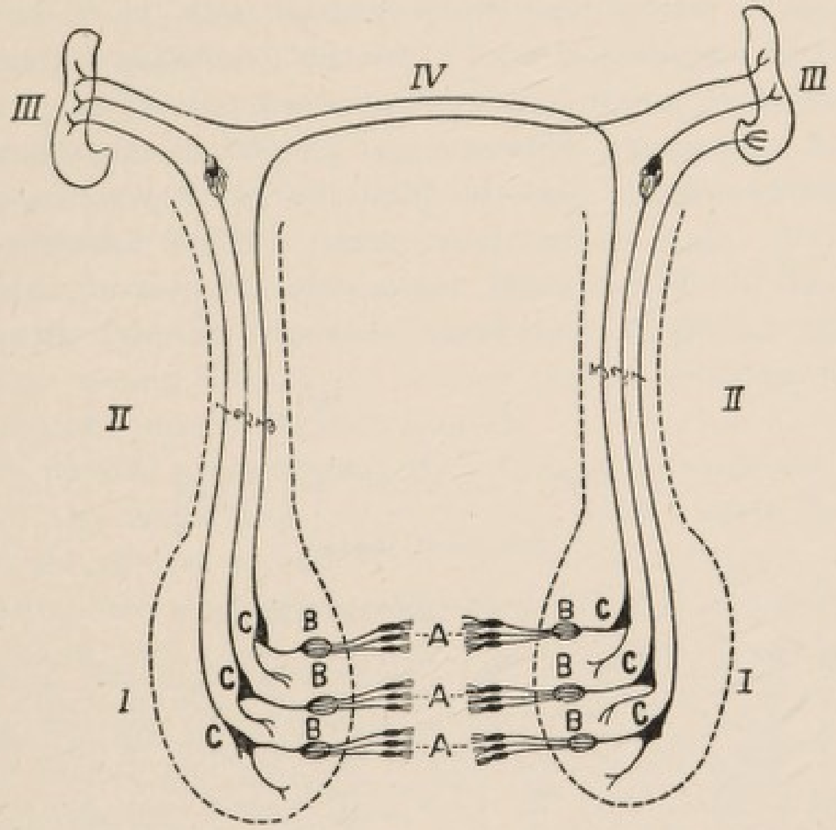


Fig. 51.—The Connections of the Olfactory Fibres. *A*, olfactory cells ; *B*, synapses in the olfactory bulb I. ; ii., olfactory tracts ; iii., olfactory centre ; iv., decussation of fibres. (Howell.)

1. **Receptors.**—Over the upper part of the nasal cavity the columnar epithelial cells are devoid of cilia, and between them are placed spindle-shaped cells (fig. 51, *A*), which send processes

through the mucous membrane, and through the cribriform plate of the ethmoid into the olfactory bulb *I*.

In the bulb these neurons form synapses, *B*, with other neurons (*C*), the axons of which pass to the base of the olfactory tracts.

2. **Connections with the Central Nervous System.**—The connections of the olfactory fibres with the cortical centre in the cerebrum (see p. 205) is shown in fig. 51, *III*.

3. **Physiology.—Stimulation of Mechanism.**—To act upon the olfactory mechanism the substance must be volatile, and must be suspended in the air. In this condition infinitesimal quantities of such substances as musk are capable of producing powerful sensations. The mucous membrane must be moist, and this is secured by the activity of Bowman's glands, situated in the mucous membrane. These are under the control of the fifth cranial nerve, and section of this leads indirectly to loss of the sense of smell through dryness of the membrane.

(*b*) For Vibration of Ether

Sense of Sight

A. General Considerations

While the addition to and withdrawal from the surface of the body of the slower ethereal waves which are the basis of heat act upon the special nerve terminations in the skin to give rise to sensations of *heat* and *cold*, a certain range of more rapid vibrations act specially upon the nerve endings in the eye to produce molecular changes which in turn affect the centres in the brain, and play a most important part in the adjustment of movements for the benefit of the body and which give rise to changes in consciousness which we call **sight**. The range of vibrations which can act in this way are comparatively limited, the slowest being about 435 billions per second, the most rapid about 764 billions. Vibrations more rapid than this, which are capable of setting up chemical changes, as in photography, do not produce visual sensations.

The action of light upon the protoplasm of lower organisms has been already considered (p. 15), and it has been seen that it may be either general or unilateral, producing the phenomena of positive and negative phototaxis. In more complex animals special sets of cells are set apart to be acted on by light, and these are generally imbedded in pigmented cells to prevent the passage of light through the protoplasm. Such an accumulation of cells constitutes an **eye**, and in the simpler organisms such an eye can have no further function than to enable the presence or absence of light or various **degrees of illumination** to produce their effects.

But in the higher animals these cells are so arranged that certain of them are stimulated by light coming in one direction, others are stimulated by light coming in another, and while the former are connected with one set of synapses in the brain, the latter are connected with another. Thus light coming from one point will stimulate one set of cells which will excite one part of the brain, and light from another will act upon other cells which will excite another part of the brain, and thus not merely the degree of illumination but the **source of illumination** becomes distinguishable.

It is by this arrangement that it becomes possible to form ideas of the **shape** of external objects. One directs the eye to the corner of the ceiling, and the idea that it is a corner is due to the fact that three different degrees of illumination are appreciated, and that these can be localised—one above, one to the right, and one to the left. One set of cells is stimulated to one degree, another set of cells to another degree, and a third set of cells to a third degree; and the different stimulation of these different sets of cells leads to a different excitation of separate sets of neurons in the brain. These changes in the brain are accompanied by the **perception** of the three parts differently illuminated. From the previous training of the nervous system we are taught to interpret this as due to a corner. But this interpretation is simply a **judgment** based upon the sensations, and it may or may not be right, and instead of actually looking at a corner we may be looking at the picture of one.

From the very first it must be remembered that the modification of our consciousness which we call **vision is not directly due to external conditions, but is a result of changes set up in the**

brain. We do not perceive the object we are looking at, but simply the changes in our brain produced by changes in the eye set up by rays of light coming from the object.

Usually such changes are set up by a certain range of vibrations of the ether, but they may be set up in other ways —*e.g.* by the mechanical stimulation of a blow on the eye; but, however set up, they give rise to the same kind of changes in consciousness—visual sensation. This fact has been formulated in the doctrine of **specific nerve energy**, that different varieties of stimuli applied to the same organ of sense always produce the same kind of sensation. And the converse that the same stimulus applied to different organs of sense produces a different kind of sensation for each also holds good.

The visual mechanism not only gives the power of appreciating the **degree** and **source of illumination**, but also of appreciating **colour**. *Physically* the different colours are simply different rates of vibration of the ether, *physiologically* they are different kinds of sensations produced by different modes of stimulation of the eye. The slowest visible vibrations produce changes accompanied by a sensation which we call red, the most rapid vibrations produce different changes which we call violet. But, as will be afterwards shown, these sensations may be produced by other modes of stimulating the eye.

The visual mechanism in this way gives a **flat picture** of the outer world, and from this flat picture *judgments* are formed of the size, distance, and thickness of the bodies looked at.

The idea of **size** is based upon the extent of the eye-cells stimulated by the light coming from the object. If a large surface is acted upon, the object seems large; if a small surface, the object seems small. But the extent of eye-cells acted on depends not merely upon the size of the object, but also upon its **distance** from the eye, since the further the object is from the eye the smaller is the image formed. Hence, our ideas of size are judgments based upon the size of the picture in the eye, and the appreciation of the distance of the object. The distance of an object, when over fifty or sixty metres from the eye, and very probably even when over as little as six metres, is judged by the modifications in its shading and colour due to the condition of the atmosphere. A range of hills will at one time be judged to be quite near, at another time to be distant. Since the estimation of the size of an object depends upon the judgment of its distance, the estimate we form of the size of such objects as a range of hills is often erroneous. When objects are near the eye, a special mechanism comes into play to enable their distance to be determined (see p. 144).

The idea of **thickness or contour** of an object is also largely a judgment based upon colour and shading. When a cube is looked at, it appears solid because of the degrees of illumination of the different sides—degrees of illumination which may be reproduced in a flat picture of such a cube. When the object is near the eyes, by using the two eyes together a means of determining solidity comes into action in such animals as monkeys (see p. 144).

B. Anatomy of the Eye

Before attempting to study the physiology of the eye, the student must dissect an ox's or a pig's eye, and then make himself familiar with the microscopic structure of the various parts.

The eye may be described as a hollow sphere of fibrous tissue (fig. 52), the posterior part, the *sclerotic* (*Scl.*), being opaque; the anterior part, the *cornea* (*Cor.*), being transparent and forming part of a sphere of smaller diameter than the sclerotic. Inside the sclerotic coat is a loose fibrous layer, the *choroid* (*Chor.*), the connective tissue cells of which are loaded with melanin, a black pigment. This is the vascular coat of the eye—the larger vessels running in its outer part, and the capillaries in its inner layer. Anteriorly, just behind the junction of the cornea and sclerotic, it is thickened and raised in a number of ridges, the *ciliary processes* (*Cil. M.*), running from behind forward and terminating abruptly in front. In these the *ciliary muscle* is situated. It consists of two sets of non-striped muscular fibres—first, radiating fibres, which take origin from the sclerotic just behind the corneo-sclerotic junction, and run backwards and outwards to be inserted with the bases of the ciliary processes; second, circular fibres which run round the processes just inside the radiating fibres. The choroid is continued forward in front of the ciliary processes to the *pupil* as the *iris*, and in it are also two sets of non-striped muscular fibres—first, the circular fibres, a well-marked band running round the pupil, and called the *sphincter pupillæ* (*Sph.P.*) muscle; second, a less well-marked set of radiating fibres, which are absent in some animals, and which constitute the *dilator pupillæ* muscle (*D.P.*). In the **horse** the pupil is elliptical, and from the edge of the iris a process like a small bunch of grapes projects, and, when the pupil is contracted, nearly occludes it.

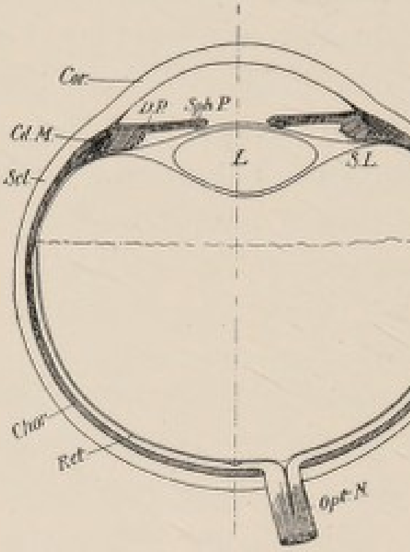


Fig. 52.—Horizontal section through the Left Eye. *Cor.*, cornea; *Scl.*, sclerotic; *Opt N.*, optic nerve; *Chor.*, choroid; *Cil.M.*, ciliary processes with ciliary muscle; *D.P.*, dilator pupillæ muscle; *Sph.P.*, sphincter pupillæ muscle; *L.*, crystalline lens; *S.L.*, hyaloid membrane forming suspensory ligament and capsule of lens; *Ret.*, retina. The vertical line passing through the axis of the eye falls upon the central spot of the retina.

The *membrana nictitans*, lying on the inner aspect of the orbit, consists of a flexible plate of elastic fibro-cartilage covered with conjunctiva. When the eye is retracted the post-orbital fat is pushed forwards and thrusts the membrane over the inner half of the eyeball.

That part of the eye in front of the iris is filled by a lymph-like fluid, the *aqueous humour*, while the part behind is occupied by a fine jelly-like mucoid tissue, the *vitreous humour*. The vitreous humour is enclosed in a delicate fibrous capsule, the *hyaloid membrane*, and just behind the ciliary processes this membrane becomes tougher, and is so firmly adherent to the processes that it is difficult to strip it off. It passes forward from the processes as the *suspensory ligament* (*S.L.*), and then splits to form the *lens capsule*. In this is held the *crystalline lens* (*L.*), a biconvex lens, with its greater curvature on its posterior aspect, and characterised by its great elasticity. Normally it is kept somewhat pressed out and flattened between the layers of the capsule, but if the suspensory ligament is relaxed its natural elasticity causes it to bulge forward. This happens when the ciliary muscle contracts and pulls forward the ciliary processes with the hyaloid membrane.

Between the hyaloid membrane and the choroid is the *retina* (*Ret.*). This is an expansion of the optic nerve, which enters the eye at 3 to 4 mm. to the inner side of the posterior optic axis (fig. 53). The white nerve fibres pass through the sclerotic, through the choroid, and through the retina, to form the white *optic disc*, and then losing their white sheath, they spread out in all directions over the front of the retina, to form its first layer—the layer of *nerve fibres* (1). These nerve fibres take origin from a layer of *nerve cells* (2) behind them, forming the second layer. The dendrites of these cells arborise with the dendrites for the next set of neurons in the third layer, the *internal molecular layer* (3). The cells of these neurons are placed in the next or fourth layer, the *inner nuclear layer* (4), and from these cells, processes pass backwards to form synapses in the fifth, or *outer molecular layer* (5), with the dendrites of the terminal neurons. These terminal neurons have their cells in the sixth or *outer nuclear layer* (6) of the retina, and they pass backwards and end in two special kinds of terminations in the seventh layer of the retina—the *rods and cones* (7). These structures are composed of two segments—a somewhat barrel-shaped basal piece, and a transparent terminal part which in the rods is cylindrical and in the cones is pointed. Over the central spot of the eye in man or apes there are no rods, but the cones lie side by side, and the other layers of the retina are thinned out. The rods and cones are imbedded in the last or eighth layer of the retina—the layer of pigment cells, or *tapetum nigrum*. The retina in front thins out, but the tapetum nigrum, along with another layer of epithelial cells representing the rest of the retinal structures, is continued forwards over the ciliary processes and over the back of the iris.

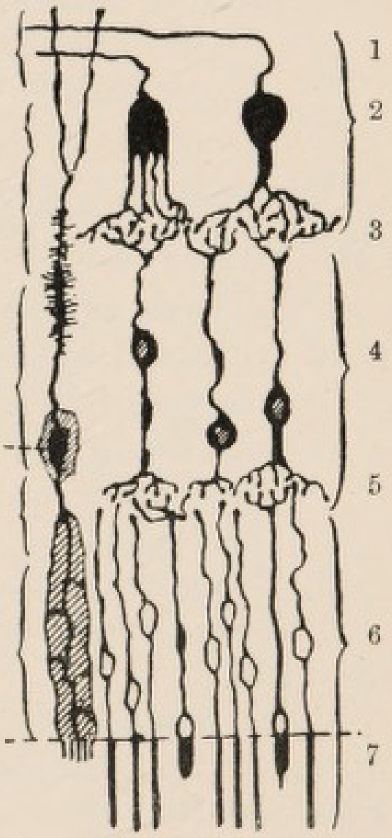


Fig. 53.—Diagram of a Section through the Retina stained by Golgi's method. For description, see text. (*From* Van Gehuchten.)

The blood vessels of the retina enter in the middle of the optic nerve, and run out and branch in the *anterior* layer of the retina.

The interior of the eye may be examined by the **Ophthalmoscope**, which consists essentially of a small mirror from which light can be reflected into the back of the eye, with a small hole in the centre through which the observer can study the illuminated part of the chamber. (*Practical Physiology.*)

C. Physiology

The study of vision may be taken up in the following order :—

1. The **mode of formation of pictures** on the nerve structures (retina) of the eye.
   (1) One eye (monocular vision).
      A. The method in which rays of light are focussed (dioptric mechanism).
      B. Stimulation of the retina.
   (2) Two eyes (binocular vision).
2. The **conduction of the nerve impulses** from the retina to the brain.
3. The position and mode of action of the parts of the brain in which the changes are set up which accompany visual sensations (**the visual centre**).

1. THE MODE OF FORMATION OF PICTURES UPON THE RETINA

(I.) Monocular Vision

A. The Dioptric Mechanism

Distant Vision.—The eye may be compared to a photographic camera, having in front a lens, or lenses, to focus the light upon the sensitive screen behind (fig. 54). The picture is formed on the screen by the luminous rays from each point outside being concentrated to a point upon the screen. This is brought about by **refraction of light** as it passes through the various media of the eye—the cornea, aqueous, crystalline lens, and vitreous. The refractive indices of these, compared with air as unity, may be expressed as follows:—

Cornea	1·33	Lens	1·45
Aqueous	1·33	Vitreous	1·33

Thus light passes from a medium of one refractive index into a medium of another refractive index—

1. At the anterior surface of the cornea;
2. At the anterior surface of the lens;
3. At the posterior surface of the lens;

and at these surfaces it is bent. The degree of bending depends upon—1st, The difference of refractive index; 2nd,

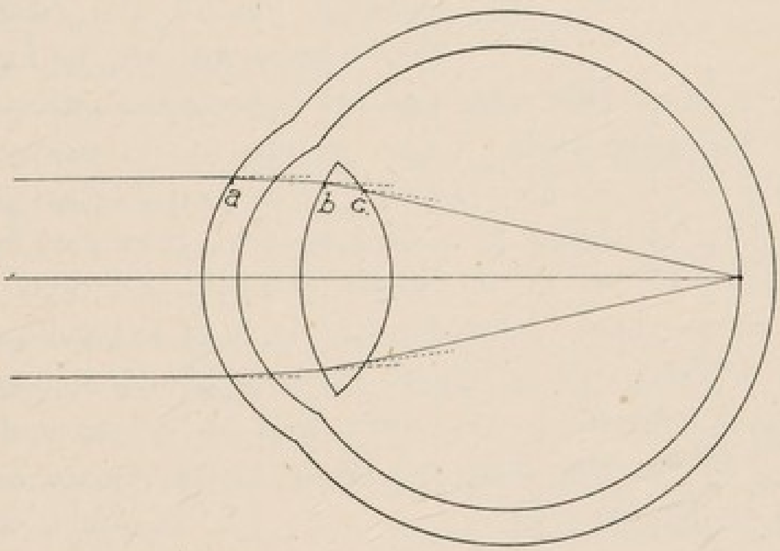


Fig. 54.—To show how parallel rays are brought to a focus on the retina by refraction at the three surfaces (*a*), anterior surface of the cornea; (*b*), anterior surface of the lens; and (*c*), posterior surface of the lens.

The obliquity with which the light hits the surface. This will vary with the convexity of the lens—being greater the greater the convexity.

The posterior surface of the lens has the greatest convexity, with a radius of 6 mm. The anterior surface of the cornea has the next greatest, with a radius of 8 mm. The anterior surface of the lens has the least, with a radius of 10 mm. A ray of light passing obliquely through these media will be bent at the three surfaces.

These media, in fact, form the physiological lens, a compound lens composed of a convexo-concave part in front, the cornea and aqueous, and a biconvex part, the crystalline lens behind. In the resting normal eye (**emmetropic eye**) the principal focus is exactly the distance behind the lens at which the layer of rods and cones in the retina is situated, and thus it is upon these that light coming from luminous points at a distance is focussed.

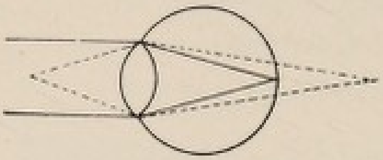


FIG. 55.—To show that rays from distant and near objects are not focussed on the retina at the same time.

Positive Accommodation.—If an object is brought nearer and nearer to the eye, the rays of light entering the eye become more and more divergent, and if the eye be set so that rays from a distance—*i.e.* parallel rays—are focussed, then rays from a nearer object will be focussed behind the retina, and a clear image will not be formed (fig. 55). This means that **near and far objects cannot be distinctly seen at the same time**, a fact which can be readily demonstrated by *Scheiner's Experiment*. (*Practical Physiology*.)

Make two pin-holes in a card so near that they fall within the diameter of the pupil. Close one eye, and hold the holes in front of the other. Get someone to hold a needle against a sheet of white paper at about three yards from the eye, and hold another needle in the same line at about a foot from the eye. When the near needle is looked at the far needle becomes double (fig. 56).

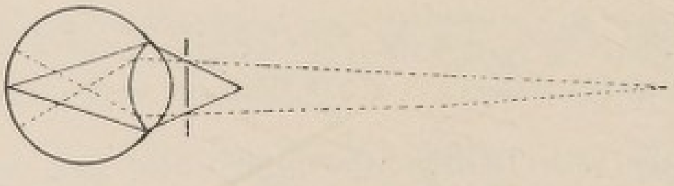


FIG. 56.—Scheiner's Experiment ——— represents rays from the near needle and - - - - rays from the far needle.

Objects may be brought nearer and nearer to the eye, and yet be seen distinctly up to a certain point, the **near point of accommodation** within which they cannot be sharply focussed upon the retina. This, however, requires a change in the lens arrangement of the eye, and this change, beginning when the object comes within about 6 metres (the **far point of accom-**

modation), becomes greater and greater, till it can increase no further when the near point is reached. The change is called **positive accommodation**, and it consists in an increased curvature of the anterior surface of the lens. This may be proved by examining the images formed from the three refracting surfaces (**Sanson's images**), when it will be found that the image from the anterior surface of the lens becomes smaller and brighter when the eye is directed to a near object. The examination of these images is facilitated by the use of the Phakoscope. (*Practical Physiology.*)

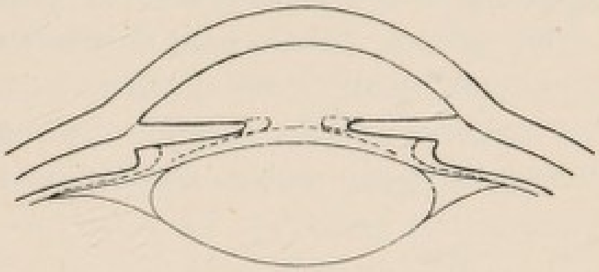


FIG. 57.—Mechanism of Positive Accommodation. The continuous lines show the parts in negative accommodation, the dotted lines the positive accommodation.

Positive accommodation is brought about by contraction of the **ciliary muscle** (see p. 119), which pulls forward the ciliary processes to which the hyaloid membrane is attached, and thus relaxes the suspensory ligament of the lens and the front of the lens capsule, and allows the natural elasticity of the lens to bulge it forward (fig. 57).

This change of positive accommodation is accompanied by a **contraction of the pupil** due to contraction of the sphincter pupillæ muscle. By this means the more divergent peripheral rays which would have been focussed behind the central ones to produce a blurred image are cut off, and **spherical aberration** is prevented.

The muscles acting in positive accommodation—the ciliary and sphincter pupillæ (fig. 57, *C.M.* and *S.P.*)—are supplied by the third cranial nerve (*III.*), while the dilator pupillæ is supplied by fibres passing up the sympathetic of the neck. The centre for the third nerve is situated under the aqueduct of Sylvius, and separate parts preside over the ciliary muscle and the sphincter pupillæ (see p. 180).

The **sphincter centre** is reflexly called into action, and the pupil contracted—1st, When strong light falls on the retina and stimulates the optic nerve. In this way the retina is protected against over-stimulation; 2nd, When the image upon the retina becomes blurred as the object approaches the eye. At the same time the centre for the ciliary muscle is also called into play to produce accommodation.

The **centre for dilatation** of the pupil is situated in the medulla oblongata. Like the centre of the sphincter it may be reflexly excited, stimulation of ingoing nerves causing a dilatation of the pupil when the medulla is intact (fig. 58).

The dilator fibres pass down the lateral columns of the spinal cord to the lower cervical and upper dorsal region, where they arborise round cells in the anterior horn. From these, fibres pass by the anterior root of the second (*2 D. N.*), possibly also of the first and third dorsal nerves, and, passing up through the inferior cervical ganglion, run on to the superior ganglion, where they arborise round cells which send axons to the Gasserian ganglion of the fifth cranial nerve (*V.*), and from there the fibres pass along the ophthalmic division and its long ciliary branches to the dilator fibres of the iris (*D.P.*).

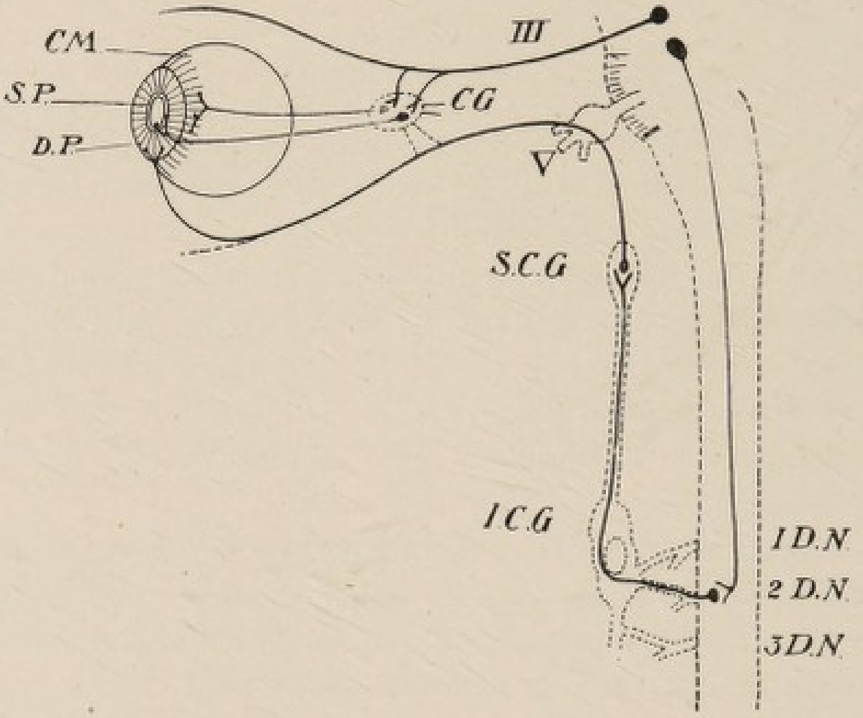


Fig. 58.—Nerve Supply of the Intrinsic Muscles of the Eye (see text).

The importance of the course taken by these dilator fibres is considerable, because diseases of the spinal cord in the lower cervical and upper dorsal region (the **cilio-spinal region**), and tumours in the upper mediastinum, may interfere with their action, and by stimulating cause chronic dilatation of the pupil, or by paralysing prevent dilatation of the pupil. Since the dilator muscle fibres of the pupil have not been demonstrated in all animals, it has been suggested that the nerve may act by inhibiting the sphincter pupillæ, but the evidence on this point is not conclusive.

A peripheral mechanism exists in the muscle of the iris which may act independently of the central nervous system, as may be seen in the eye of a decapitated cat, and various drugs act directly upon it—*e.g.* physostigmin causing a contraction of the pupil by acting upon the nerve endings and pilocarpine by acting on the muscle fibres. Adrenalin causes a dilatation by acting on the nerve endings and atropine by acting in the same way.

Imperfections of the Dioptric Mechanism

(1) **Hypermetropia.**—The eye is sometimes too short from before backwards, and thus, in the resting state, parallel rays are focussed behind the retina, and in order to see even a distant object the individual has to use his positive accommodation. As the object is approached to the eye it is focussed with greater and greater difficulty, and the near point is further off than in the emmetropic eye (fig. 58, *C*).

The long-sighted eye differs from the slightly presbyopic in the fact that not merely divergent, but also parallel rays, are unfocussed in the resting state.

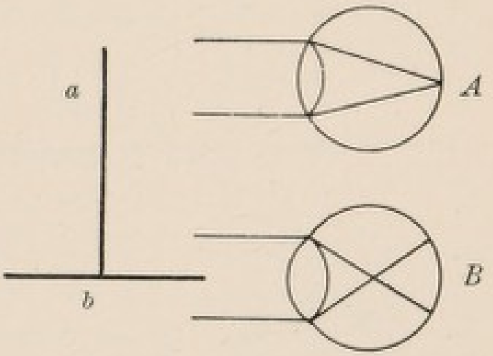


Fig. 59.—To show the cause of Astigmatism. *A*, a slight curvature of the cornea in the vertical plane ; *B*, more marked curvature in the horizontal plane, leading to rays from *b*—a horizontal line being focussed in front of the retina when *a*—a vertical line—is looked at.

(2) **Myopia.**—In certain cases the antero-posterior diameter of the eye is too long, and as a result parallel rays—rays from distant objects—are focussed in front of the retina, and it is only when the object is brought near to the eye that a perfect image can be formed. In such an eye no positive accommodation is needed till the object is well within the normal far point, and the near point is approximated to the eye.

(3) **Astigmatism** is a defect due to unequal curvature of one or more of the refracting surfaces in different planes. If the vertical curvature of the cornea is greater than the horizontal, when a vertical line is looked at, horizontal lines will not be sharply focussed at the same time (fig. 59).

B. Stimulation of the Retina

1. Reaction to Varying Illuminations.—(1) **The Blind Spot.**—At the entrance of the optic nerve the retina cannot be stimulated because there are no end organs in that situation.

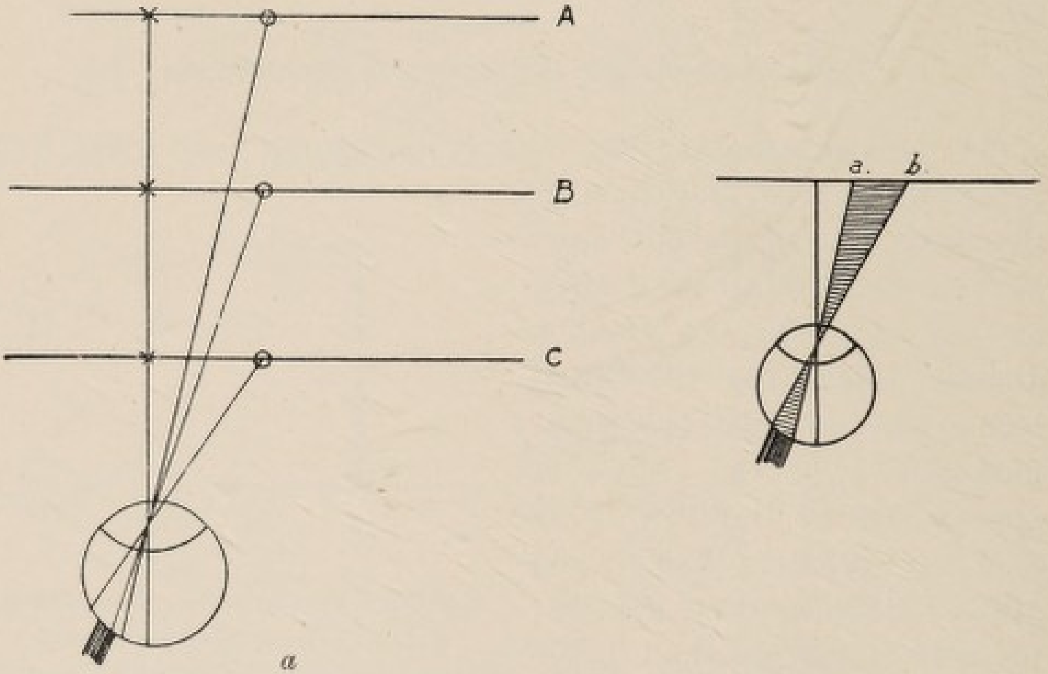


FIG. 60.—Methods of demonstrating the Blind Spot: *a*, by Mariotte's experiment; *b*, by moving a pencil along a sheet of paper.

The existence of such a blind spot may be demonstrated—1st, By Mariotte's experiment, which consists in making two marks in a horizontal line on a piece of paper, closing the left eye, fixing the right eye on the left-hand mark with the paper held at a distance from the eye, when both marks are visible, then bringing the paper nearer to the eye, when the right-hand mark will first disappear, and, when the paper is brought still nearer, will reappear (fig. 60, *a*) (*Practical Physiology*); 2nd, By making a mark on a sheet of paper, and with the head close to the paper moving the point of a pencil to the right for the right eye, or to the left for the left eye, when the point will disappear and again reappear (fig. 60, *b*). (*Practical Physiology.*) The eye is blind for all objects in the shaded region. By resolving the various triangles the distance of the blind spot from the central spot of the eye may be determined (3 to 4 mm.), and the diameter of the blind spot (1·5 mm.) may also be ascertained.

(2) **The Field of Vision.**—The rest of the retina forward to the edge is capable of stimulation, and the whole range of objects which can be seen at one time constitutes the field of vision, and it may be indicated by the optical angle subtended by that range of objects. As the distance from the eye increases the field of vision extends.

(3) The **layer of the retina capable of stimulation** is the layer of rods and cones. This is proved by the experiment of **Purkinje's images**, which depends upon the fact that if a ray of light is thrown through the sclerotic coat of the eye the shadow of the blood vessels stimulates a subjacent layer (fig. 61, *c*), and these vessels appear as a series of wriggling lines on the surface looked at. If the light be moved, the lines seem to move, and, by resolving the triangles, it is possible to calculate the distance behind the vessels of the part stimulated, and this distance is found to correspond to the thickness of the retina. The shadows of the blood vessels are not seen in ordinary vision, because they then fall upon parts of the retina which are insensitive. (*Practical Physiology.*)

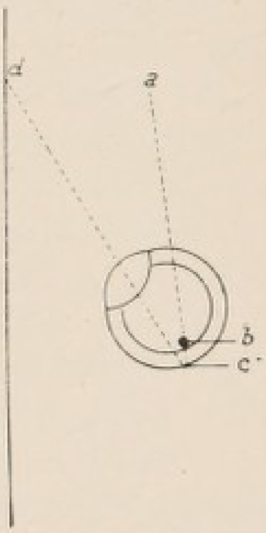


FIG. 61.—To show that the hindmost layer of the retina is stimulated. (*Purkinje's Images.*) *a*, source of light; *b*, blood vessel of retina; *c*, shadow of vessel on rods and cones; *d*, image of shadow mentally projected on to the wall.

The cones are the more specialised elements of the retina, and they react more particularly to bright light, which soon exhausts the rods. The rods, again, react to faint illumination. This explains why it is that, when we go out into a dark night from a brightly lighted room, we at first can see nothing, but after a time, when the rods have recovered, we begin to see objects more distinctly. It also explains why it is that if we direct our eye to a small faintly shining star we may fail to see it, because its image falls on cones alone, while it becomes visible if the eye be directed slightly from it. The rods seem incapable of giving rise to colour sensation, and when the solar spectrum is looked at in a very dim light it appears as a greyish band of illumination with the red end wanting, because the slow red vibrations fail to stimulate the rods. It is because the blue end of the spectrum is the more active in faint illumination that the illusion of a moonlight scene may be got by looking through a blue glass, while looking through a yellow glass gives the idea of sunlight and brilliant illumination. (*Practical Physiology.*)

(4) **Modes of Stimulation.**—The rods and cones are generally stimulated by the ethereal light vibration, but they may be stimulated by mechanical violence or by sudden changes in an electric current. But, however stimulated, the kind of sensation is always of the same kind—a visual sensation (see p. 118).

(5) Of the **nature of the changes in the retina** when stimulated we know little. But we know that—

1*st.* Under the influence of light the cells of the tapetum nigrum expand forward between the rods and cones.

2*nd.* A purple pigment which exists in the outer segment of the rods is bleached. Even although there is no purple in the cones, which alone occupy the sensitive central spot of the eye, this change in colour suggests that a chemical decomposition accompanies stimulation.

3*rd.* Electrical changes occur.

(6) **Fatigue.**—If a bright light be looked at for some time, the part of the retina acted upon is temporarily blinded, and hence when the eye is taken off the bright light a dark spot is seen. This is sometimes called a **negative after image.** When coloured lights are used the phenomena of complemental colours are produced (p. 135). (*Practical Physiology.*)

Sometimes the stimulation of the retina or of the brain neurons connected with it may last after the withdrawal of the stimulus, when a continuance of the sensation—a **positive after image**—is seen. This may be observed if, on opening the eyes in the morning, a well-illuminated window is looked at and the eyes closed. A persisting image of the window may be seen.

2. The Power of Localising the Source or Direction of Illumination.—This may be determined in the same way as in studying the sense of touch—by finding how near two points may be stimulated and still give rise to a double sensation.

3. Colour Sensation — Physics of Light Vibration.—Physically the various colours are essentially different rates of vibration of the ether, and only a comparatively small range of these vibrations stimulate the retina. The slowest acting vibrations are at the rate of about 435 billions per second, while the fastest are not more than 764 billions—the relationship of the slowest to the fastest is something like four to seven. The apparent colour of objects is due to the fact that they absorb certain parts of the spectrum, and either transmit onwards other parts, or reflect other parts. The vast variety of colours which are perceived in nature is due to the fact that the pure spectral colours are modified by the *brightness* of illumination, and by *admixture* with other parts of the spectrum. Thus a surface which in bright sunlight appears of a brilliant red, becomes maroon, and finally brown and black, as the light fades. Again, a pure red when diluted with all the spectrum—*i.e.* with white light—becomes pink as it becomes less and less saturated. (*Practical Physiology.*)

Physiology of Colour Sensation.—1. The **peripheral part of the retina is colour blind**—is incapable of acting so as to produce colour sensations. This may be shown by means of the perimeter and coloured chalks. Until the chalk is brought well within the field of vision its colour cannot be made out. As the image of the chalk travels in along the retina it is found that yellow and blue can be distinguished before red and green—that is, that there is a zone of retina which is blind to red and green, but which can distinguish blue and yellow. Only the central part of the retina is capable of being stimulated by all colours. These zones are not sharply defined, and vary in extent with the size and brightness of the coloured image (fig. 62). (*Practical Physiology.*)

2. While the various sensations which we call colour are generally produced by vibrations of different lengths falling

on the retina, **colour sensations are also produced in various other ways.**

(*a*) By mechanical stimulation of the retina. By pressing on the eyeball as far back as possible a yellow ring, or part of a ring, may often be seen. (*Practical Physiology.*)

(*b*) Simple alternation of white and black upon the retina may produce colour sensation, as when a disc of paper marked with lines is rotated rapidly before the eye. (*Practical Physiology.*)

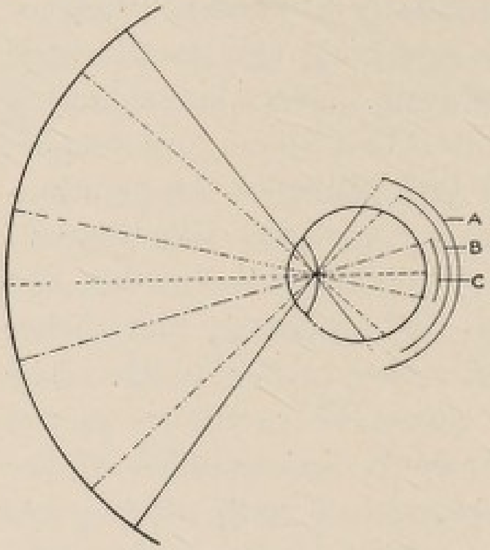


FIG. 62.—Distribution of Colour Sensation in relationship to the surface of the retina (*Colour Perimeter*). *A* indicates the extent of retina stimulated by white and black; *B*, the part also capable of stimulation by blue and yellow; and *C*, the central part capable also of stimulation by red and green.

3. By allowing different parts of the spectrum to fall upon the eye at the same time, it is possible to produce either a sensation of white or of some other part of the spectrum. (*Practical Physiology.*) To produce a sensation of white from two or three different parts of the spectrum, a due proportion of each part must be taken, since different parts have different sensational activity. This may be represented by a plotting out the various parts of the spectrum on a curve, and joining them to a central spot by means of lines. The length of the line then represents the relative sensitive activity of the particular part of the spectrum to which it passes (fig. 63).

This means that by different modes of stimulation of the retina the same sensation may be produced. The sensation of orange may be produced either when vibrations at about 580 billions per second fall on the eye, or when two sets of vibrations, one about 640 and one about 560 billions, reach it. By no possible physical combination of the two is it possible to produce the intermediate rate of vibration.

The sensation of colour, therefore, depends upon the nature of the change set up in the retina, and not upon the condition producing that change.

What we call colours are particular changes in our consciousness which accompany particular changes in our brain neurons produced by particular changes set up in the retina, in whatever way these changes may have been produced.

4. After looking for some time at any one colour, on removing the colour another appears in its place—the **complemental colour.** If the first colour is—

Red, the second will be green blue;
Orange, ,, ,, blue;
Green, ,, ,, pink;
Yellow, ,, ,, indigo blue;

and *vice versâ*. (*Practical Physiology.*)

Theories of Colour Vision.—1. From consideration of the peripheral colour-blind zone of the retina and of the more limited area giving sensations only of blue and yellow when stimulated, and of the most limited central part giving also sensations of red and green, it would seem that some special substance or substances must exist in each of these areas which by its or their stimulation give rise to the various sensations.

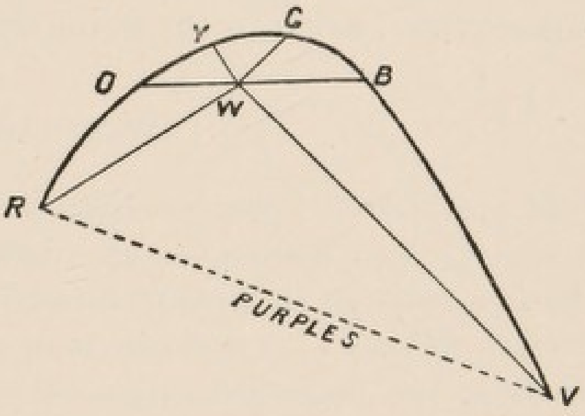


FIG. 63.

2. Considered along with this, the phenomena of complemental colours suggest the possibility of there being one substance which when undergoing one change, say breaking down, produces yellow, and when undergoing another change, say building up, produces blue, and another substance which when undergoing one change produces red, and another change produces green. If such a view be correct, it becomes almost necessary to postulate the existence of another substance which when stimulated gives rise to sensations which we call white. Or there might be four different substances, one when changed giving rise to yellow, another to blue, another to red, and another to green. When the substance giving

the sensation of yellow is used up, then the parts stimulated by the rest of the spectrum would react to white light and give a complemental colour, and so on through the other substances.

It has also been suggested that the facts may be explained on the assumption that there are *three* substances in the retina, one more especially stimulated by the red rays but also acted on by the others, one chiefly stimulated by the green rays, and one chiefly acted on by the blue rays. Such theories, however, do not call for consideration from the ordinary student.

Colour-blindness.—While everyone is **colour blind** at the periphery of the retina, a certain proportion of people—about 5 per cent.—are unable to distinguish reds and green, even at the centre of the retina. It is impossible to say how far this condition exists in the lower animals.

(II.) BINOCULAR VISION

In most of the lower animals, the field of vision of each eye is separate and distinct at all times, but in the horse and dog the two eyes can be directed forwards so that the fields of vision overlap as they always do in man and in apes. When in this position, the combined action of the eyes affords a means of determining the distance and solidity of near objects.

1. **Distance of Near Objects.**—As an object is approached, the two eyes have to be turned forwards by the internal recti muscles, and by the degree of contraction of these, an estimation of the distance is made.

2. **Solidity of an Object.**—If the object is near, a slightly different picture is given on each retina, and experience has taught us that this *stereoscopic vision* indicates solidity.

Movements of Eyeballs.—To secure the harmonious action of the two eyes, it is necessary that they should be freely movable. Each eye in its orbit is a ball and socket joint in which the eyeball moves round every axis (fig. 64). The axis of the eye (*a*) in man and in monkeys, is set obliquely to the axis of the orbit (*b*), and the centre of rotation is behind the centre of the ball. The movements are produced by three pairs of muscles.

1. The internal and external recti (*I.R.* and *Ex.R.*).

2. The superior and inferior recti acting along the lines indicated (*S.R.*).

3. The superior and inferior obliques acting in the line (*S.ob.*).

The internal rectus rotates the pupil inwards.
,, external ,, ,, ,, outwards.
,, superior ,, ,, ,, upwards and inwards.
,, inferior ,, ,, ,, downwards and inwards.
,, superior oblique ,, ,, downwards and outwards.
,, inferior ,, ,, ,, upwards and outwards.

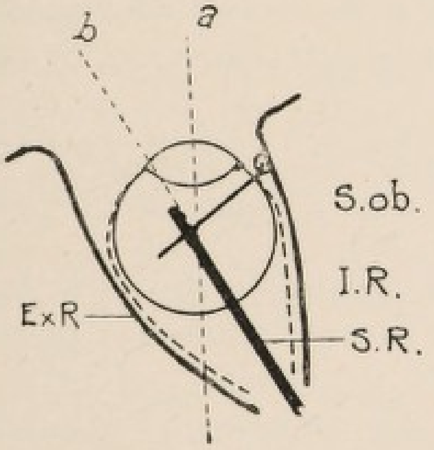


FIG. 64.—The left Eyeball in the Orbit, with the Muscles acting upon it. (*Man and Ape.*)

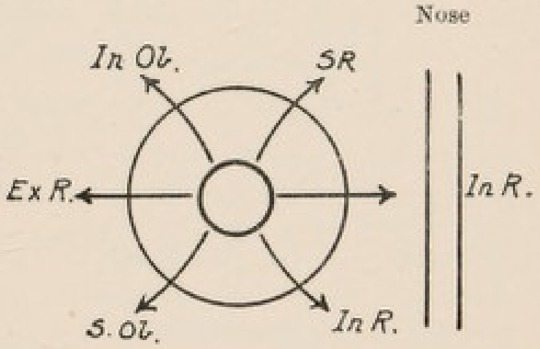


FIG. 65.—The Movements of the Pupil caused by the various Muscles of the Eye. (Right Eye.) (*Man and Ape.*)

In the **horse**, **dog**, and other similar animals the eye is set more nearly in the axis of the orbit, and the obliques do not pass backwards upon the ball, but act more purely as rotators; the superior oblique swinging the outer angle of the pupil upwards and inwards, the inferior oblique downwards and inwards. The superior and inferior recti move the pupil more directly upwards and downwards.

In the **horse** and other herbivora a retractor oculi muscle is inserted all round the ball inside these muscles just described, and it can retract the eye in the orbit, and at the same time pushes forward the fatty tissue to which the nictitating membrane is attached and thus thrusts this over the front of the eye.

When the eyes are allowed to sweep over a landscape or any series of objects, or when these move rapidly past the eyes or the eyes rapidly past them, as in travelling by train, the axes are directed in a **series of glances** to different points, and the succession of pictures thus got gives the idea of the continuous series of objects. This jerking movement of the eyes may be well seen in a passenger looking out of a railway carriage in motion.

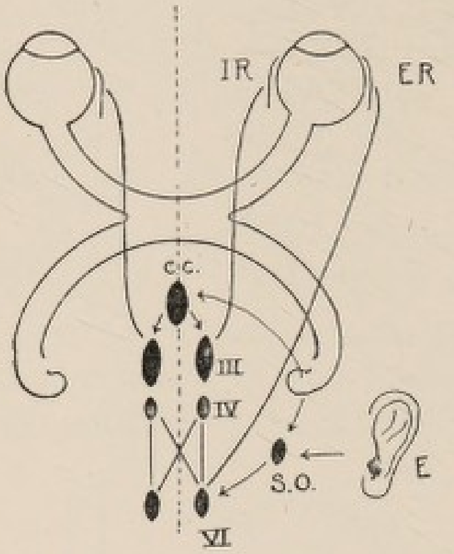


Fig. 66.—The Nervous Mechanism presiding over the combined movements of the two Eyes in man and apes. *I.R.*, internal rectus; *E.R.*, external rectus; *C.C.*, convergent centre acting on the internal recti through the nuclei of the third nerve; *S.O.*, superior olive (centre for lateral divergence) acting on the external rectus of the same side through the nucleus of the sixth, and on the internal rectus of the opposite side through the nucleus of the third; *E.*, ear.

Nervous Mechanism.—A somewhat complex **nervous mechanism** presides over these various movements of the eyes. All the muscles are supplied by the third cranial nerve, except the superior oblique, which is supplied by the fourth nerve, and the external rectus, which is supplied by the sixth nerve (fig. 66; see also fig. 95, p. 179).

The centres for the third and fourth nerves are situated in the floor of the aqueduct of Sylvius under the corpora quadrigemina, while the centre for the sixth is in the pons Varolii (fig. 96, p. 181, and fig. 95, p. 179). The various centres are joined by bands of nerve fibres which pass between the sixth and fourth and third centres, and in part at least cross the middle line.

A combined mechanism, each part of which acts harmoniously with the other parts, thus presides over the ocular movements, and this mechanism is controlled by impulses constantly received from the two retinæ, from the ear and from the brain. Thus in convergence of the optic axes the parts of the nuclei of the third nerves which supply the internal recti muscles must act harmoniously together, and hence a mechanism to direct this convergence may be postulated. In lateral deviation of the eyes that part of the nucleus of the third nerve which presides over the internal rectus of one side acts harmoniously with the sixth nerve supplying the external rectus of the other side, and hence it may be supposed that a directing mechanism for lateral deviation exists possibly in the superior olive. Similarly a centre or centres presiding over the movements of the eyes in a vertical plain may be supposed to exist.

The movements of the eyes involve not merely the contraction of definite muscles, but also the co-ordinated inhibition of others (see p. 138).

2. CONNECTIONS OF THE EYES WITH THE CENTRAL NERVOUS SYSTEM

From each eye the optic nerve extends backwards and inwards to join the other optic nerve at the chiasma.

A partial crossing of the fibres takes place in the chiasma, the extent of decussation varying in different animals and being fairly extensive in the **horse.** From the chiasma the two optic tracts pass upwards round the crura cerebri to end in two divisions—

1. A posterior division passing to the anterior corpora quadrigemina on the same side (fig. 67, *A.C.Q.*).
2. An anterior division running to the geniculate body on the posterior aspect of the thalamus opticus (fig. 73, *Op. Th.*).

The fibres of the posterior termination of the optic tract end in synapses with neurons in the corpora quadrigemina, and the fibres of these neurons pass downwards and control the oculo-motor mechanism already described (fig. 66, p. 136).

The fibres of the anterior division make synapses with other neurons in the posterior part of the thalamus, and these neurons send their fibres backwards to the occipital lobe of the brain, where they connect with the cortical neurons (fig. 67, *Occ.*, p. 138).

3. THE VISUAL CENTRE

A response to stimulation on the part of the neurons in the occipital lobe of the brain (p. 201) is the physical basis of visual sensations, and hence this part of the brain is called the **visual centre.** Usually the visual centre is stimulated by changes in the chain of neurons passing from the retina and set in action by retinal changes; but direct stimulation of the occipital lobe may induce visual sensations.

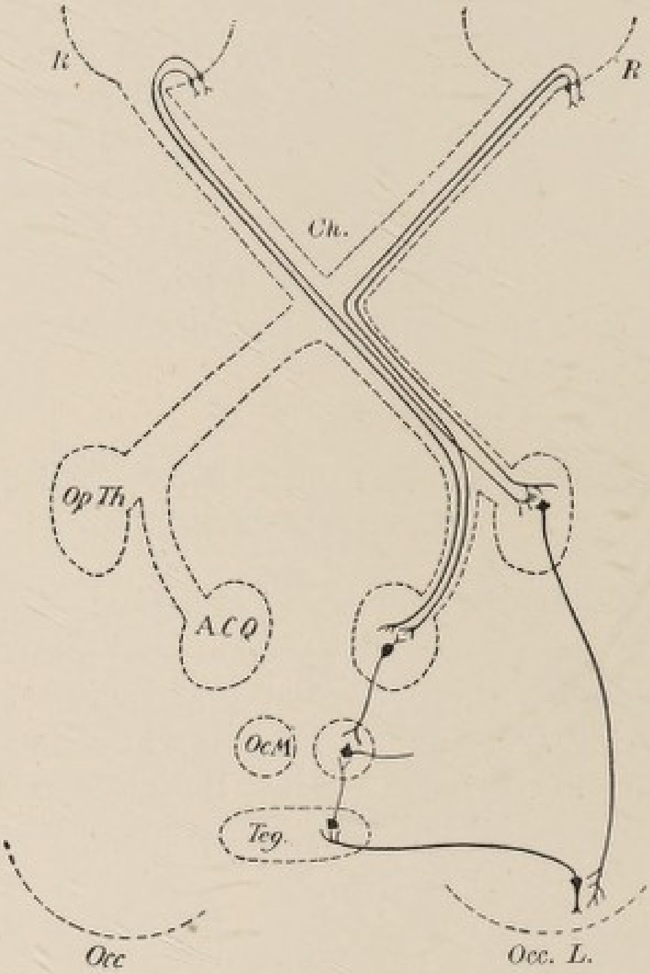


Fig. 67.—The Connections of the Retinæ with the Central Nervous System in man and apes. *R*, retinæ; *Ch.*, chiasma leading to optic tract; *Op.Th.*, optic thalamus; *A.C.Q.*, anterior corpora quadrigemina; *Oc.M.*, oculo-motor mechanism (fig. 66); *Occ.L.*, occipital lobe of the cerebrum; *Teg.*, tegmentum.

(*c*) For Vibration of Air

Sense of Hearing

1. General Considerations

While through the tactile mechanism differences of pressure act as stimuli, through the ear certain vibratory changes of pressure stimulate and may affect the consciousness. Even simple organisms, devoid of any special organ of hearing, may be affected by vibratory changes, and in fish it is difficult to be certain how far such vibrations produce their effect through the ear or through the body generally. But in higher vertebrates it is chiefly through the ears that they act. In these there is a special arrangement by which the vibrations of the air are converted into vibrations of a fluid in a sac situated in the side of the head into which the free ends of neurons project (fig. 68).

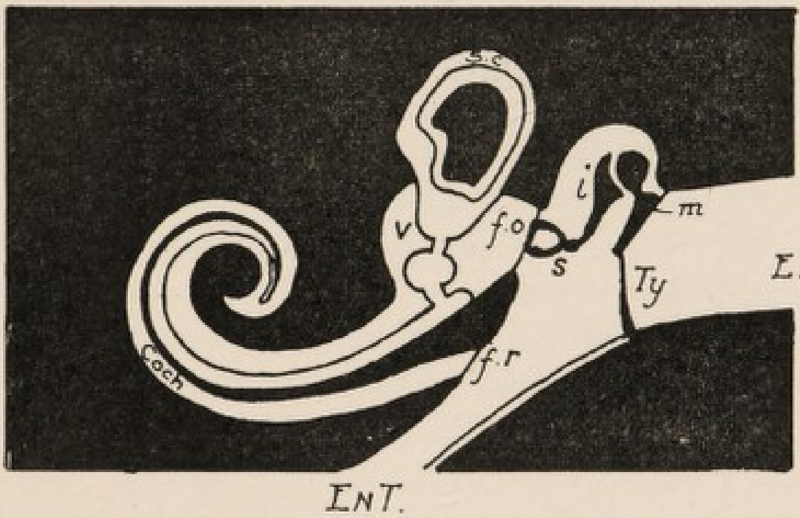


Fig. 68.—Diagram of the Ear. *Ex.M.*, external meatus; *Ty.*, tympanic membrane; *m.*, malleus; *i.*, incus; *s.*, stapes; *f.o.*, fenestra ovalis; *f.r.*, fenestra rotunda; *En.T.*, Eustachian tube; *v.*, vestibule with the utricle and saccule; *s.c.*, semicircular canal; *Coch.*, cochlea.

The importance of such a mechanism in the anterior part of the animal in warning it of danger or making it aware of the presence of its prey is manifest.

In mammals the organ of hearing consists of an external, a middle, and an internal ear. The first is to conduct the vibrations of the air to the second, in which these vibrations produce to and fro movements of a bony lever, by which the fluid in the third is alternately compressed and relaxed.

2. External Ear

The structure of this presents no point of special physiological interest. In lower animals the pinna is under the control of muscles, and is of use in determining the direction from which sound comes.

3. Middle Ear

The object of the middle ear is to overcome the mechanical difficulty of changing vibrations of air into vibrations of a fluid. It consists of a chamber, the **tympanic cavity,** placed outside of the petrous part of the temporal bone (fig. 68). Its outer wall is formed by a membrane, the **membrana tympani** (*Ty.*), which is attached to a ring of bone. Its inner wall presents two openings into the internal ear — the **fenestra ovalis** (*f.o.*), an oval opening, situated anteriorly and above, and the **fenestra rotunda** (*f.r.*), a round opening placed below and behind. Throughout life these are closed, the former by the foot of the stapes, which is attached to the margin of the hole by a membrane, and the latter by a membrane. The posterior wall shows openings into the mastoid cells, and presents a small bony projection which transmits the **stapedius muscle.** The anterior wall has above a bony canal carrying the **tensor tympani muscle,** and below this the canal of the **Eustachian tube**, which communicates with the posterior nares (fig. 68, *Ent.*).

In the tympanic cavity are three ossicles—the **malleus** (*m.*), **incus** (*i.*), and **stapes** (*s.*), forming a chain between the membrana tympani and the fenestra ovalis. The handle of the **malleus** is attached to the membrana tympani, and each time a wave of condensation hits the membrane, it drives in the handle of the malleus. This, by a small process, pushes inwards the long process of the **incus**, which thrusts the **stapes** into the fenestra ovalis, and thus increases the pressure in the enclosed fluid of the internal ear. The fenestra rotunda (*f.r.*) with its membrane acts as a safety valve. The bones rotate round an antero-posterior axis passing through the heads of the malleus and incus. They thus form a lever with the arm to which the power is applied—the handle of the malleus—longer than the other arm. The advantage of this is that, while the range of movement of the stapes in the fenestra ovalis is reduced, its force is proportionately increased.

The range of movement is still further controlled by the **stapedius** muscle, which twists the stapes in the fenestra. This muscle seems to act when loud sounds fall on the ear, and when its nerve supply, derived from the facial nerve, is paralysed, such sounds are heard with painful intensity.

If the membrana tympani is violently forced outwards by closing the nose and mouth and forcing air up the Eustachian tube, the incus and stapes do not accompany the malleus and membrane, since the malleo-incal articulation becomes unlocked.

The membrana tympani is so loosely slung that it has no proper note of its own, and responds to a very large range of vibrations. By the attachment to it of the handle of the malleus it is well damped, and stops vibrating as soon as waves of condensation and rarefaction have ceased to fall upon it. The **tensor tympani** muscle, supplied by the fifth cranial nerve, has some action in favouring the vibration of the membrane, and its paralysis diminishes the acuteness of hearing.

Fig. 69.—Transverse Section through Cartilaginous lower part of Eustachian Tube to show the Cartilaginous Arch cut across and the way in which it is pulled down and the tube opened in swallowing (shaded).

The **Eustachian tube** has a double function. It allows the escape of mucus from the middle ear, and it allows the entrance of air, so that the pressure is kept equal on both sides of the membrana tympani. Its lower part is generally closed, but opens in the act of swallowing. It is surrounded by an arch of cartilage, to one side of which fibres of the tensor palati are attached, so that when this muscle acts in swallowing, the arch of cartilage is drawn down and flattened, and the tube opened up (fig. 69).

When the Eustachian tube gets occluded, as a result of catarrh of the pharynx, the oxygen in the middle ear is absorbed by the tissues, and the pressure falls. As a result, the membrane is driven inwards by the atmospheric pressure, and does not readily vibrate, and hearing is impaired.

4. Internal Ear

The internal ear is a somewhat complex cavity in the petrous part of the temporal bone, **the osseous labyrinth.** It is filled with fluid, the **perilymph.** It consists of a central space, the **vestibule** (*V.*), into which the fenestra ovalis opens. From the anterior part of this, a canal makes two and a half turns round a central pillar, and then, turning sharply on itself, makes the same number of turns down again, and ends at the fenestra rotunda. This is the **osseous cochlea** (fig. 68, *Coch.*). The ascending and descending canals are separated from one another, partly by a bony plate, partly by a membranous partition—the **basilar membrane.** At the base, the bony lamella is broad, but at the apex its place is chiefly taken by the membrane, which measures at the apex more than ten times its width at the base.

From the posterior and superior aspect of the vestibule a mechanism unconnected with hearing has been evolved. Three **semicircular canals** (fig. 70), each with a swelling at one end, open into the vestibule. One runs in the horizontal plane, and has the swelling or ampulla anteriorly (fig. 70, *h.c.*). The other two run in vertical planes placed obliquely to the middle plane, as is indicated in fig. 70. The anterior or superior canal (*s.c.*), has its ampulla in front and the posterior (*p.c.*) has its ampulla behind. They join together, and enter the vestibule by a common orifice.

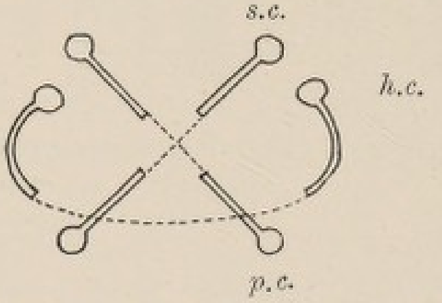


Fig. 70.—The Relationship of the Semicircular Canals to one another. *h.c.*, horizontal canal; *s.c.*, superior canal; *p.c.*, posterior canal.

In the **perilymph** of the bony labyrinth lies a complex membranous bag, the **membranous labyrinth.**

In the vestibule this is divided into two little sacs, the **utricle**, related to the semicircular canals, and the **saccule**, related to the cochlea. They are joined together by a slender canal. From the saccule comes off a canal which runs into the cochlea upon the basilar membrane, forming a middle channel between the other two, the **scala media** or membranous cochlea. This terminates blindly at the apex. From the utricle a membranous canal extends into each of the bony semicircular canals, being provided with an ampulla, which nearly fills up the bony ampulla, while the canal portion is small, and occupies only a small part of the bony canal (fig. 68, p. 139).

In the membranous cochlea the lining cells form the **organ**

of Corti (fig. 71). This is set upon the basilar membrane, and consists from within, outwards, of—1*st*. A set of elongated supporting cells; 2*nd*. A row of columnar cells, with short, stiff, hair-like processes projecting from their free border; 3*rd*. The inner rods of Corti, each of which may be compared to an ulnar bone attached by its terminal end, and fitting on to the heads of the outer rods; 4*th*. The outer rods of Corti, each resembling a swan's head and neck—the neck attached to the basilar membrane, and the back of the head fitting into the hollow surface of the inner rods; 5*th*. Several rows of outer hair cells, with some spindle-shaped cells among them; 6*th*. The outer supporting cells; 7*th*. Lying over the inner and outer hair cells is the membrana reticularis, resembling a net, through the meshes of which the hairs project; 8*th*. Arching over this organ is a homogeneous membrane—the membrana tectoria.

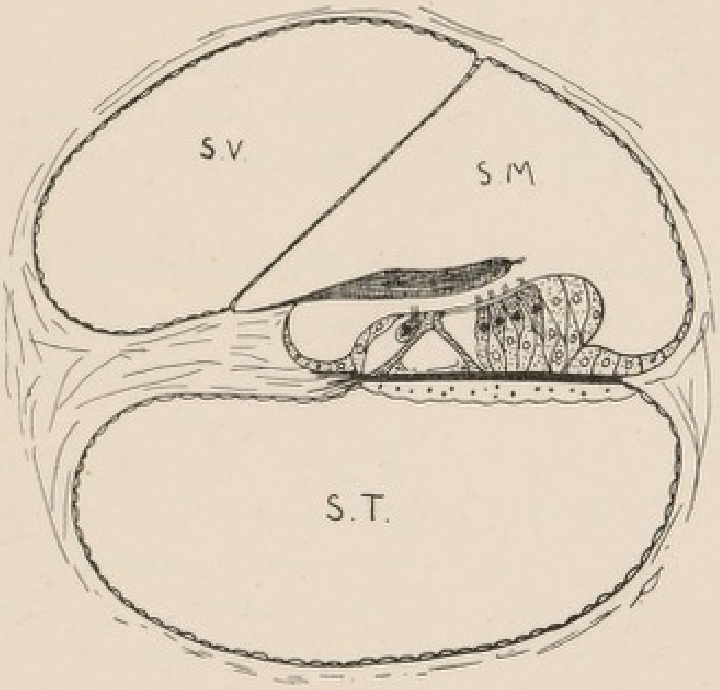


FIG. 71.—Transverse Section through one turn of the Cochlea to show the Organ of Corti on the Basilar Membrane. *S.M.*, scala media; *S.V.* scala vestibuli; *S.T.*, scala tympani.

The membranous labyrinth is attached to the inner wall of the bony labyrinth at certain points, through which fibres of the VIII. nerve to the terminal organs enter it. One set of fibres goes to the utricle and to the ampullæ. A quite independent set, the true auditory nerve, goes to the saccule and the cochlea.

The membranous labyrinth has an outer fibrous coat, and inside this a homogeneous layer which is markedly thickened where the nerves enter it. It is lined by flattened epithelium, which becomes columnar, and is covered with stiff hair-like processes over the thickenings at the entrance of the nerves. On the top of these hair-like processes lies a little mass of calcareous nodules imbedded in a mucus-like substance, the **otoliths.** In the fish and some lower animals the otoliths are large structures.

The terminal neurons of both the vestibule and the cochlea end in dendrites between the hair cells, and the cell of these neurons is upon their course to the medulla.

5. Connection with the Central Nervous System

The **VIII. nerve** is essentially double, consisting of a dorsal **cochlear** or auditory part, and a ventral labyrinthine or **vestibular** part.

Cochlear Root (fig. 72).—This is the true nerve of hearing. Its fibres (*Coch.R.*) begin in dendrites between the hair cells of the organ of Corti, have a cell upon their course, and when they enter the medulla branch into two divisions, which end either in the tuberculum acusticum or the nucleus accessorius (*N. Acc.*), where they form synapses. From the cells, axons pass (*a*) to the oculo-motor mechanism of the same side and the opposite side (*N.* vi.), and (*b*) up to the cerebrum (*CB.*) of the same and of the opposite side.

Vestibular Root (fig. 73).—The fibres of this root take origin in dendrites between the cells of the maculæ in the ampullæ of the semi-circular canals and of the saccule, and have their nerve cells upon their course (*Ves.R.*). As they enter the medulla they divide into two, forming an ascending and a descending branch. (1) The ascending branch sends fibres on to the cerebrum (*CB.*), and to the superior vermis of the cerebellum (*CBL.*). These fibres give off collaterals to the nucleus of Deiters (*N. Deit.*), from the cells of which fibres pass, which divide, some running on the same side, some on the opposite side; one branch passing up to the oculo-motor mechanism (*N.* vi.), the other passing down the spinal cord to send collaterals to the cells in the grey matter. (2) The descending branch forms connections with the medullary nuclei as it passes down.

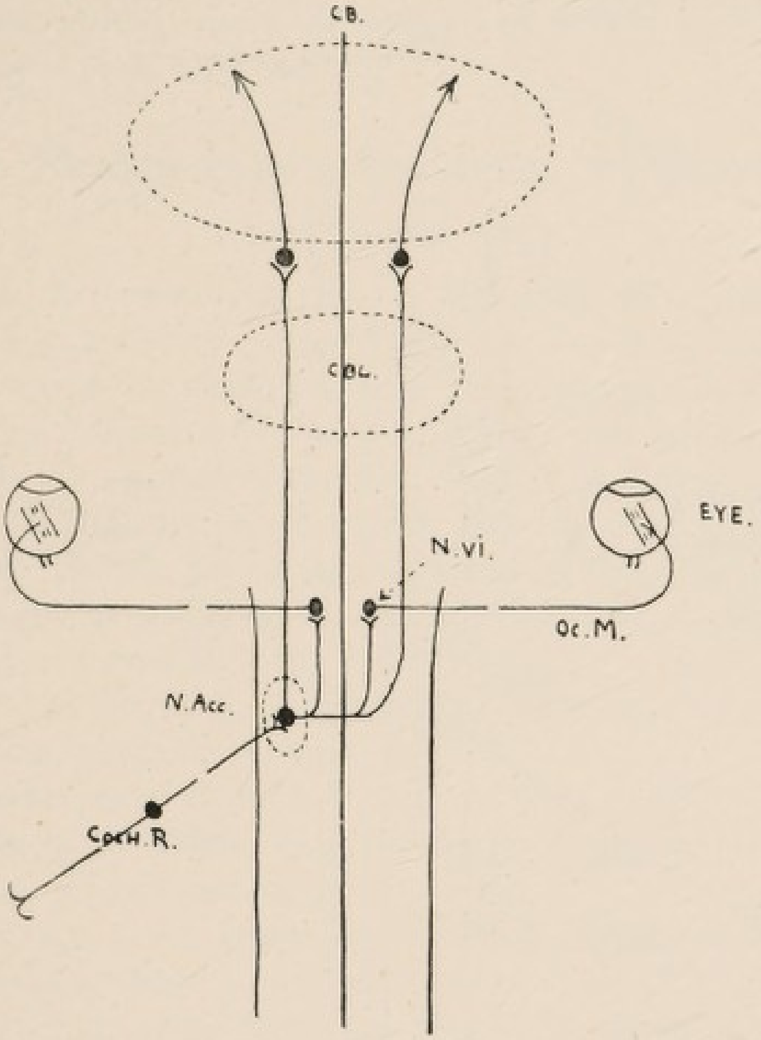


Fig. 72.—Connections of Cochlea with Central Nervous System. *Coch.R.*, cochlear root of eighth nerve ; *N. Acc.*, tuberculum acusticum and nucleus accessorius sending fibres to the cerebrum (*CB.*) and to the oculo-motor mechanism (*N.* vi.) ; *CBL.*, cerebellum.

6. The Auditory Centre and the Physiology of Hearing

The qualities of sound which can be distinguished by the sense of hearing are **loudness**—amplitude of vibration ; **pitch**—rate of vibration ; and **quality**—the character of the sound given by the over-tones. The perception of this last is essentially a perception of pitch.

Loudness.—It is easy to understand how the peripheral neurons in the internal ear are more powerfully stimulated by the greater variations in the degree of pressure which are produced by more powerful aerial waves, and how the greater

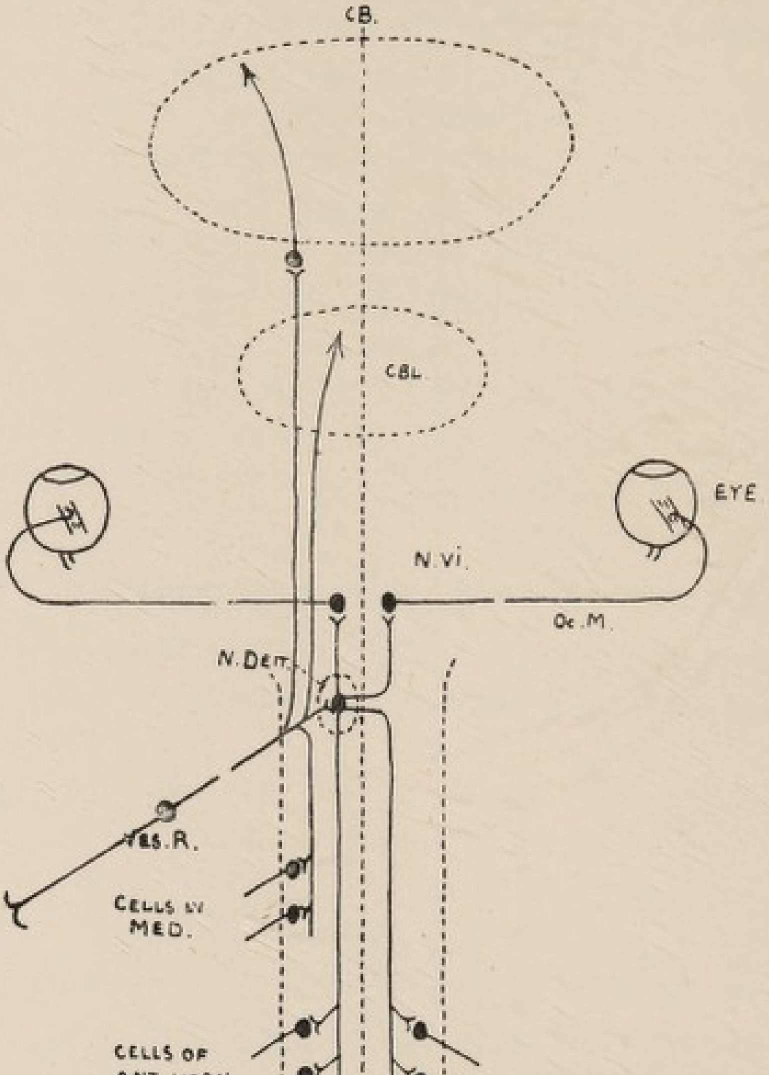


FIG. 73.—Connections of Semicircular Canals with Central Nervous System, *Ves. R.*, Vestibular root of eighth nerve sending fibres upwards to *CB.* (cerebrum) and *CBL.* (cerebellum), downwards to the centre in medulla oblongata (*Med.*), and to Deiters' nucleus (*N. Deit.*), from which fibres pass to the oculo-motor mechanism (*N.vi.*) and to the centres in the anterior horn of the spinal cord.

stimulation of the receptive centre in the brain will be accompanied by a sensation of greater *loudness*.

Pitch.—A study of the structure of the cochlea seems to show a mechanism well suited to afford a means of estimating the *pitch* of a note and the existence of over-tones. The fibres of the basilar membrane may be compared to the strings of a piano, each one of which, or each set of which, will be made to vibrate by a particular note.

D. PROPRIO-CEPTIVE MECHANISM OF THE HEAD

Labyrinthine Sense

Just as the reflex response of the limbs to external stimuli leads to a stimulation of the proprio-ceptive mechanism in the muscles and joints which plays an important part in guiding the subsequent movement (see p. 107), so the reflex response to visual stimuli in the muscles of the head and neck brings into play a delicate proprio-ceptive mechanism developed from the internal ear which has an important action in guiding the movements of the body as a whole, and very specially in guiding the co-ordinated movements of the eye muscles.

This is the labyrinthine mechanism consisting of the utricles and the semi-circular canals.

The **structure** of this mechanism has been described on p. 142.

The **mode of action** may be analysed by a study of the sensations which accompany its activity.

That there is no special mechanism making us aware of uniform movement is proved by the fact that we are not conscious of whirling through space with the earth's surface, and that in a smoothly running train we lose all sense of forward movement. It is only as the train starts or stops that we have a sensation of movement or retardation. The same thing has been demonstrated by strapping a man to a table rotating smoothly round a vertical axis and setting the table spinning. A sense of rotation is experienced as the table starts, but is lost when the movement becomes uniform. Stopping the table gives rise to a sensation of being rotated in the opposite direction.

The semicircular canals are the mechanism which act in this way. They are arranged in pairs in the two ears. The two horizontal canals are in a horizontal plane, the superior canal of one side and the posterior canal of the other are in parallel planes oblique to the mesial plane of the body (fig. 74, *a*).

The horizontal canals may be considered as forming the arc of a circle with an ampulla at each end. The superior canal of one side has its ampulla in front, while its twin—the posterior of the opposite side—has its ampulla behind, and they together form the arc of a circle with an ampulla at each end (fig. 74, *a*).

The membranous canals are very narrow, and occupy but a small part of the osseous canals. The membranous ampullæ are large and almost fill the osseous ampullæ (fig. 74, *b*).

If the head is moved in any plane, certain changes will be set up in the ampullæ towards which the head is moving, and converse changes in the ampullæ at the other end of the arc of the circle.

If, for example, the head is suddenly turned to the right, the inertia of the endolymph and perilymph tend to make them lag behind. Thus the endolymph in the ampulla of the left horizontal canal will tend to flow into the canal, but the canal is so small that it will merely accumulate in the ampulla, and thus a high pressure will be produced (fig. 74, *b* + +). The perilymph will tend to lag behind, and a low pressure will result outside (fig 74, *b* −). The converse will take place in the opposite horizontal canal.

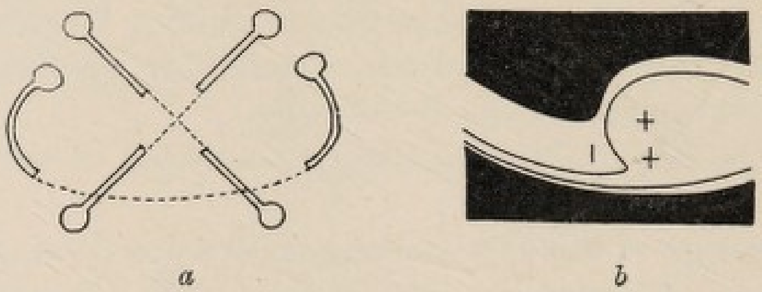


FIG. 74.—(*a*) Arrangement of the semicircular canals on the two sides ; (*b*) bony and membranous canal and ampulla to illustrate their mode of action.

When the movement is continued the pressures will be readjusted, and, on stopping the movement, the opposite conditions will be induced, and a sensation of moving in an opposite direction will be experienced.

In forward movement, the two superior canals have the pressure of endolymph increased in their ampullæ—in backward movement this occurs in the two posterior canals. In nodding to the right the superior and posterior canals of the right ear undergo this change. In all probability the utricle with its otoliths mounted on the top of the hair cells also plays a part in the labyrinthine mechanism. As the head is moved the pressure of the otolith will change from one part of the macula to another, and may thus give different stimuli for different positions of the head.

The importance of this labyrinthine mechanism in muscular co-ordination is shown by the effect of its destruction. This leads to inco-ordinate movements of the eyes, head, and limbs, and to loss of tone in the muscles. When injury to the labyrinth is sudden, as when a "knock-out" blow is received on the chin, driving the condyles of the lower jaw against the petrous part of the temporal, the general loss of muscular tone may be so complete that the individual collapses. The muscles chiefly under the tonic influence of this mechanism are those of the neck and trunk, and the extensor and abductor muscles of the limbs of the same side.

Just as the eye dominates the *movements* of the muscles of the body through the cerebrum (see p. 142), so the labyrinthine mechanism dominates the *tonus* of the muscles as a whole through the cerebellum (see p. 177).

5. THE CONNECTIONS BETWEEN THE RECEIVING AND REACTING MECHANISMS

1. THE SPINAL NERVES

The connections between the peripheral receiving mechanisms and the central nervous system, the activity of which leads to the appropriate reaction of muscles, have been in part studied in connection with the various special senses.

The main connecting channels between the peripheral receiving organs and the central nervous system on the one hand, and the central nervous system and the reacting structures on the other, may now be considered more generally.

These connections are seen in their most typical arrangement in the spinal nerves, a pair of which comes off, one on each side, from each level of the spinal cord, and passes outwards between the vertebræ.

General Arrangement

These nerves may be classified as **ingoing** and **outgoing**, and they may be divided into those connected with the body wall and its appendages and those connected with the viscera.

A dorsal root (*P.R.*) comes off from the dorso-lateral aspect of the cord and has a swelling upon it, the ganglion of the dorsal root. It joins a ventral root (*A.R.*) coming from the ventro-lateral margin. These form the spinal nerve which is distributed to the body wall. Lying in front of this is a swelling or ganglion (*S.l.*) joined to the nerve by two roots, a white ramus (*W.R*). and a grey ramus (*G.R.*); and from this a nerve extends towards the viscera (*V.N.*). Before this nerve reaches its final distribution it passes through another ganglion.

Roots of the Spinal Nerves.—The dorsal root is the great ingoing channel to the spinal cord, and the ventral root is the great outgoing channel. Section of a series of dorsal roots leads to (*a*) loss of sensation in the structures from which the fibres come, and (*b*) to a loss of muscular co-ordination, as a result of cutting off the afferent impressions connected with the kinæsthetic sense (p. 102).

As a result of this section, the parts of the fibres cut off from the cells of the ganglia on the dorsal root die and degenerate (see p. 85). Therefore, if the root is cut inside the ganglion, the degeneration extends inwards and up the dorsal columns of the cord, and if it is cut outside, the degeneration passes outwards to the periphery.

Section of the ventral root causes paralysis of the muscles and other structures supplied by the outgoing fibres, and the fibres die and degenerate.

The nerve to the somatopleur or body wall (*S.N.*) is composed of incoming and outgoing fibres. 1*st*. *Incoming* fibres are medullated and take origin in the various peripheral sense organs. As they pass through the ganglion on the dorsal root each fibre is connected by a side branch with a nerve cell —the trophic centre of the neuron—and it then enters the spinal cord, and either passes to the dorso-lateral column, or forms synapses in the cord (see p. 87). 2*nd*. *Outgoing* fibres are medullated, and take origin from the large cells in the ventral horn of the grey matter of the cord and pass on to be connected with muscle fibres by end plates or to gland cells by less definite synapses.

The nerve to the viscera or splanchnopleur (*V.N.*), and to the involuntary structures in the somatopleur, contains—1*st.* *Incoming Fibres.*—These take origin either in definite peripheral structures, such as Pacinian corpuscles, or in some less defined endings, and as medullated fibres pass through the various ganglia, and have their cell stations in the ganglion on the ventral root. The nerve fibres coming from Pacinian bodies and from muscles, like the similar fibres in the somatic branch, are large and are connected with large cells in the spinal ganglion, and they become myelinated at the same time. A set of smaller fibres similar to those coming from the skin in the somatic branch are also found in the visceral branch, and they seem to be connected with smaller cells in the ganglion.

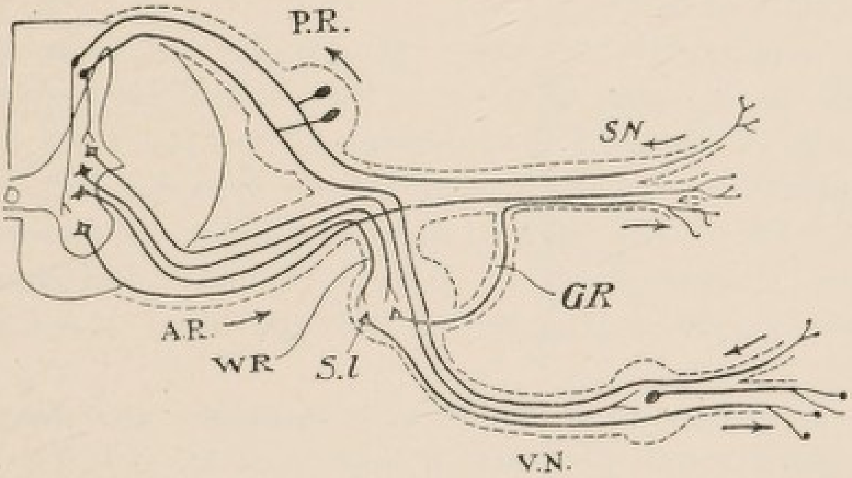


FIG. 75.—Structure of a Typical Spinal Nerve. *P.R.*, dorsal root (with ganglion; *A.R.*, ventral root; *S.l.*, ganglion of sympathetic chain; *W.R.*, its white ramus; *G.R.*, its grey ramus; *V.N.*, visceral nerve with collateral ganglion; *S.N.*, somatic nerve.

2*nd.* The *Outgoing Fibres* are characterised by their small size, take origin chiefly in a lateral column of cells, which is well developed in the dorsal region of the cord, and pass out as medullated fibres by the ventral root. From this they pass by the *white* root to a sympathetic ganglion, whence they may proceed in one of two different ways (fig. 75).

(*a*) They may form synapses with cells, and fibres from these cells may pass—

1. Outwards with the splanchnic nerves; or,

2. Back into the spinal nerve by the grey root, and so down the somatic nerve to blood vessels, muscles of the hairs, sweat glands, etc. The ganglia from which fibres pass back into spinal nerve are known as *lateral ganglia.*

(*b*) They may pass through these ganglia on to one more peripherally situated in which they form synapses and are continued onwards. These ganglia from which fibres do not pass back are called *collateral ganglia.* Before their first interruption they are termed *pre-ganglionic fibres,* after their interruption *post-ganglionic.*

The various fibres after their interruption proceed as non-medullated or grey fibres to their termination, where they join a network of anastomosing fibres with cells—a sort of *terminal ganglion.* Many drugs have a special action on the *terminal ganglia, e.g.* apocodein paralyses them, while adrenalin —the extract of the medullary part of the suprarenals—stimulates certain of them.

The interruption of fibres in ganglia, or their passage through these structures, has been determined by taking advantage of the fact that *nicotine* in one per cent. solution when painted on a ganglion poisons the synapses but does not influence the fibres. Hence, when a ganglion is painted with nicotine, if stimulation of the fibres on its proximal side produces an effect, it is proved that the break is not in that ganglion.

The arrangement of **epicritic**, **protopathic** and **deep fibres** in the neuron and plexuses is considered at p. 170.

Distribution

A. SOMATIC FIBRES

(*a*) *Outgoing Fibres.*—The course of these must be studied in the dissecting-room.

(*b*) *Ingoing Fibres.*—The fibres passing in by each pair of nerves come from zones of skin encircling the body. These are, however, interrupted by the limbs. Each limb may be considered to be an outgrowth at right angles to the trunk, composed of a pre-axial and post-axial part.

B. SPLANCHNIC FIBRES

(*a*) *The Outgoing Fibres* may be divided into (fig. 76)—

A. *The Thoracico-Abdominal Fibres,* which come out in the middle region of the spinal cord and pass through the lateral ganglia of the sympathetic chain—

(1) *Head and Neck.*—These leave the spinal cord by the upper dorsal nerves and pass upwards in the sympathetic cord of the neck to the superior cervical ganglion where they have their cell stations. From these, fibres are distributed to the parts supplied. The chief functions of these fibres are—1*st*. Vaso-constrictor to the vessels of the face and head; 2*nd*. Pupilo-dilator (see p. 126); 3*rd*. Motor to the muscle of Müller; 4*th*. Secretory to the salivary glands, lachrymal

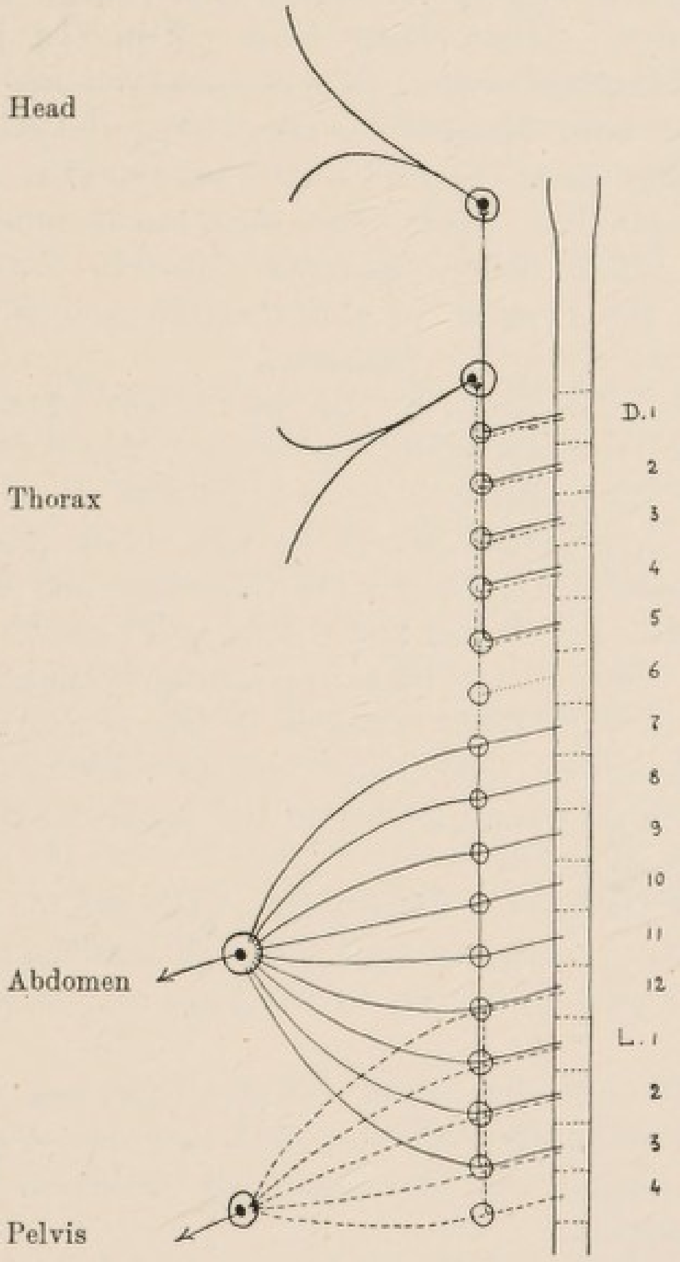


Fig. 76.—Scheme of distribution of Splanchnic Nerves.

gland, and sweat glands. The course of these fibres is of importance in medicine, since tumours in the upper part of the thorax may press upon them.

(2) *Thorax.*—The fibres to the thoracic organs also come off in the upper dorsal nerves, have their cell stations in the stellate ganglion, and pass to the heart and lungs.

(3) *Abdomen.*—These fibres come off in the lower dorsal and upper lumbar nerves. They course through the lateral ganglia and form synapses in the collateral ganglia of the abdomen—the solar plexus and the superior and inferior mesenteric ganglia. From these they are distributed to the abdominal organs, being vaso-constrictor to the vessels, inhibitory to the muscles of the stomach and intestine, and possibly secretory to the pancreas.

(4) *Pelvis.*—The fibres for the pelvis leave the cord by the lower dorsal and upper lumbar nerves, and have their cell stations in the inferior mesenteric ganglia, from which they run in the hypogastric nerves to the pelvic ganglia. They are vaso-constrictor, inhibitory to the colon, and motor to the bladder, uterus and vagina and the retractor penis.

(5) *Fore Limb.*—These fibres, coming out by the upper and mid dorsal nerves, have their synapses in the sympathetic ganglia of the sympathetic chain, and passing back into the spinal nerves by the grey rami, course to the blood vessels, hairs, and sweat glands of the limb.

(6) *Hind Limb.*—The fibres take origin from the lower dorsal and upper lumbar nerves, have their cell stations in the lateral ganglia, and pass to the leg in the same way as do the fibres to the arm.

B. *The Cranial and Sacral Fibres.*—These pass out from the upper and lower ends of the cord, and they do not pass through the lateral ganglia but have their cell station in some of the collateral ganglia.

(1) The *third cranial nerve* carries fibres which have their synapses in the ciliary ganglion, and pass on to the sphincter pupillæ and ciliary muscle.

(2) The *seventh nerve* carries fibres through the chorda tympani to cell stations in the submaxillary and sublingual ganglia. These are secretory to the submaxillary and sublingual glands.

(3) The *ninth nerve* sends fibres to the parotid gland, which have their cell station in the otic ganglion.

(4) The *vagus* sends inhibitory fibres to the heart, which form synapses in the cardiac plexus. It also sends motor fibres to the œsophagus and stomach, which, in some animals at least, have the cell stations in the ganglion of the trunk.

(5) The *nervi erigentes* come off from the second and third sacral nerves, and pass to the hypogastric plexus near the bladder where the fibres have their cell stations. They are the vaso-dilator nerves to the pelvic organs, inhibit the retractor penis, and are motor to the bladder, colon, and rectum.

(*b*) *Ingoing Fibres.*—The course of these from the viscera is not so clearly known; but they appear to enter the main nerve largely by the white rami. In the normal condition stimulation of their peripheral endings does not lead to modifications of consciousness, and is therefore not accompanied by pain. But in abnormal conditions painful sensations are produced. In some cases abnormal stimulation of visceral nerves leads to painful sensations referred to the cutaneous distribution of the spinal nerve with which they are connected. Thus, disease of the heart is often accompanied by pain in the distribution of the upper dorsal nerves in the left arm, with which the visceral fibres to the heart are associated.

2. THE CENTRAL NERVOUS SYSTEM

Spinal Cord and Brain

The anatomy and histology of each part of the central nervous system should be mastered before its physiology is studied. An outline sufficient to make the description of the physiology intelligible is all that is given here.

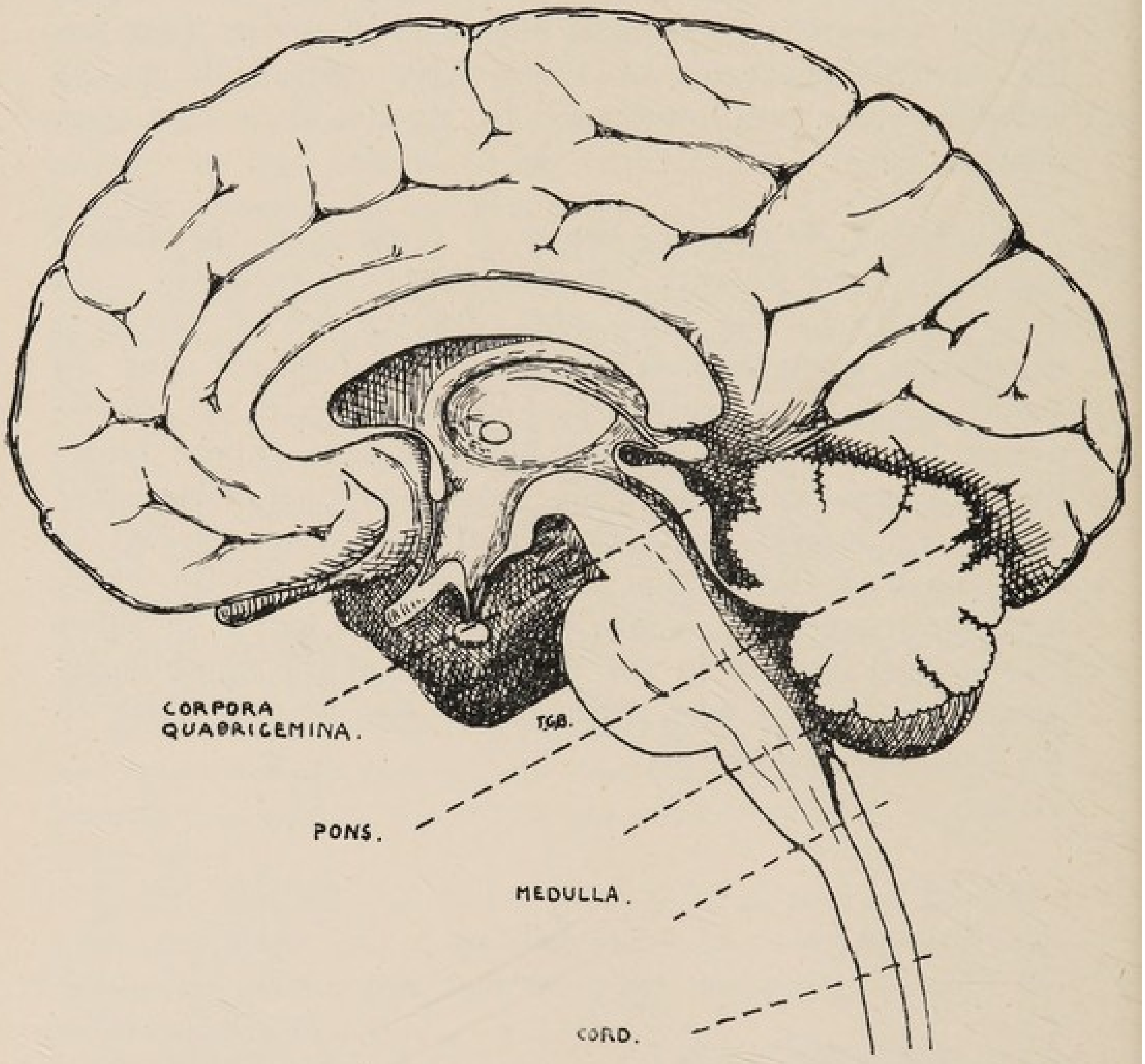


Fig. 77.—Mesial Section through the Brain and upper part of the Spinal Cord to show the positions at which the sections figured in later diagrams have been made. Cord, p. 157, fig. 78 ; Medulla, figs. 84 and 85 ; Pons, fig. 87, p. 173 ; Corpora, fig. 90, p. 179.

A. SPINAL CORD

Structure

THE spinal cord is a more or less cylindrical mass of nerve tissue which passes from the base of the brain down the vertebral canal. There are two enlargements upon it, one in the cervical region, one in the lumbar region, and from these the nerves to the arms and legs come off. A fine central canal runs down the middle, and the two sides are almost completely separated from one another by a ventral and a dorsal mesial fissure (fig. 78). Each half is composed of a core of grey matter arranged in two processes or horns—

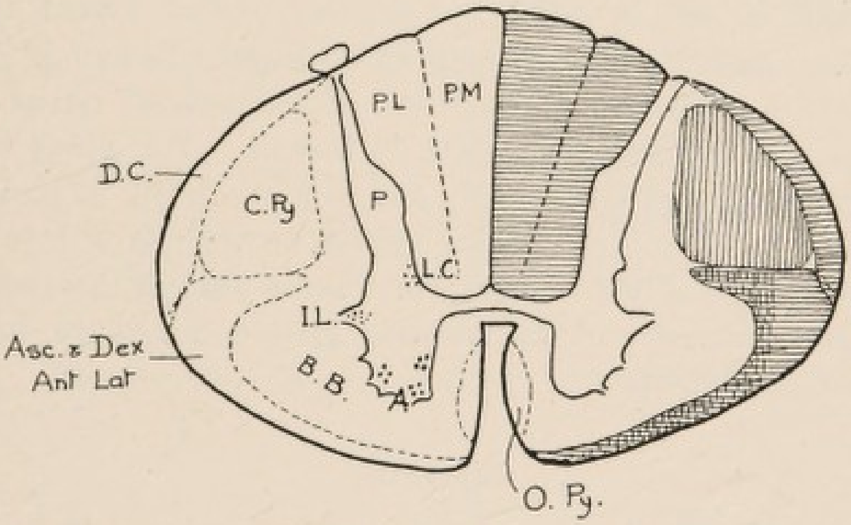


FIG. 78.—Cross Section of the Spinal Cord through the Second Dorsal Segment, to show disposition of grey and white matter. *P.*, dorsal horn ; *A.*, ventral horn with large cells ; *I.L.*, intermedio-lateral horn with small cells ; *L.C.*, Lockhart Clarke's column of cells ; *P.M. and P.L.* dorso-median and dorso-lateral columns ; *D.C.*, direct cerebellar tract *Asc. and Desc. Ant. Lat.*, ascending and descending ventro-lateral or spino-ventral tracts ; *B.B.*, basis bundles ; *C.Py.*, crossed pyramidal tract ; *O.Py.*, direct pyramidal tract. On opposite side, tracts which degenerate headwards are marked with horizontal lines ; tracts degenerating from the head with vertical lines. (*After* BRUCK.)

the ventral and dorsal horns (*A. and P.*)—which divide the white matter surrounding the grey into a dorsal, a lateral, and a ventral column. In the dorsal region a lateral horn of grey matter projects into the lateral column (*I.L.*). The grey matter on each side is joined to that of the opposite side by bands of grey matter; the ventral and dorsal grey commissures, one below and one above the central canal.

The grey matter is composed very largely of cells and synapses of neurons supported by branching neuroglia cells. The cells of the grey matter are largest and most numerous in the ventral horn, where they constitute the cells from which the majority of nerve fibres come off. In the dorsal region a group of cells in the lateral horn, the intermedio-lateral cells, give off visceral fibres (*I.L.*). In the dorsal region also a set of cells lie on the mesial aspect of the dorsal horn constituting the cells of Lockhart Clarke (*L.C.*).

The white substance is composed of medullated nerve fibres in which the neurilemmal sheath is absent. The fibres chiefly course up and down the cord, and some run in a horizontal direction:—1. The fibres of the spinal nerves; 2. Fibres passing from grey to white matter; 3. Fibres joining the two sides of the cord in front of the ventral grey commissure forming the white commissure.

Functions

The spinal cord is the great mechanism of reflex action, and the great channel of conduction between the brain and the peripheral structures.

A. Reflex Functions

If the brain of such an animal as a frog be destroyed, the animal lies prone on its belly and immovable for any length of time; but the legs tend to be drawn up alongside the body, and the muscles are in a state of slight tonic contraction very different from the flaccid condition found after destruction of the cord. The study of the spinal reflexes (p. 90) has shown that *the animal has the power of reflex movements with definite co-ordination of its muscles, but it has no power of balancing itself, and manifests no spontaneous movements.*

These reflex functions of the cord in mammals have been very fully investigated by Sherrington in dogs and cats in which the cerebrum has been separated from the rest of the nervous system, and his results have been considered on p. 92. On suspending such animals in the normal horizontal position, with legs dependent, it is found that all four legs are in a state of tonic slight extension as they are in supporting the body. This he terms "decerebration rigidity." It appears to be due to impulses passing down from the semicircular canal mechanism, which reinforce the spinal reflex arcs. That this is so is shown by the fact that section of the posterior roots of the spinal nerves removes the rigidity. Stimulation of definite areas of skin at once causes the animal to strike a special attitude (p. 95). Thus stimulation of the left fore paw produces the attitude of walking, which is assumed normally when that paw reaches the ground. Stimulation of the left pinna produces the attitude assumed if the animal were turning away from the stimulus.

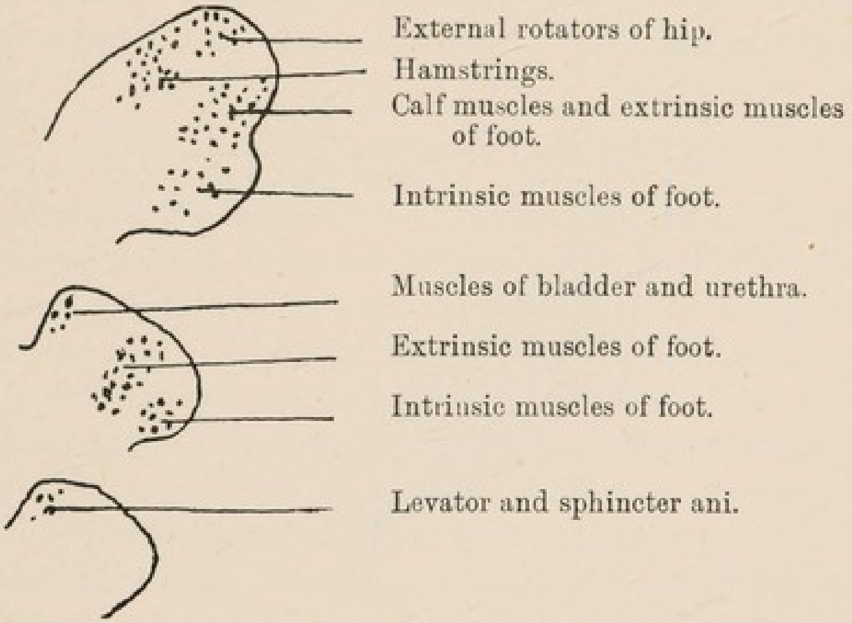


FIG. 79.—The Groups of Cells in the Ventral Horn of grey matter at the level of the 2nd, 3rd, and 4th sacral nerves. (*From* BRUCE.)

The anatomical connection between the different levels of the cord involved in such reflexes has been demonstrated by Sherrington by keeping a dog in which the spinal cord is cut in the neck till all the down-going tracts below the point of section have completely degenerated so as to leave a clean slate, and then cutting the cord at a lower level when the proprio-spinal fibres connecting the different levels of the cord degenerate. They are chiefly situated in the lateral columns of the cord.

In man the cutaneous reflexes connected with various groups of **skeletal muscles** are definitely associated with different levels of the cord.

Reflex actions in connection with various **visceral muscles** are also connected with the spinal cord. Many of these are complex reflexes involving inhibition of certain muscles and increased action of others, some visceral, some skeletal. The best marked of these are the reflex acts of **micturition** (p. 427), **defæcation** (p. 376), **erection,** and **ejaculation** (p. 434). The lumbar enlargement is the part of the cord involved.

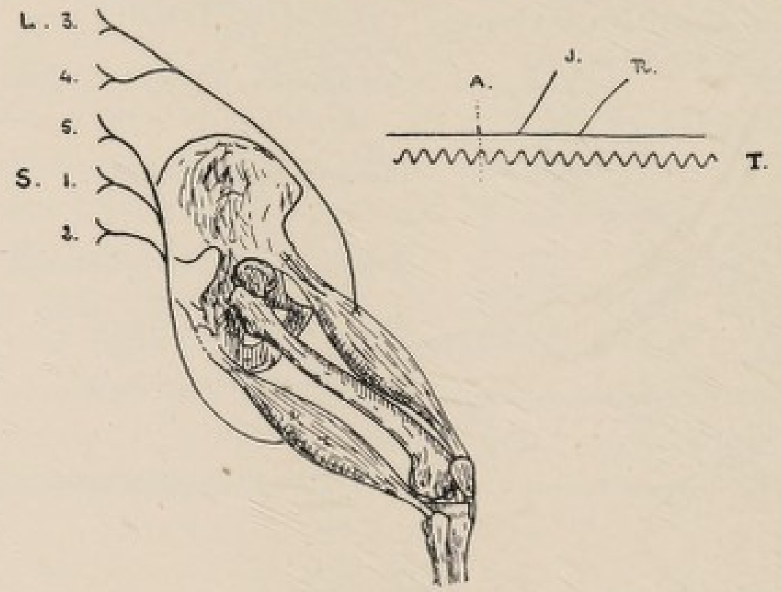


Fig. 80.—The neuro-muscular mechanism concerned in the knee jerk, and the time of the knee jerk (*A.J.*) compared with the time of a reflex action (*A.R.*).

The synapses in the cord are not only capable of acting reflexly to set up definite contractions in muscles, but they also exercise a constant **tonic action** upon them, due to the constant inflow of incoming impressions (p. 42). When this tonic action is interfered with by any condition which interferes with the integrity of the reflex arc, the effect of directly stimulating a muscle is diminished. This is very well seen in the contraction of the quadriceps extensor femoris which occurs when the ligamentum patellæ is struck sharply, causing a kick at the knee joint—the **knee jerk** (fig. 80). When the reflex arc in the lower lumbar region of the cord is interfered with, the knee jerk is diminished or is absent, and when the activity of the arc is increased, by the removal of the influence of the brain, the jerk is increased. That the jerk is probably not a true reflex is shown by the fact that the latent period is very much shorter than that of most reflex actions (fig. 80). The reflex arc, however, is necessary for the tonus. This tonus is increased by tension of the muscles and also by fatigue of the nervous system, and this condition may lead to cramp.

The degeneration of special groups of cells—the anterior horn of grey matter—which follows amputation of the leg at different levels seems to indicate that the various groups of cells have definite connections with individual muscles (see fig. 79).

B. Conducting Paths

The study of the course of the ingoing and outgoing fibres in the cord has proved to be one of great difficulty. It is possible in animals to divide the cord completely or to divide one half, or to divide any one of the white columns, and to observe any loss of muscular action which may ensue and to trace the course of degenerated fibres; but to determine what changes in the sensibility have resulted on animals, unable to give any expression to their sensations, is practically impossible.

On the other hand, the clinical method of carefully studying the changes in sensibility during life and determining post-mortem the exact site of the lesion which has produced these symptoms has generally proved somewhat unsatisfactory on account of the want of precision in the lesions produced by injury or disease of the cord.

A. Ingoing Fibres.—In the cord there seems to be a sorting of fibres into those the stimulation of which can effect consciousness and give rise to sensations and those which simply produce reflex responses. Thus, those kinæsthetic fibres which give rise to the muscle and joint *sense* run up in the posterior columns and cross above the cord, while those which are concerned with the *unconscious adjustment* of muscular action through the agency of the cerebellum are shunted off through the synapses in Clarke's column to the direct cerebellar tract of the same side and the spino-ventral cerebellar tract of the opposite side. In all probability fibres connected with the tactile sense are similarly sorted out, and possibly even those connected with the conduction of thermal and of nocuous stimuli.

As regards the course of the *Ingoing Fibres*, the most valuable advance has been made by the study of the results of lesions of the cord in the light of the observations of Head and his co-workers on the course of these fibres in the peripheral nerves (see p. 111).

While section of a cutaneous nerve destroys epicritic and protopathic sensibility, and leaves deep sensibility intact, lesions of the spinal cord are apt to interrupt the passage of the impulses concerned with different *kinds* of sensation. Thus, section of a cutaneous nerve abolishes any sensation of pain from the surface of the skin, but leaves the possibility of the sensation of pain being produced by severe pressure on deep structures, while a lesion of the cord is apt to interrupt the passage of all stimuli producing pain, whether coming by epicritic, protopathic or deep fibres. A redistribution has taken place—all the various fibres carrying the impulses derived from nocuous stimulation have got shunted into one tract carrying them up to the brain. Similarly the impulses connected with thermal sensation coming by epicritic and by protopathic fibres, and those connected with the sense of touch and pressure, each get shunted into specific tracts (figs. 81 and 82).

This must mean that these impulses get sorted out by passing through synapses in the cord, and the position of these synapses and the course of the axons running from them to the brain have been deduced partly from histological investigation of the fibres of the posterior roots, partly by careful study of the symptoms and of the degenerations which follow definite lesions of the cord.

By the developmental method, by the different characters of the fibres, and by the degenerative changes, a posterior root has been divided into four main bundles :

1. A set of large fibres passing forward to form synapses with the cells of the ventral horn at the same and other levels of the cord.
2. A second passing up the dorsal columns of the same side, some running right on to the top of the cord, but many entering the grey matter as they course upwards.

3. A third set forming synapses with the cells of Lockhart Clarke's column.
4. A fourth ending at once in synapses with the cells of the dorsal horn or running for a short distance up the dorsal column before forming synapses.

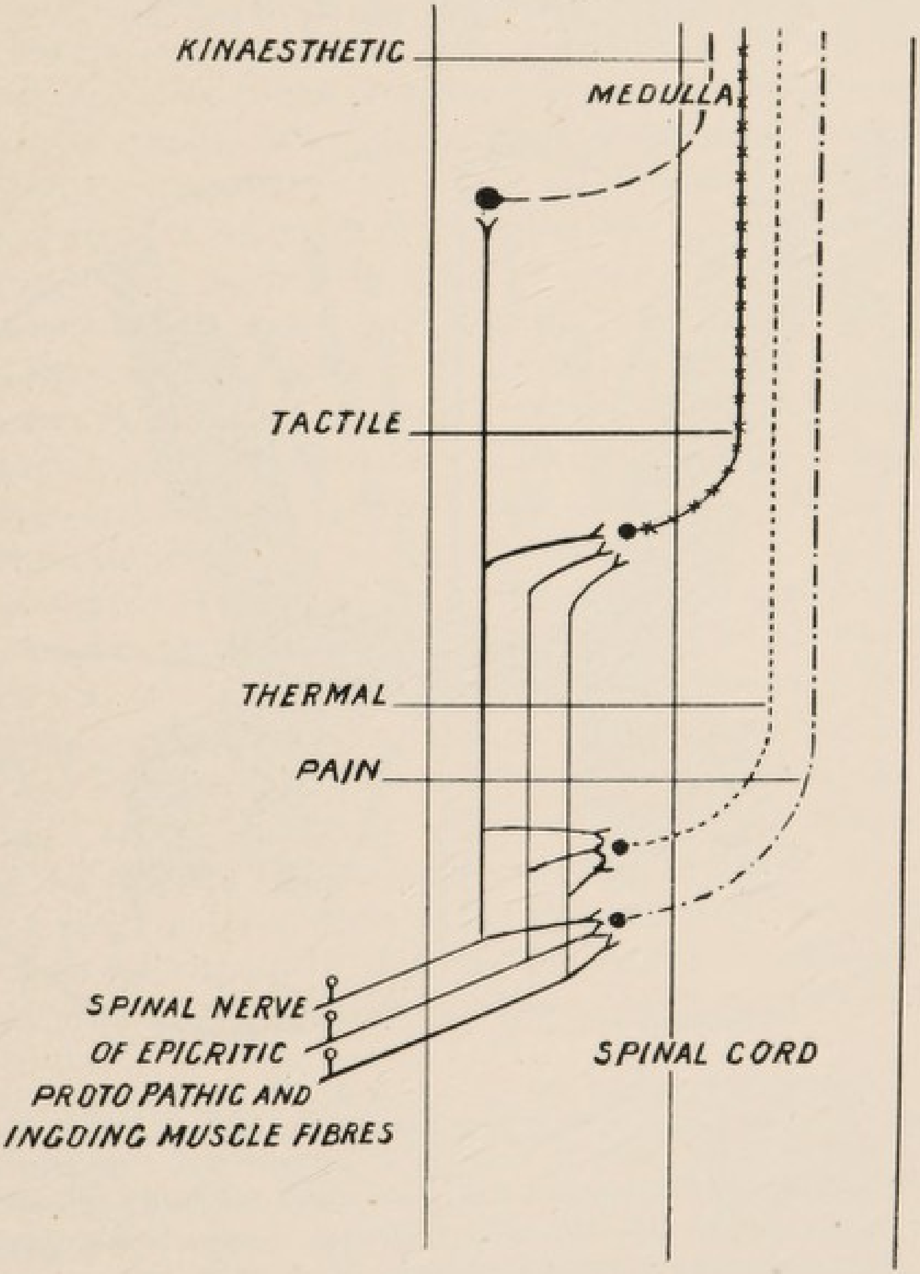


FIG. 81.—To show redistribution of impulses in the cord and the general course of impulses of different kinds.

1. The first set of fibres are those concerned in ordinary **simple reflex action** (fig. 82, 4).

2. The second set make up the **dorsal columns.** When

interrupted the result is a loss of the kinæsthetic sense and a loss of the tactile sense for a short distance below the lesion, but not of the rest of the tactile sense or of the thermal sense or of pain. They form synapses in the nuclei of the dorsal columns in the medulla in which they terminate, and, from these synapses, fibres cross the middle line to run headwards to the brain in the fillet (see p. 175) (fig 82, 1 and *A*).

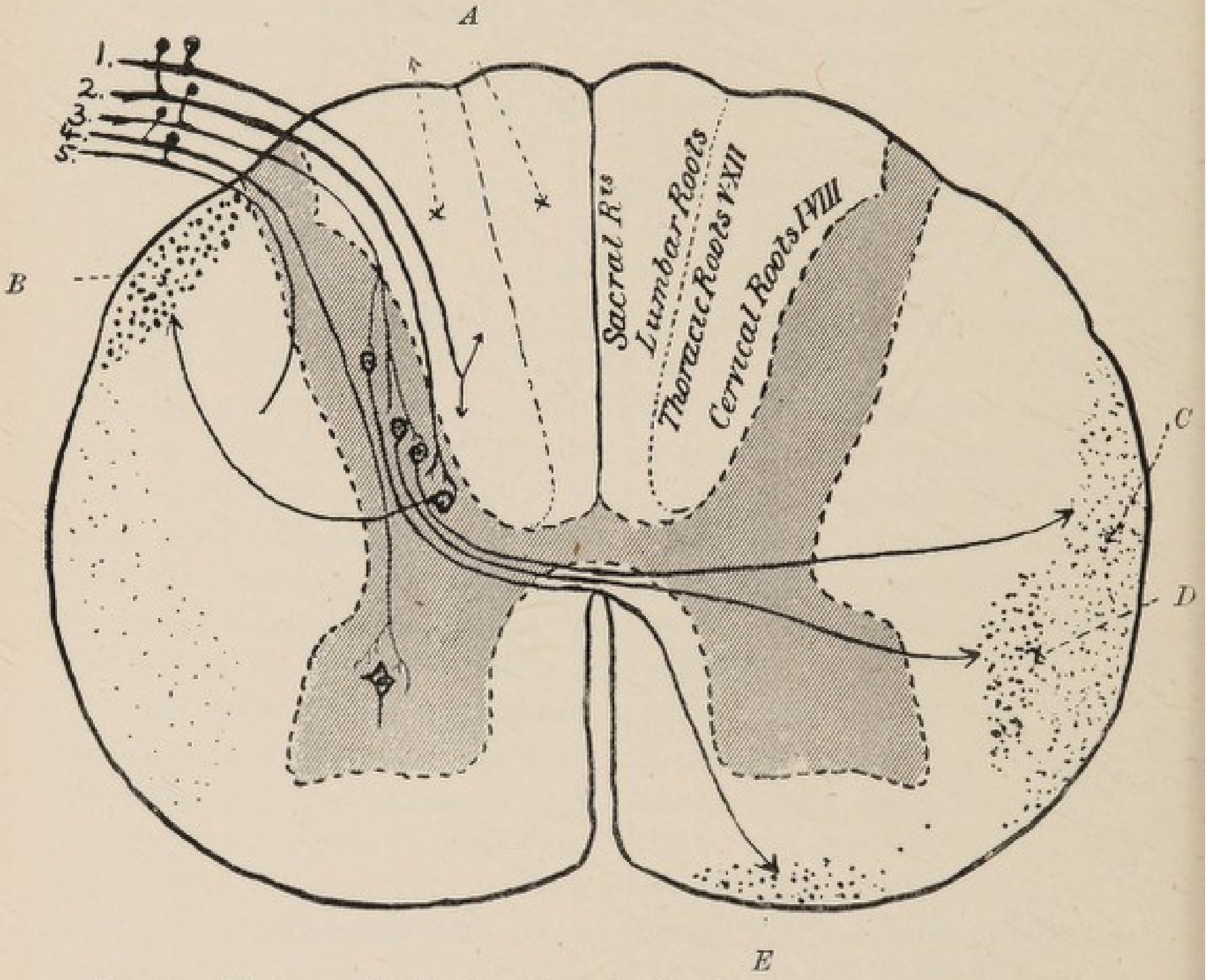


FIG. 82.—To show redistribution of impulses in the spinal cord. 1 to 5, incoming fibres of dorsal root; *A*, tract of kinæsthetic sense; *B*, tract of unconscious impulses for muscular co-ordination and tone; *C*, same as *B*, but on opposite side; *D*, tract of impulses of pain. heat and cold; *E*, tract of impulses of touch and pressure. (PAGE MAY.)

3. From the cells of Lockhart Clarke, with which the third set of fibres form synapses—(1) axons sweep outwards to take up a position on the dorso-lateral margin of the cord and to constitute the **direct cerebellar tract** which runs up to the cerebellum (fig 82, 2 and *B*); (2) other axons cross the ventral

white commissure to the opposite side of the cord and come to lie on the lateral margin just ventral to the direct cerebellar tract. They may be termed the **ventro-spinal cerebellar tract**, and they too pass to the cerebellum, but by a different route from those of the direct tract (see p. 177) (fig. 82, 3 and *C*).

4. The fourth set of fibres form synapses with the cells in the dorsal horn. From these, axons cross the ventral white commissure to the opposite side of the cord, and have been traced headwards to the posterior part of the thalamus opticus. They may thus be called the **spino-thalamic tract**. They seem to run in two groups:—(1) Those concerned with the sensations of pain, of heat and of cold cross near their point of entry and take up a position in close association with those of the ascending ventro-lateral cerebellar tract (fig. 82, *D*). (2) Those concerned with the tactile sense, whether of light touch or of pressure, run for a short distance up the dorsal columns, then form synapses. The fibres from these cross at a higher level than the last, and when they have crossed take up a position on the ventral margin of the cord (fig. 82, *E*).

As regards the side of the cord on which these fibres lie as they course upwards to the brain, it has been demonstrated, by section of one-half of the cord, that sensations of pain, temperature, and to a less extent of touch, are lost on the opposite side below the point of section, and that the kinæsthetic sense and partly the tactile sense are lost on the same side. These symptoms are explained by fig. 81.

The position of the fibres in the different columns of the cord has been determined by studying the results of section of the different columns and by following out the degenerations which result.

The degeneration method, or Wallerian method, is based upon the fact, that nerve fibres separated from their cell die and degenerate (see p. 85). These degenerations may be demonstrated when recent by Marchi's method of staining, which depends upon the fact that, while the white sheath of normal fibres is not stained black when the tissue is placed in a solution of chrome salt with osmic acid, it is so stained when it begins to degenerate (p. 85). When, at a later period, the white sheaths have entirely disappeared, the degeneration is best demonstrated by Weigert's method of staining the white sheaths of normal fibres with hæmatoxylin, which leaves the degenerated tracts of fibres unstained. The fibres in the central nervous system do not regenerate, probably because they are devoid of the neurilemmal sheath.

B. Outgoing Fibres.—The course of these fibres is much more easily determined than that of the ingoing fibres. The effects of experimental or clinical lesions of the cord upon the muscular movements, the downward degeneration which follows such lesions, and lastly the fact that, generally speaking, these outgoing fibres get their medullary sheath at a later date than the ingoing fibres, all enable the position of the outgoing tracts to be defined. They may be grouped in four sets—

1. A very strong band of fibres lying in the dorsal part of the lateral column, just inside the direct cerebellar tract, and becoming smaller as the posterior part of the cord is reached. This is the *crossed pyramidal tract* (fig. 87, *C.Py.*), which comes from the cells of the cortex cerebri of the opposite side, and gives off collateral branches to the cells in the ventral horn of the spinal cord (fig. 41, *D*, p. 88).

2. Certain fibres from the cortex cerebri do not cross, but run down, some in the crossed pyramidal tract, some in the *direct pyramidal tract* (fig. 87, *O.Py.*), which runs along the margin of the ventral fissure, and extends tailwards only into the dorsal region. These fibres decussate in the cord.

3. A set of fibres just inside the ventro-lateral ascending tract, which may be called the *ventro-lateral descending tract* (fig. 87, *Desc.Ant.Lat.*). This comes from Deiters' nucleus (see fig. 87), and as it passes down, gives off fibres to the cells in the anterior horn of the grey matter of the cord. Deiters' nucleus receives fibres from the cerebellum, and the ventro-lateral descending tract thus carries down impulses from that organ.

4. From the red nucleus (p. 184) some fibres pass down the cord as the *pre-pyramidal tract* just ventral to the crossed pyramidal tract.

C. Fibres not Degenerating beyond the Cord.—*Proprio-Spinal Fibres.*—Round the grey matter, a band of fibres—the *basis bundles* (fig. 87, *B.B.*)—and outside of these, scattered through the white matter chiefly of the lateral columns, other fibres degenerate in the cord and seem to be commissural between different levels of the grey matter (see p. 167).

Other tracts of fibres have been described, such as *Lissauer's tract* and the *septo-marginal tract*, but their relations have not been satisfactorily investigated.

B. THE MEDULLA OBLONGATA

1. Structure

The medulla oblongata may be regarded as the upper end of the spinal cord, which it connects with the brain (fig. 83). The cord expands and the dorsal median fissure is opened out, so that the central canal comes to the surface, and expands into a lozenge-shaped area—the *floor of the fourth ventricle.* The lateral columns of the cord pass outwards tc the cerebellum to form part of its inferior peduncles—the *restiform bodies.* Between the lateral and the ventral columns an almond-shaped swelling, the *olive*, appears (fig. 85, *O.*). In front of this the medulla is encircled by a mass of transverse fibres—the middle peduncles of the cerebellum, or the *pons Varolii* (fig. 87, *P.*). The floor of the fourth ventricle is constricted above by the approximation of the superior peduncles of the cerebellum (fig. 83, *p.c.s.*) to again become a canal. The **grey matter** of the cord gets broken up into separate masses, of which the most important are—

1. The *nuclei of the dorsal columns*—the nucleus gracilis and nucleus cuneatus (fig. 84, *N.C.* and *N.G.*)—masses of cells and synapses in which the fibres of the dorsal columns end, and from which the upgoing fibres of the *fillet* start.

2. The *inferior olivary nucleus* (fig. 85, *O.*), which lies in the olive, and which is connected by bands of fibres with the dentate nucleus of the cerebellum (fig. 87, *Dent.*).

3. The *nucleus of Deiters* (fig. 87, *Deit.*), lying higher up in the pons Varolii, and connected with fibres from the cerebellum and from the semicircular canals (see fig. 81).

4. The *nuclei of the cranial nerves*, masses of cells from which the nerves take origin (fig. 86).

2. Conducting Paths

A. Ingoing.—1. The dorsal columns of the spinal cord terminate in two masses of grey matter on each side, the nucleus gracilis and nucleus cuneatus. From these, fibres pass forwards (*i.e.* towards the ventral aspect of the medulla) and cross the middle line forming the *decussation of the fillet* (fig. 84, *F.*). The crossed fibres (fig. 85, *F.*) then pass up in a vertical series on each side of the middle line until the pons

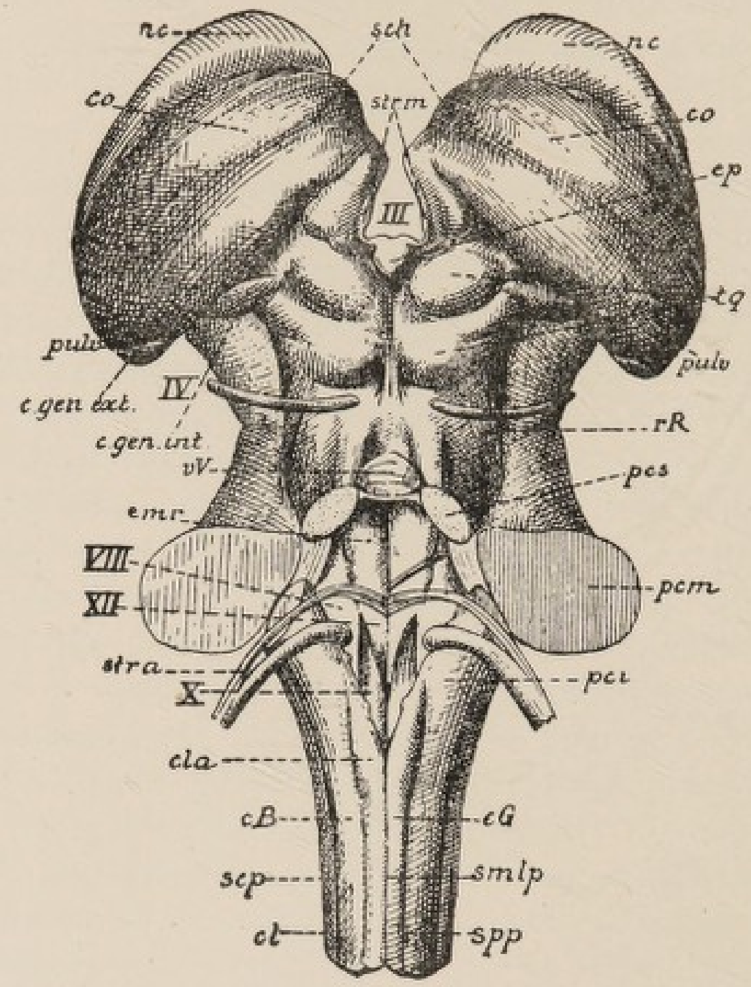


FIG. 83.—View of the Medulla Oblongata, Corpora Quadrigemina, and the Optic Thalami from above. *c.l.a.*, posterior columns of cord; *VIII.*, *XII.*, *X.* indicate the roots of these cranial nerves; *p.c.i.*, the restiform body; *p.c.m.*, the middle peduncle of the cerebellum; *p.c.s.*, the superior peduncle of the cerebellum; *t.q.*, the anterior and posterior corpora quadrigemina; *c.o.*, the optic thalamus with pulvinar (*pulv.*) and external and internal geniculate bodies behind it; *e.p.*, the pineal body. The separation of the posterior columns of the cord and the opening out of the floor of the fourth ventricle is shown. (VAN GEHUCHTEN.)

Varolii is reached, when they spread out horizontally like a fan (fig. 87, *F.*) dorsally to the deep transverse fibres. Above the pons they divide into two sets (fig. 90, *F.*) — a *lateral fillet*, which ends in the anterior corpora quadrigemina, and a *mesial fillet*, which passes on to the optic thalamus, and there ends by forming synapses.

2. The *spino-thalamic tract* passes up through the medulla, and with the mesial fillet ends in the thalamus.

3. The *direct cerebellar tract* passes up into the restiform body, and so on to the superior vermis of the cerebellum (p. 182). Its fibres form synapses round cells chiefly on the opposite side.

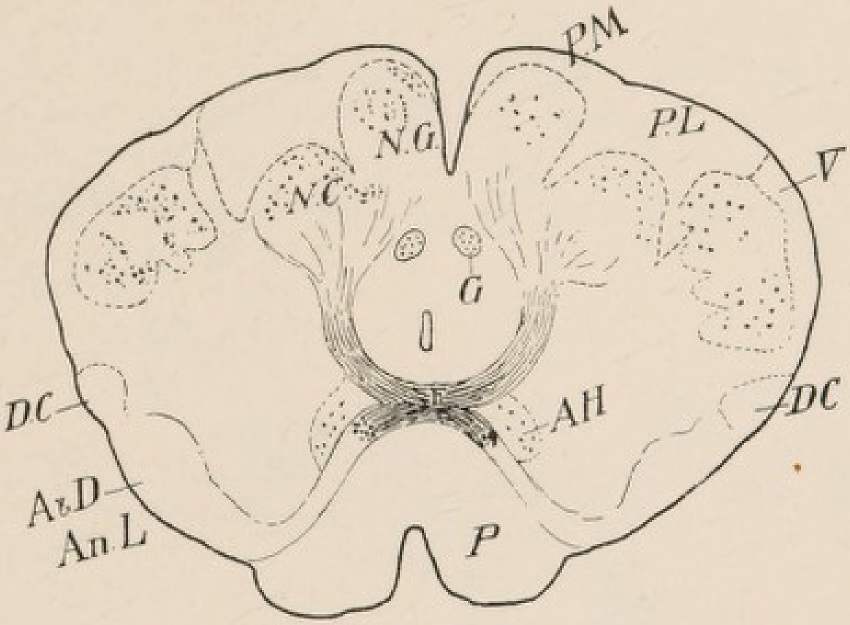


Fig. 84 —Cross Section through Medulla Oblongata above the decussation of the Pyramids. *P.M. and P.L.*, postero-median and postero-lateral tracts of the cord ; *N.G. and N.C.*, nucleus gracilis and cuneatus, giving off the fillet fibres crossing at *F.* ; *V.*, ascending root of fifth nerve ; *G.*, nucleus of glossopharyngeal nerve ; *A.H.*, anterior horn of spinal cord ; *P.*, the anterior pyramids ; *D.C.*, direct cerebellar tract ; *A. and D. Ant.L.*, ascending and descending antero-lateral tracts. (*After* Bruce.)

4. The *ventro-spinal cerebellar tract* passes up beside the last, but it leaves it in the restiform body and courses forward, to arch back into the cerebellum round the superior cerebellar peduncle and to form synapses with the cells of the superior vermis (fig. 87, p. 173).

B. Outgoing.—1. The fibres from the cerebral cortex, which form in the cord the crossed and direct pyramidal tracts, pass down in the middle part of the crusta (fig. 90, *P.*) of the crura cerebri, and, after coursing between the superficial and deep transverse fibres of the pons (fig. 87, *P.*), come to lie in the ventral pyramids of the medulla (fig. 84, *P.*). At the lower end of the medulla most of these fibres cross (p. 174) to the lateral column of the cord; some, however, run down the direct and crossed pyramidal tracts of the same side.

2. The fibres of the descending ventro-lateral tract, coming originally from the deep nuclei of the cerebellum, take origin, in part at least, in a mass of nerve cells (Deiters' nucleus), which lies in the dorsal and lateral part of the pons Varolii (fig. 87, *Deit.*).

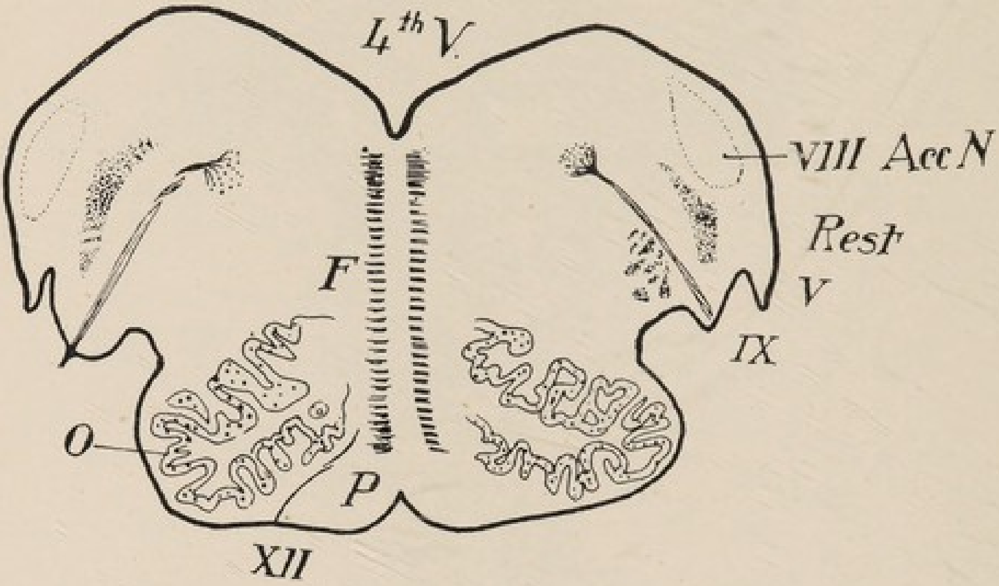


Fig. 85.—Cross Section of Medulla through the Olive. The central canal has opened out to form the floor of the fourth ventricle, *4th V.*, the lateral columns are passing out to form the inferior peduncles of the cerebellum; *F.*, fillet; *O.*, inferior olivary nucleus; *P.*, anterior pyramids; *Rest.*, fibres of restiform body; *V.*, ascending root of fifth nerve; *VIII. Acc.N.*, accessory nucleus of the eighth nerve. (*After* Bruce.)

C. Commissural Fibres.

1. The basis bundles of the cord form in the medulla a strong band of fibres connecting the grey matter at different levels, the *dorsal longitudinal fasciculus.*

2. A set of fibres run from each olivary body across the middle line to the dentate nucleus of the cerebellum of the opposite side.

3. Cranial Nerves

(*The physiology of these should be studied while dissecting them.*) The nerves springing from and entering the medulla do not come off in the same regular fashion as do the spinal nerves, although they, like the spinal nerves, must be considered as forming part of the spinal arcs. The outgoing fibres of each spring from a more or less definite mass of cells. The ingoing fibres generally form synapses with cells arranged in definite groups. In this way the so-called *nuclei of the cranial nerves* are formed. The position of these is indicated in fig. 86. In the cranial nerves no sharp differentiation into ventral and dorsal roots can be made out. Nevertheless they contain the same component elements as the spinal nerves, the fibres running either together or separately.

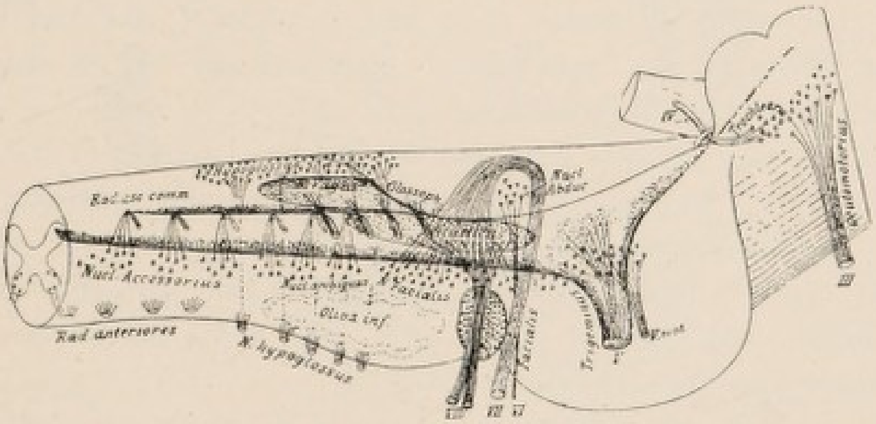


Fig. 86.—The Nuclei and Roots of the Cranial Nerves. (*After* Edinger.)

Ingoing Fibres.—Somatic and splanchnic fibres (p. 158) enter the medulla and have their cell stations in ganglia upon the nerves.

Outgoing Fibres.—Somatic and splanchnic fibres pass out, the latter being characterised by their small size, and by forming synapses before their final distribution.

The XII. (Hypoglossus) is purely a ventral root nerve, and is motor to the muscles of the tongue.

The X. (Vagus), and the XI. (Spinal Accessory) are practically one nerve, consisting partly of dorsal and partly of ventral root fibres. The vagus is the great ingoing nerve from the abdomen, thorax, larynx, and gullet, while, by outgoing fibres, passing through it or through the accessorius, it is augmentor for the muscles of the bronchi and alimentary canal, inhibitory to the heart, dilator to blood vessels of the thorax and abdomen, and motor to the muscles of the larynx and to the levator palati. The accessorius is also motor to the sterno-cleido-mastoid and trapezius.

The IX. (Glossopharyngeus) is essentially a dorsal root, and is the ingoing nerve for the back of the mouth, the Eustachian tube, and tympanic cavity. It transmits outgoing fibres which are motor to the stylo-pharyngeus and middle constrictor of the pharynx.

The VII. (Facial) is almost purely a ventral root, transmitting the motor fibres to the muscles of expression, and secretory fibres to the submaxillary and sublingual glands and the glands of the mouth. It, however, carries ingoing fibres from the anterior two-thirds of the tongue.

The V. (Trigeminal) is chiefly a dorsal root, but it has a distinct ventral or motor root which joins it, and carries the motor fibres to the muscles of mastication. It is the great ingoing nerve for all the face.

The VI. (Abducens) supplies the external rectus of the eye.

The IV. (Trochlearis) supplies the superior oblique. The III. (Oculo-motorius) supplies all the muscles of the eye except those supplied by VI. and IV. The anterior part of the nucleus consists of small cells and gives off fibres to the sphincter pupillæ and ciliary muscles.

The fibres coming from the nuclei of these cranial nerves do not always pass out in the nerve itself. Thus, fibres from the nucleus of the III. to the orbicularis oculi pass out in the VII., while fibres for the posterior belly of the digastric which pass out in the VII. probably come from the nucleus of the XII.

4. Reflexes of the Medulla

The extensive series of synapses in the medulla form arrangements by which various combined and co-ordinated movements are controlled. Thus, part of the nucleus of the vagus governs the movements of respiration, while other parts preside over the slowing mechanism of the heart. To these various reflex arrangements the name of *centres* has been given, and their mode of action will be considered when dealing with the mechanism of circulation, respiration, and digestion.

C. REGION OF PONS VAROLII

This region consists of the upper part of the medulla embraced by the transverse fibres of the middle peduncles of the cerebellum (fig. 87).

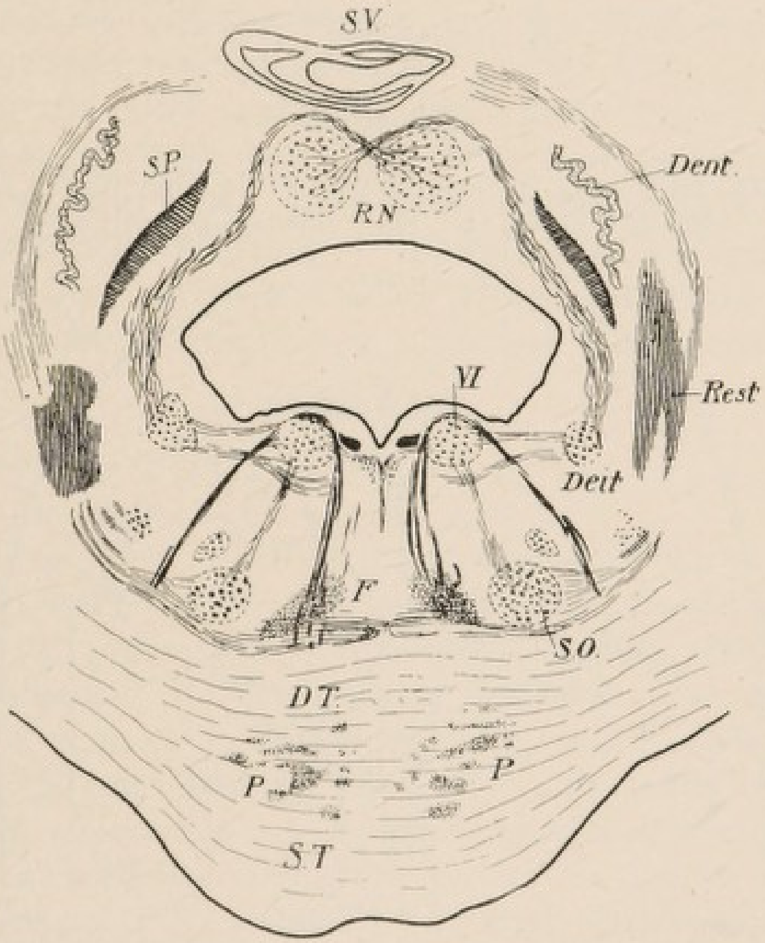


FIG. 87.—Cross Section through Region of Pons, Cerebellum, and Fourth Ventricle. *S.V.*, superior vermis; *R.N.*, roof nucleus; *Dent.*, dentate nucleus; *Rest.*, restiform body; *S.P.*, superior peduncle of cerebellum; *Deit.*, Deiters' nucleus; *VI.*, nucleus of the sixth nerve; *F.*, fillet; *S.O.*, superior olive; *D.T. and S.T.*, deep and superficial transverse fibres; *P.*, pyramidal fibres. (*After* BRUCE.)

Outgoing Fibres.—1. The fibres to the face muscles cross the middle line to become associated with the various nuclei of the cranial nerves. For this reason a tumour in one side of the pons may cause paralysis of the face muscles on one side and of the muscles of the rest of the body on the opposite side.

2. Fibres to the limbs and trunk run down between the deep and superficial transverse fibres (fig. 87, *P.*).

Ingoing Fibres.—The fillet fibres in the pons, instead of running up on each side of the middle line, spread out into a horizontal arrangement above the crossed fibres (fig. 87, *F.*).

The **nucleus of Deiters** and the nuclei of various cranial nerves lie in this region of the brain.

The connections of the transverse fibres are considered on p. 177.

D. CEREBELLUM

Structure

The cerebellum (fig. 86) or lesser brain lies above the fourth ventricle, and is joined to the cerebro-spinal axis by three peduncles on each side (figs. 81 and 89). It consists of a central lobe, the upper part of which is the *superior vermis* (fig. 87, *S.V.*), and two lateral lobes, each with a secondary small lobe, the *flocculus*. Its surface is raised into long ridge-like folds running in the horizonal plane, and is covered over with grey matter, the cortex.

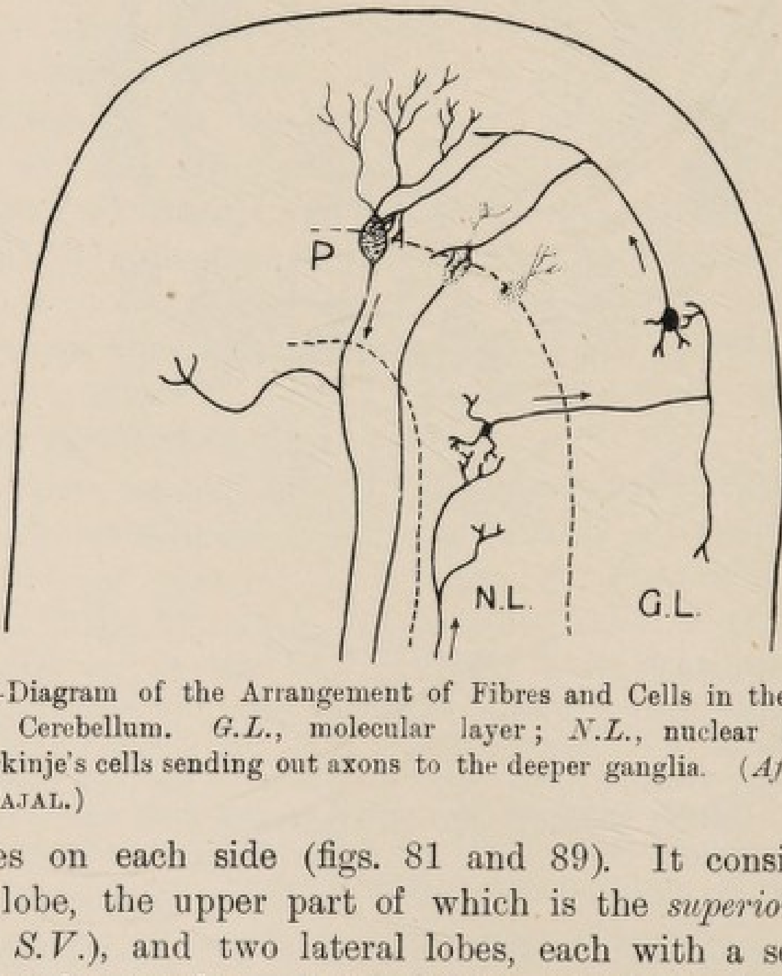


FIG. 88.—Diagram of the Arrangement of Fibres and Cells in the Cortex of the Cerebellum. *G.L.*, molecular layer; *N.L.*, nuclear layer; *P.*, Purkinje's cells sending out axons to the deeper ganglia. (*After* RÁMON Y CAJAL.)

In the substance of the white matter forming the centre of the organ are several masses of grey matter on each side, the most important of which are—1, the *roof nucleus*; and 2, the *dentate nucleus* (fig. 87, *R.N.* and *Dent.*).

The **cortex** may be divided into an outer somewhat homogeneous layer (the *molecular layer*, fig. 88, *G.L.*) and an inner layer studded with cells (the *nuclear layer*, *N.L.*). Between these is a layer of large cells—the cells of Purkinje (*P.*).

By Golgi's method the arrangement of fibres and cells in the cerebellar cortex has been shown to be as follows:—

Fibres coming into the cortex from the white matter end either in synapses round cells in the nuclear layer, or proceed at once to the outer layer (fig. 88). From the cells in the nuclear layer, processes pass to the outer layer and there form synapses with other cells. From these, processes pass to the cells of Purkinje, round which they arborise, and from Purkinje's cells the outgoing fibres of the cerebellum pass into the white matter, and so to the deeper ganglia, and to Deiters' nuclei (fig. 87).

Connections

The cerebellum is connected (fig. 89):—

i. *With the Spinal Cord.*

a. Incoming Fibres.—1. The direct cerebellar tract (p. 172) passes up in the restiform body to end chiefly in the superior vermis. 2. The ascending ventro-lateral tract (p. 174) passes to the cerebellum in the superior peduncle and ends in the superior vermis. 3. Fibres from the nuclei of the dorsal columns of the same side (fig. 84, p. 177) pass in the restiform body to the cerebellum. 4. Fibres from the vestibular root of the eighth nerve also pass to the cerebellum (fig. 81, p. 152).

b. Commissural Fibres.—Strong bands of fibres connect the inferior olive of one side with the dentate nucleus of the other.

c. Outgoing Fibres.—Fibres pass from the superior vermis to the deep nuclei, and, from these, fibres run to Deiters' nuclei (fig. 87), from which fibres pass down in the descending ventro-lateral tract of the cord.

ii. *With the Cerebrum.*—1. The fibres of the middle peduncles cross in the middle line embracing the medulla, and forming the pons Varolii, and become associated with cells from which fibres pass up in the lateral parts of the crura cerebri to the cerebral cortex (fig. 90, *CC. CC.*, p. 187).

2. The fibres of the superior peduncle, coming chiefly from the dentate nucleus and superior vermis, cross the middle line and end partly in the red nucleus of the opposite side and partly in the thalamus opticus (fig. 90, *S.C.P.*). The red nucleus fibres seem to pass upwards to the cerebrum and downwards into the pre-pyramidal tract of the spinal cord. How far the former are upward conducting and how far downward is not definitely known.

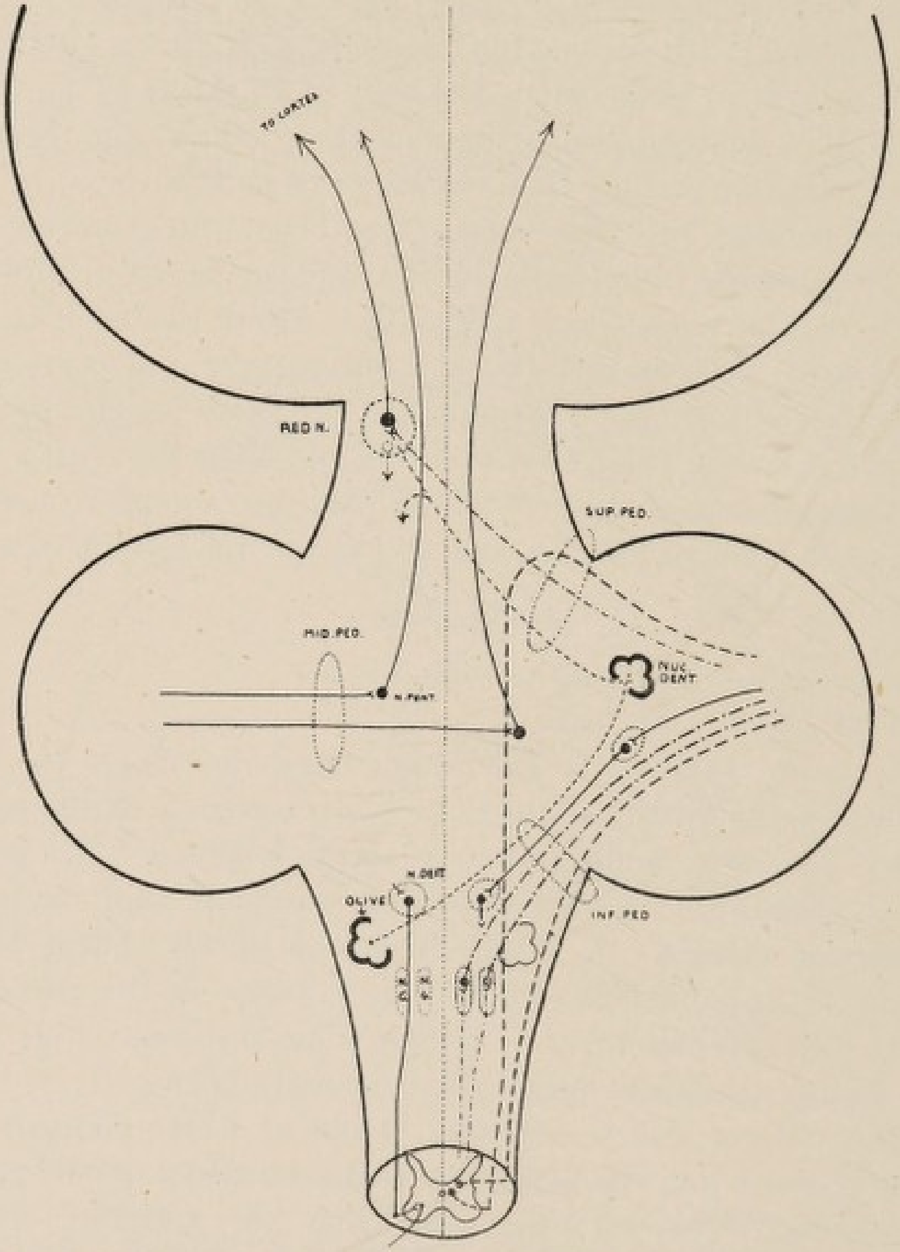


FIG. 89.—Connections of the Cerebellum with the Cerebro-spinal Axis (for explanation, see text).

The cerebellum thus constitutes the central part of one of the great nervous arcs, the ingoing fibres terminating in the cortex which sends fibres to the basal ganglia, which in turn send out the outgoing fibres.

Functions

Removal of the cerebellum deprives the animal, for a time at least, of the power of balancing itself. This may be easily demonstrated in the pigeon (fig. 96, p. 185). But in some cases, when slowly progressing disease has destroyed the organ, no loss of equilibration has appeared, and in other cases the cerebellum has been congenitally almost absent, and yet the individual has not shown any sign of want of power of maintaining his balance. Evidently, therefore, some other part of the brain can compensate for its absence.

The manner in which the cerebellum acts has been chiefly elucidated by removing parts of the organ and keeping the animals under observation for prolonged periods. If one side of the cerebellum be removed the first symptoms are (1) a tonic contraction of the muscles of the limbs of the same side by which the fore limbs may be powerfully extended, and an arching of the body with the convexity towards the side of the lesion, while the animal may be driven round its long axis to the opposite side. (2) These irritative symptoms soon pass off, and the animal then manifests inadequacy or weakness in the limbs of the affected side, so that it droops to that side, and, if a quadruped, may circle to that side. (3) After some weeks these symptoms disappear, and the loss of one side of the cerebellum is apparently completely compensated for.

When in the dog compensation has been established, destruction of the cerebral cortex of the opposite side leads to a reappearance of the muscular inadequacy.

Electrical stimulation of the cerebellum has yielded results somewhat difficult of interpretation, but the most recent investigations seem to show that stimulation of the cortex with currents strong enough to produce movements when applied to the discharging part of the cerebral cortex (see p. 209) do not produce manifest effects, but that comparatively weak currents applied to the basal ganglia do produce movements, the most manifest of which are the conjugate movements of the eyes, and the eyes and head to the side stimulated.

It has been further found that powerful stimulation may also cause flexion of the elbow of the same side and entension of the opposite elbow with entension of the trunk and lower limbs. This may be associated with the maintenance of the body in the erect position and the alternate movements of the limbs in the act of progression.

Taking into consideration the fact that lesions of the posterior nerve roots cause loss of muscular co-ordination, while destruction of the ascending cerebellar tracts produces decrease of muscular tone on the same side, it may be concluded that both the kinæsthetic mechanism, which plays so important a part in maintaining the balance of the body, and the labyrinthine mechanism, have an important central station in the cerebellum.

It would thus appear that the cerebellum is to be regarded as a *mechanism supplementary to the great cerebro-spinal mechanism, and that it has for its purpose more especially the muscular co-ordination and adjustment required in maintaining the balance.* This it may do in one or both of two ways—

1. By receiving impulses from without, and sending impulses downwards to act upon the spinal mechanism.

2. By receiving impulses, and sending impulses upwards to the cerebrum to modify its action. Channel for such impulses exists (1) in the fibres of the pons which cross the middle line to connect with cells from which fibres pass upwards to the occipital and frontal lobes of the cerebrum (fig. 41, p. 88) and (2) in the superior peduncles.

To maintain the constant muscular adjustments involved in balancing the body an **arrangement whereby any disturbance of the equilibrium can produce an appropriate reaction** is required.

The ingoing impulses which are more especially of service in this way are derived from (1) the *kinæsthetic mechanism* (see p. 170); (2) the *tactile mechanism* from the soles of the feet; (3) the *eye*; and (4) the *labyrinthine mechanism* (p. 152).

When the information as to the relationship of the animal with its surroundings derived from these various sources is not concordant—*e.g.* when the semicircular canals indicate movement and the eyes an absence of movement—balancing becomes difficult. This may be readily demonstrated by setting a poker vertically on the floor, holding it in the hand, placing the forehead on the top, walking rapidly three times round it, then standing up and trying to walk out of the room. The sudden stoppage of the rotatory movement causes a disturbance in the semicircular canals giving a sense of rotation in the opposite direction, while the eyes show that no rotation is taking place. The feeling of *giddiness* is, however, not the cause of the loss of balancing, but a mere accompaniment. (*Practical Physiology.*)

E. THE CRURA CEREBRI AND CORPORA QUADRIGEMINA

Above the pons Varolii, the two halves of the medulla diverge from one another and form the peduncles of the cerebrum (fig. 90, *CC.*, *P.*), while posteriorly the two superior peduncles of the cerebellum come together (*S.C.P.*). Above these, two swellings develop on each side—the anterior and posterior corpora quadrigemina (fig. 83, p. 168).

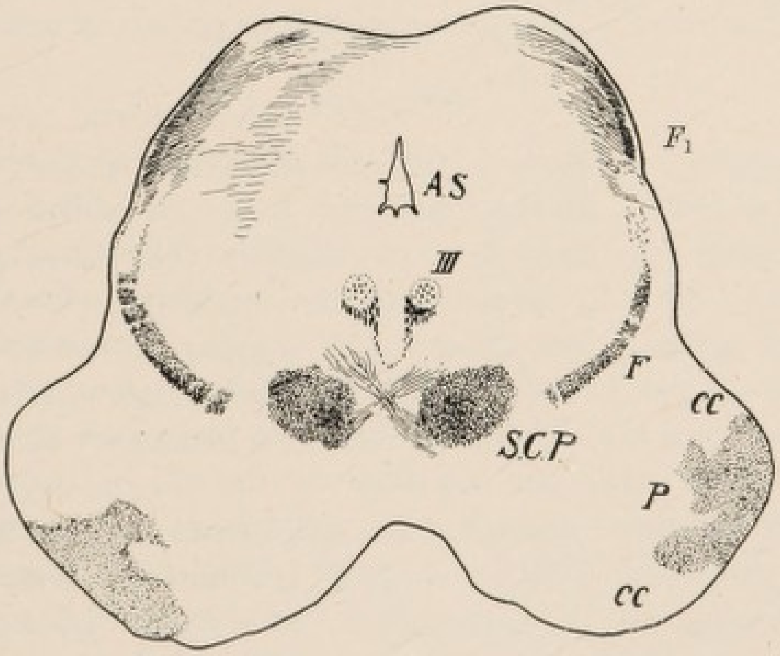


FIG. 90.—Cross Section through Anterior Corpora Quadrigemina and Cerebral Peduncles. *A.S.*, aqueduct of Sylvius; *III.*, nucleus of third nerve; *S.C.P.*, superior cerebellar peduncles; *F.*, mesial fillet; F_1, lateral fillet; *P.*, pyramidal tract; *CC.*, cerebello-cerebral fibres (Human). (*After* BRUCE.)

The *crusta*, or anterior parts of each peduncle of the cerebrum, is composed, in its central part, of the pyramidal fibres passing down from the cerebrum to the spinal cord (*P.*), and, on each side, of the cerebello-cerebral fibres passing upwards from the pons (*CC.*). The posterior part, or *tegmentum*, contains—1*st.* The fillet fibres going partly to the corpora quadrigemina, partly onwards to the thalamus opticus (*F.*); 2*nd.* The nuclei of the 3rd and 4th cranial nerves; 3*rd.* The fibres of the superior peduncles of the cerebellum which cross the middle line (*S.C.P.*); and 4*th.* The red nuclei in which most of these fibres end.

The functions of this segment of the brain are chiefly conducting, but the anterior corpora quadrigemina form the shunting station between the incoming fibres of the optic tract and the oculo-motor mechanism (see p. 141).

F. THE CEREBRUM

Structure

Each crus or peduncle terminates in its half of the cerebrum (fig. 76, p. 164). As the fibres pass from peduncle to cerebrum and *vice versâ* they come into relationship with three masses of grey matter lying in the midst of the cerebrum. These are the *thalamus opticus*, into which the ingoing fibres enter; the *lenticular nucleus*, between which and the thalamus the outgoing fibres run; and the *caudate* nucleus, the main part of which lies in front of the other two (fig. 91).

The fibres, above these nuclei, spread out to form the *corona radiata* and enter a crust of grey matter, the *cortex cerebri*, which covers over the cerebrum, and which in the higher animals is raised into a number of folds or convolutions marked off from one another by fissures and sulci.

In the lower vertebrata the differentiation of the cortex from the basal ganglia is incomplete, and it is only in the higher mammals, monkeys and man, that the cortex reaches its full physiological importance.

The structure of the cortex cerebri as regards the arrangement of cells and fibres is somewhat complex, and varies greatly at different parts, but the general type is as follows (see fig. 95):—

A. **Cells** (fig. 95 *A*).—1. Plexiform layer. At the surface of the cortex is a thin layer of small irregular cells.

2. Layer of small pyramidal cells.

3. Layer of medium pyramidal cells.

4. External layer of large pyramidal cells.

Some writers class layers 2, 3, and 4 as one.

5. Layer of stellate cells. This is a thin but well-defined layer of minute polymorphic cells lying rather more than halfway down the thickness of the cortex.

6. Internal layers of large pyramidal cells.

7. Layer of spindle-shaped cells.

B. **Fibres.**—The relationship of the medullated fibres to these layers is shown in fig. 95 *B*).

1. On the surface is a fibreless layer.

2. Under this is a thin layer of more or less horizontal fibres, the zonal layer.

3. Under this is a thicker irregular layer of fibres, the supraradiary layer.

4. Next comes a band of fibres often so well developed as to make a white streak in the grey matter. This is the line of Baillarger. In the regions of the calcarine fissure in apes and in man, when it is specially marked, it is known as the layer of Gennari.

5. Radiary zone. A thick layer of white fibres chiefly passing to and from the subjacent white substance.

It should be remembered that the layer of stellate cells lie just outside Baillarger's layer of fibres.

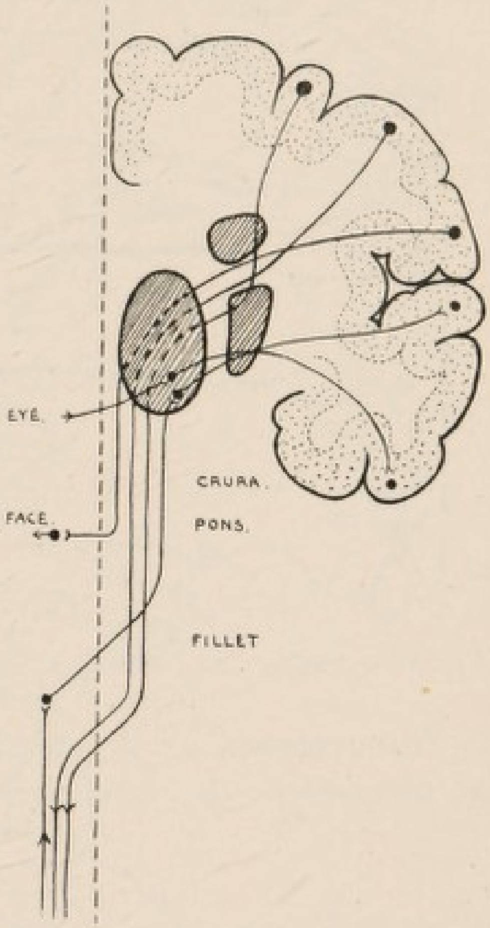


Fig. 91.—Diagrammatic Horizontal Section through Base of Cerebral Hemisphere, showing (1) the outgoing fibres for the leg, arm, and face springing from the cortex of the rolandic areas, passing through the internal capsule between the thalamus and the lenticular nucleus. The face fibres cross in the pons, the leg and arm fibres in the medulla. (2) The incoming fibres (fillet, eye) form their stations in the thalamus, and then pass on to the cortex

Fig. 92 shows the way in which the dendrites of these cells form a dense plexus at the surface and the way in which incoming fibres (1) become associated with them.

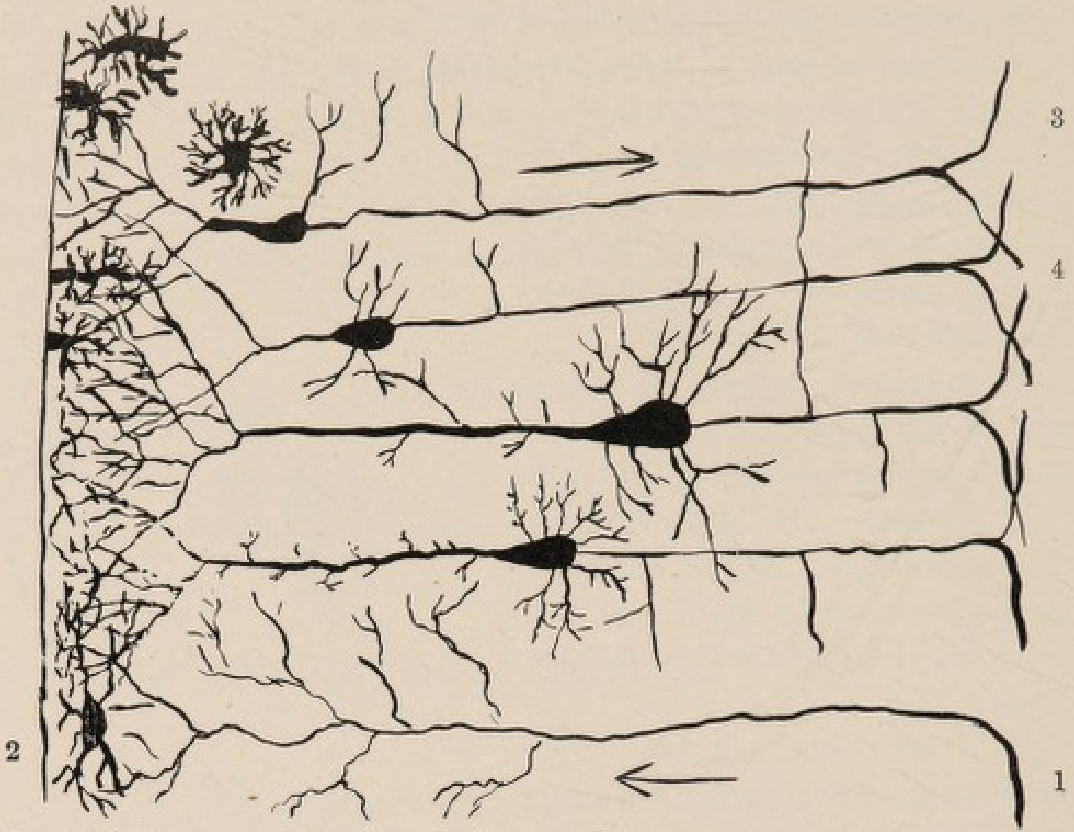


Fig. 92.—Diagram of the arrangement of cells in a typical part of the cerebral cortex. (*After* Rámon y Cajal.)

This arrangement is considerably modified in certain regions of the cortex, the large pyramidal cells being best developed

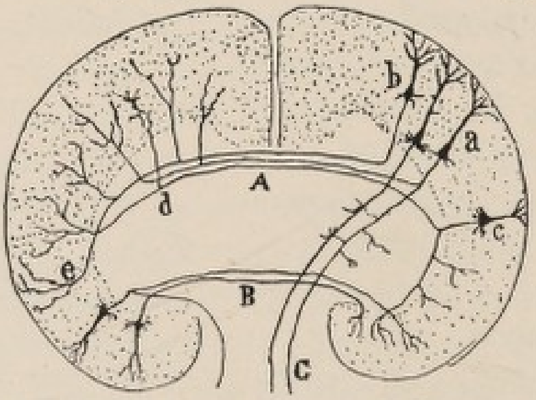


Fig. 93.—Diagram of collateral connections of different parts of the cerebral cortex. *a*, *b*, *c*, pyramidal cells of the cortex, all connected by collateral branches with other parts of the cortex in the same and in the opposite hemisphere. *a* give off the pyramidal fibres to the cord. (*After* Rámon y Cajal.)

in those parts from which the great mass of fibres pass down to the spinal cord, and being known as the cells of Betz.

From the various fibres, collaterals come off which connect different parts of the cortex of the same side, and which also connect the cortex of one side with that of the other, and with the basal ganglia (fig. 93).

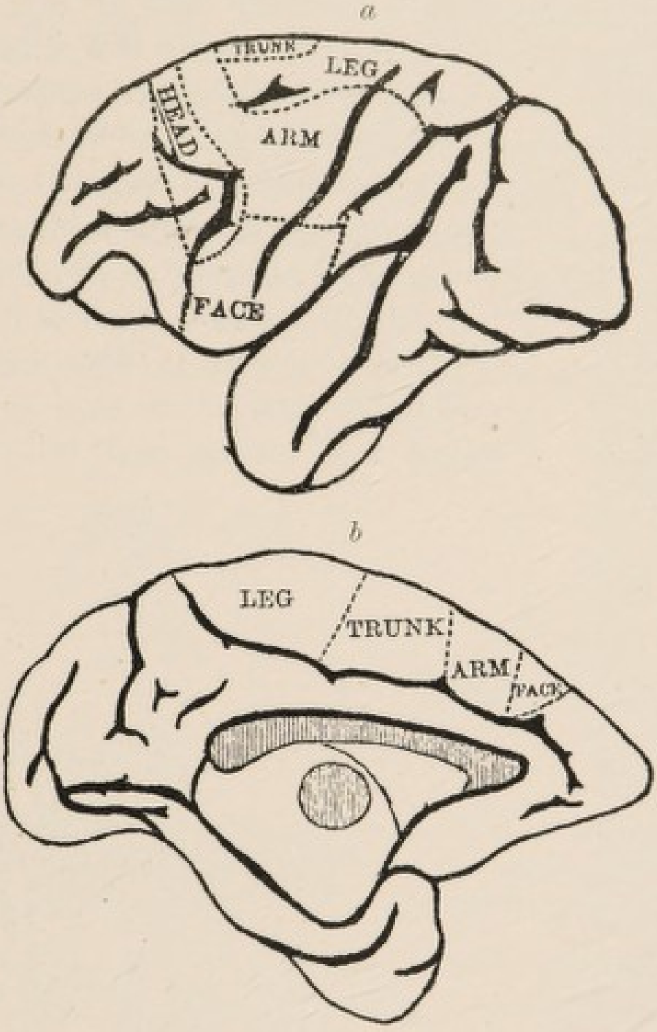


Fig. 94.—(*a*) Surface of the left Cerebral Hemisphere of a Monkey to show the situations of some of the Discharging Mechanisms (front to left); (*b*) Mesial Surface of the same Hemisphere (front to right).

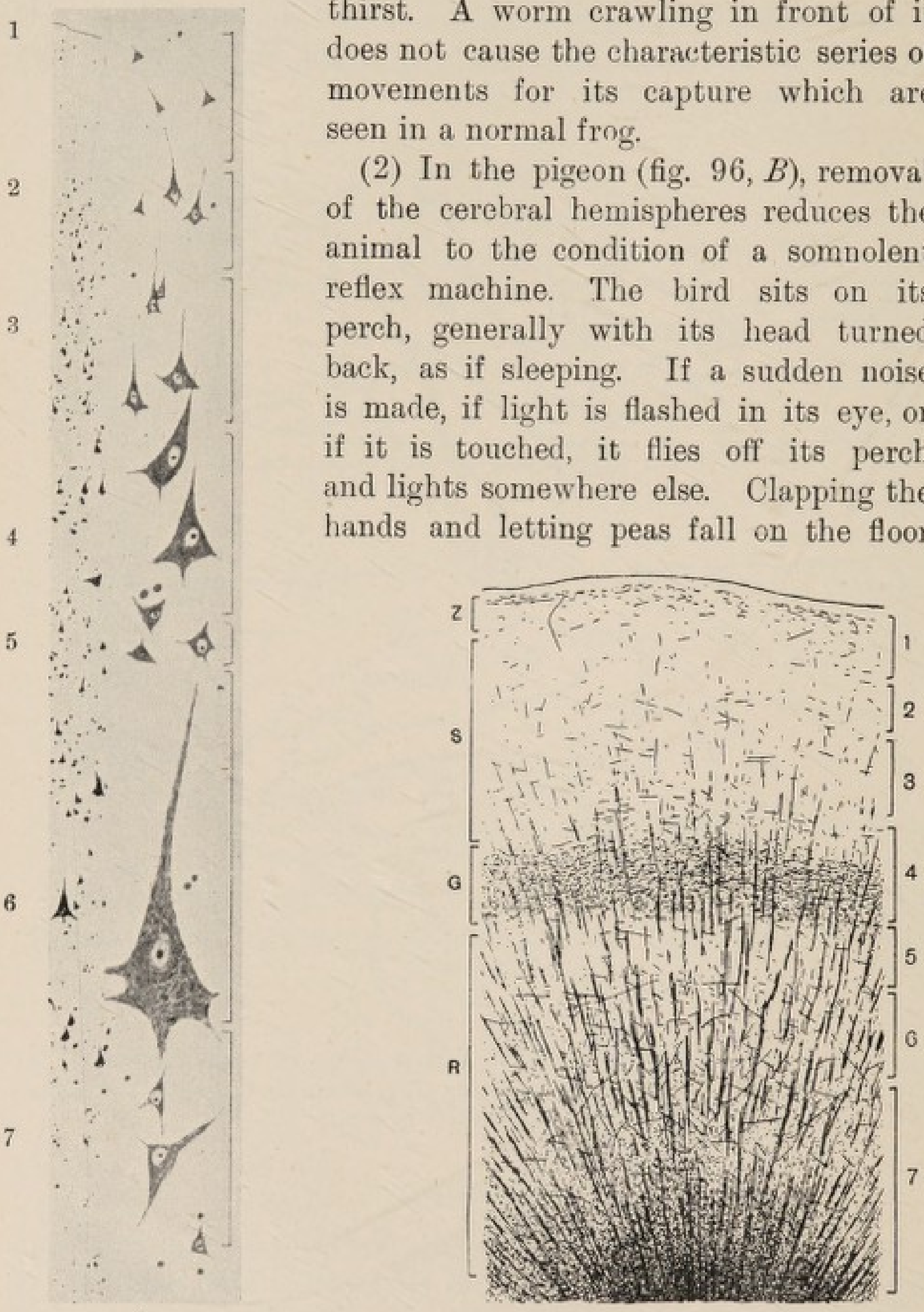
Physiology

1. **General Considerations.**—The functions of the cerebrum may be best understood by first contrasting the condition of animals with, and of animals without, this part of the brain.

(1) In the frog the cerebral lobes may easily be removed. The animal sits in its characteristic attitude. When touched it jumps, when thrown into water it swims. It is a perfect reflex machine, with the power of balancing itself unimpaired. But it differs from a normal frog in moving only when

directly stimulated, and in showing no signs of hunger or of thirst. A worm crawling in front of it does not cause the characteristic series of movements for its capture which are seen in a normal frog.

(2) In the pigeon (fig. 96, *B*), removal of the cerebral hemispheres reduces the animal to the condition of a somnolent reflex machine. The bird sits on its perch, generally with its head turned back, as if sleeping. If a sudden noise is made, if light is flashed in its eye, or if it is touched, it flies off its perch and lights somewhere else. Clapping the hands and letting peas fall on the floor



A *B*

Fig. 95.—*A*, Section of cerebral cortex in the pre-Rolandic lobe—a motor area; on the left, under a low power to show the distribution of the cells; on the right, a few of the cells from each zone more highly magnified. (For description of zones, see text.) *B*, Section through Cerebral Cortex in the region of the calcarine fissure (visual area), stained to show the arrangement of the fibres (Human). (For description of zones, see text.) (Campbell.)

both produce a start, but the bird makes no endeavour to secure the peas, as it would do in the normal state.

(3) In the dog, by a succession of operations, Goltz removed the greater part of the cerebral cortex without causing paralysis of the muscles. The animal became dull and listless, and did not take food unless it was given to it. It showed no sign of recognising persons or other dogs, and did not respond in the usual way when petted or spoken to. But it snapped when pinched, shut its eyes and turned its head away from a bright light, and shook its ears at a loud sound. It did not sit still, but walked constantly to and fro when awake. It slept very heavily. In fact all the responses of the animal might be classed as reflex responses to immediate excitation.

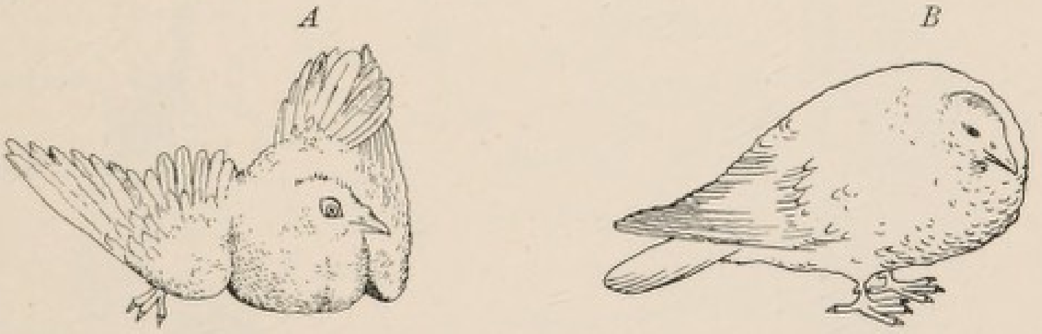


Fig. 96.—*A*, pigeon with the cerebellum destroyed to show struggle to maintain the balance; *B*, pigeon with cerebrum removed to show balance maintained, but the animal reduced to a somnolent condition.

(4) In monkeys, removal of the cerebral cortex leads to such loss of the so-called voluntary movements that all other symptoms are masked.

After section through the crura cerebri, so as to remove the influence of the cerebrum, a condition of increased tonic contraction of the muscles occurs known as **decerebration rigidity.** This appears to be due to the uncontrolled action of the kinæsthetic and labyrinthine mechanisms acting through the cerebellum. It is often well seen in old cases of apoplexy where a hæmorrhage has cut the fibres coming down from the cerebrum.

By destroying the cerebrum the animal is deprived of a most important mechanism for the co-ordination of incoming impressions from the peripherally-placed receptors with the combinations of muscular movements by which appropriate reactions are brought about. With the cerebrum intact this co-ordination is far more complete.

The reactions are, in part at least, determined by—

(1) The previous training and education of the brain. For, just as in the spinal cord channels of action are formed, so in the cerebrum, if a given reaction once follows a given stimulus, it will tend to follow it again. (*a*) This training is in part *hereditary*. Each individual of a race is born with well-established lines of action in the process of development, and throughout life these inherited channels play an important part in determining the results of stimulation. (*b*) But it is also largely *acquired* by the individual, since the reception of each stimulus and the performance of a resulting action, however this be determined, tends to lay down a path which will again be followed.

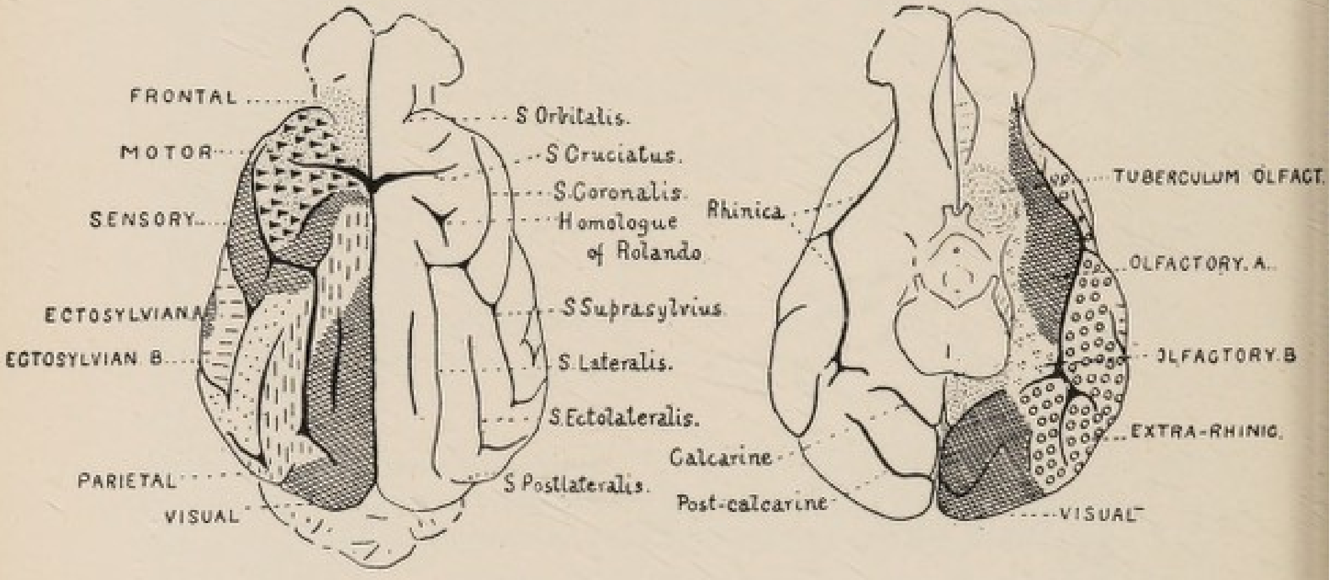


Fig. 97.—Superior and inferior aspects of the brain of the dog to show the various sulci and the distribution of the chief receiving and reacting mechanisms.

(2) Not only will the previous training of the brain thus act as the directive force in the response to stimuli, but the *nutrition of the brain* also plays an important part. The action of a brain when well nourished and freely supplied with pure blood is often very different to that of the same brain when badly nourished or imperfectly supplied with healthy blood. Since the education of the brain really consists in developing proper responses to various stimuli, the importance of the brain

being in a healthy and well-nourished condition during the training is manifest.

The power of differentiating various stimuli and their reactions is correlated with the development of the cerebrum and becomes more perfect as the animal scale is ascended. The complexity

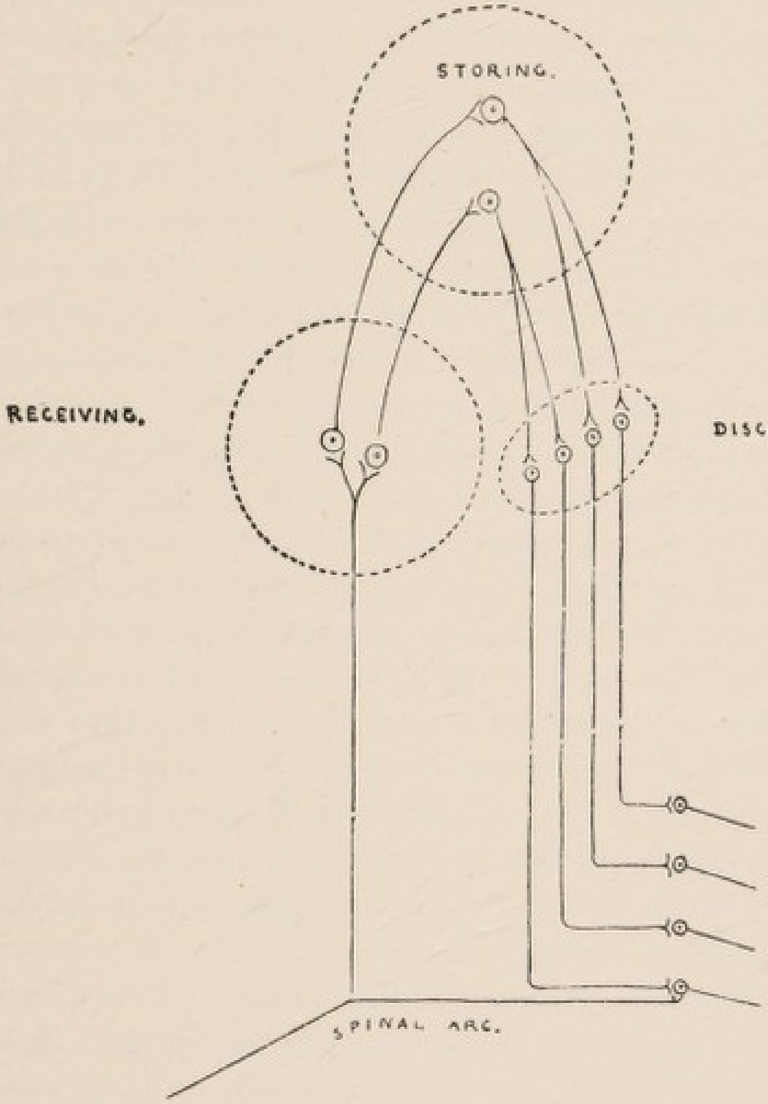


FIG. 98.—Diagram to illustrate different *possible* channels of cerebral response to stimulation, and to show how, through reflex action of the lower arcs, the action of the higher arcs may be simulated.

of the cerebral action in the higher animals has its basis in the greater number of distinct impressions which have been received and reacted to. Each separate stimulus leaves its mark upon the brain, or, as we may say, is *stored* in the brain, and each subsequent similar stimulus is sent into these channels, or is *associated* with the past reactions, and thus the present *response* is determined. For appropriate reaction the whole mechanism must be normal—a very small injury to any part may not only entirely alter the reactions or conduct of the animal but may also modify its mental condition.

Cerebral action frequently goes on without consciousness being implicated; but so far as we know, consciousness without accompanying cerebral action is unknown, and there is evidence that it is only when the actions of the various parts of the cerebrum are co-ordinated that consciousness is possible. In cases of Jacksonian epilepsy in man, as a result of a small centre of irritation on the surface of the brain, a violently excessive action of the cerebral neurons starts at the part irritated and passes to involve more and more of the brain. In such fits it is found that at first the patient's consciousness is not lost, but that, when a sufficient area of brain is involved in this excessive and inco-ordinated action, consciousness disappears.

The study of the action of drugs which abolish consciousness —*e.g.* chloroform and morphine—on the dendrites of brain cells suggests a physical explanation of the loss of consciousness. It is found that these drugs cause a general extension of the gemmules of all the dendrites; and, if we imagine that the co-ordinated action of any part of the brain is secured by definite dendrites of one set of neurons coming into relationship with definite dendrites of another set of neurons by their gemmules so as to establish definite paths, the want of co-ordinate relationship established by the general expansion would explain the disappearance of the definite sensations which constitute consciousness.

It is manifest that the range of consciousness must necessarily be wider where the stored impressions are most abundant, and where the present stimulus most readily calls into action these previous lines of cerebral activity. The storage of impressions is the basis of MEMORY. The power of associating these stored impressions with the present stimulus is the basis of RECOLLECTION. It is the implication of consciousness in this part of brain action which is the basis of mental activity.

How far the mental action is a mere accompaniment of the physical changes, and how far it can react upon them, is a question which cannot be discussed here. But the study of the insane seems to point to the conclusion that the individual may do certain things and have certain ideas as concomitants of faulty brain action, rather than that his actions are a result of the modified ideas.

2. **Time of Cerebral Action.**—The cerebral mechanism takes a very appreciable time to act, and the time varies with the complexity of the action and with the condition of the nervous apparatus.

Of the time between the presentation of a flash of light to the eye or a touch to the skin and a signal made when it is perceived by the person acted upon, part is occupied by the passage of the nerve impulses up and down the nerves and in the latent period of muscle action, but a varying period remains, representing the time occupied in the cerebral action. (*Practical Physiology.*)

Prolonged action of the nerve centres soon leads to a prolongation of the reaction time, and the same thing is produced by the action of alcohol, chloroform, and other poisons.

3. **Fatigue of Cerebral Mechanism.**—This naturally leads to the consideration of **fatigue** of the cerebral mechanism. The way in which, as a result of poisons, the definite co-relationship of certain sets of neurons with certain other sets is probably abolished by the generalised expansion of the gemmules of the dendrites has been already dealt with. In all probability the same thing occurs in fatigue, and by interrupting the definite chain of action allows rest and recovery to supervene. But continued action may further lead to well-marked changes in the cell protoplasm of the neurons. The Nissl's granules diminish and the nucleus shrivels and becomes poorer in chromatin.

In all reflex action, whether spinal or cerebral, it is the central part of the mechanism which first becomes fatigued. If, by reflex excitation of the central nervous system of a frog, muscular movements are caused for some time, the stimulation ultimately fails to act; but, if the nerves going to the muscles are stimulated, the muscles at once respond, showing that the central mechanism has given out before the peripheral structures.

Fatigue of the central nervous system is manifest both upon the receiving and reacting mechanism; upon the receiving, on the physical side by prolongation of the reaction period, and on the metaphysical side by diminished power of attention. Upon the reacting side it is shown by lessened power of muscular contraction. (See also p. 53.)

4. **Sleep.**—Fatigue of the cerebral mechanism is closely connected with **sleep.** As the result of fatigue, external stimuli produce less and less effect, and thus the changes which are the physical basis of consciousness become less and less marked. At the same time, by artificial means stimuli are usually excluded as far as possible. Absence of light, of noise, and of tactile and thermal stimuli all conduce to sleep. Consciousness fades away, and, as the cerebral activity diminishes, the arterioles throughout the body dilate, and the arterial blood pressure falls, and thus less blood is sent to the brain, and the organ becomes more bloodless. The eyelids close, the eyeballs turn upwards, the pupils contract, and the voluntary muscles relax.

The depth of sleep may be measured by the strength of the stimuli required to overcome it. In man it is usually deepest at about the end of an hour, and that it then rapidly becomes more and more shallow, until as the result of some stimulus, or when the brain has regained its normal condition, it terminates. In the later hours of sleep the consciousness may be temporarily aroused without the other conditions of sleep disappearing, and as a result of this **dreams** may ensue. Or, on the other hand, without consciousness being necessarily restored, stimuli may lead to muscular responses of a perfectly definite and purposive character, and to such phenomena as **sleep-walking**.

Hypnosis is a condition in some respects allied to sleep. It may be produced in many individuals by powerfully arresting the attention, and is probably due to a removal of the influence of the higher centres over the lower. When the condition is produced, the respirations and pulse become quickened, the pupils expand, and the sensitiveness of the neuro-muscular mechanism is so increased that merely stroking a group of muscles may throw them into firm contraction. The individual becomes a reflex machine even as regards the cerebral arcs, and each stimulus is followed by an immediate reaction. The power of suggestion is exaggerated. If a hypnotised person is told that he sees anything he acts at once as if he did actually see it.

5. **Localisation of Functions.**—The question must next be considered whether special parts of the brain are more especially connected with its three great functions—

A. The reception of stimuli.
B. The storing of effects, and the associating of present stimuli with these stored impressions.
C. The production of the resulting actions.

A. **Reception of Stimuli.**—In investigating the existence of special mechanisms for this purpose, several methods of inquiry are available.

1*st*. By removing or stimulating parts of the brain in the lower animals and studying the results.

2*nd*. By observations during life on the sensations or absence of sensations in patients suffering from disease of the brain, and the determination of the seat of the lesion after death.

3*rd*. By the histological study of the different parts of the cortex cerebri.

4*th*. By the embryological study of the development of the myeline sheaths of the various bundles of nerve fibres.

1*st*. Sensations are the usual accompaniment of the activity of the receiving mechanism. But in the lower animals it is not possible to have a direct expression of whether sensations are experienced or not, and, therefore, in determining whether **removal** of any part of the brain has taken away the power of receiving impressions, we have to depend on the absence of the usual modes of response to any given stimulus. But the absence of the usual response may mean, not that the receiving mechanism is destroyed, but either that the reacting mechanism is out of action or that the channels of conduction have been interfered with. (See fig. 98.)

Thus, if light be flashed in the eye of a monkey, it responds by glancing towards the source of illumination; and if these movements are absent this may be due (1) to loss of the receiving mechanism, to (2) loss of the mechanism causing the movements, or (3) to interruption of the channels between them.

Again, it is quite possible that, after removing the receiving mechanism in the cerebrum, external stimuli may lead to the usual response by acting through lower reflex arcs (fig. 98). If, for instance, we suppose the receiving part of the cerebrum connected with the reception of tactile impressions entirely destroyed, scratching the sole of the foot may still cause the leg to be drawn up, just as if a sensation had been experienced. Here although the upper arc is out of action the lower arc still acts.

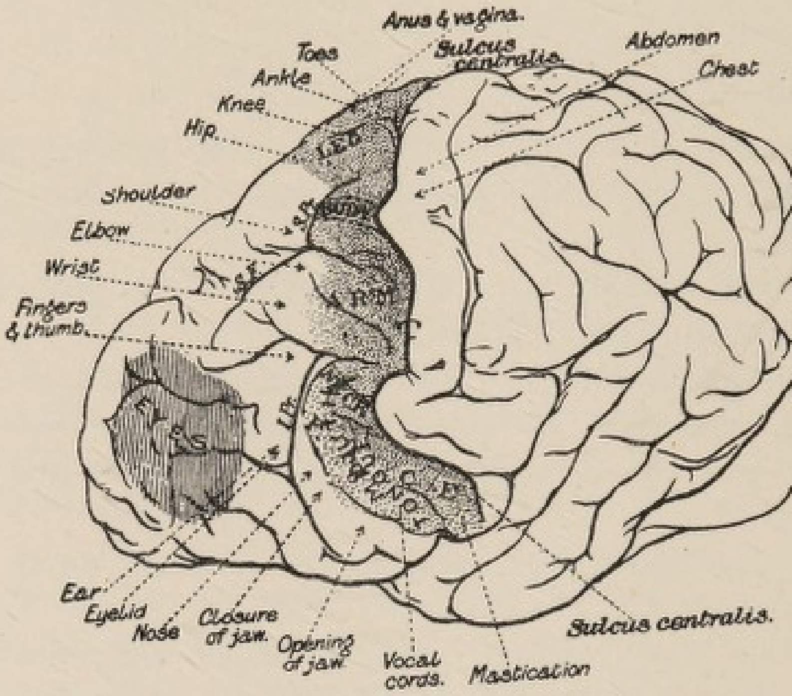


FIG. 99.—Left Hemisphere of Brain of Chimpanzee to show the results of stimulating different parts. The Sulcus Centralis is the fissure of Rolando. (*From* GRÜNBAUM and SHERRINGTON.)

In the lower animals, **stimulation** of a part of the brain, if it be connected with the reception of impressions, may cause the series of movements which naturally follow such an impression. But these movements may also be caused by directly stimulating the reacting mechanism. When, however, removal of a part of the brain causes no loss of power of movement, and yet prevents a stimulus from causing its natural response, it is justifiable to conclude that that part of the brain is connected with reception.

2nd. In man, the chief difficulty of obtaining information is in finding cases where only a limited part of the brain is affected. But such cases have been observed. Tumours of the inner aspect of an occipital lobe, for instance, have been found to be associated with loss of visual sensations without loss of muscular power, and thus the conclusion has been drawn that this part of the occipital lobe is the receiving mechanism for stimuli from the eyes.

3rd. When it has been found possible to assign a definite function to any area of the cortex, the extent and limits of the area may be determined by the extent and distribution of the particular character of the arrangement and structure of the nerve cells.

4th. Flechsig has found that bands of fibres going to certain parts of cortex get their medullary sheaths earlier than others, and that the fibres to each part of the cortex become medullated at a definite date. The areas, the fibres of which first get their sheath, he calls the primary projection areas, and they correspond very closely with the receiving areas determined by other methods (fig. 100 A and B).

Visual Centre (fig. 97).—The way in which the fibres, coming from the two retinæ, are connected with each thalamus opticus and occipital lobe has been already considered, and it has been shown that the optic tract passes into the geniculate bodies on the posterior aspect of the thalamus, and that a strong band of fibres, the optic radiation, extends from these backwards to the occipital lobes (fig. 67, p. 138). In man an extensive lesion of one—say the right—occipital lobe, especially if on the inner aspect round the calcarine fissure, is accompanied by no loss of muscular power but by blindness for all objects in the opposite side of the field of vision—*i.e.* the right side of each retina is blind. The central spot of neither eye is completely blinded because the fibres from the macula lutea only partially decussate at the chiasma.

Stimulation in this region causes movement of the eyes to the opposite side, as if some object were perceived there.

Histologically this area is characterised by a well-defined band of white fibres between the layer of stellate cells and the internal layer of pyramidal cells, the band of Gennari (fig. 95 *G*, p. 184), and by a characteristic arrangement of cells (fig. 101). This arrangement becomes more and more defined as we pass from the simpler mammals with separate vision for the two eyes to the primates with combined vision with the two eyes.

Probably each part of the centre is connected with definite parts of the two retinæ. Certain it is that there is no part of this cortical mechanism connected with the blind spot, and hence this is not perceived in ordinary vision.

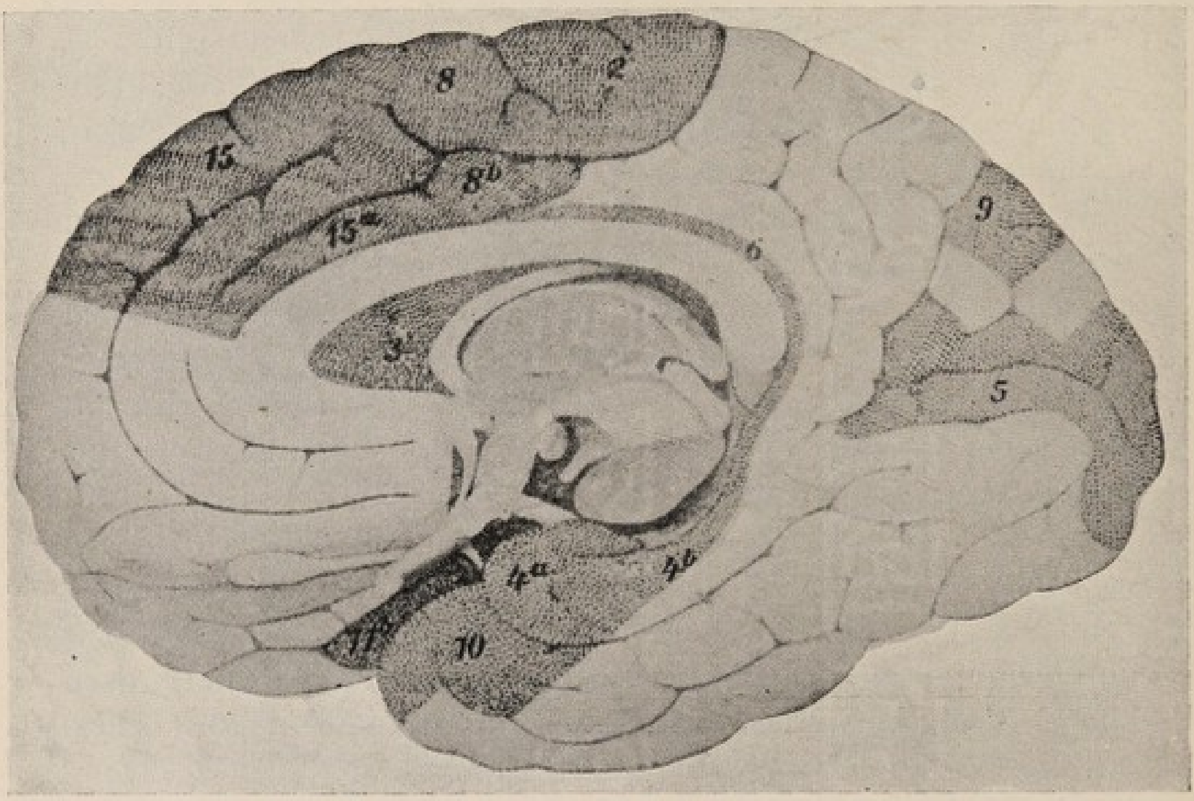


Fig. 100A.—To show Flechsig's Primary Projection Areas on the inner aspect of the Cerebral Cortex (*see* text). (Howell.)

Colour perception seems to be a less fundamental function of the visual apparatus than perception of the degree and direction of illumination, and hence colour perception may be lost in cases of comparatively slight lesions of the occipital lobes without the other functions being impaired. One of the most recently acquired functions of the mechanism is the power of appreciating the significance of the signs used in written language, and it is found that in small and superficial lesions this function may alone be lost.

Flechsig finds that this area is supplied by a band of fibres which very early get their myelin sheath (fig. 100A 5).

Around this area is a zone, lesions in which cause disturbances in vision less profound in character than those produced in the region of the calcarine fissure. This zone has a characteristic cell arrangement, but no line of Gennari. It is very slightly developed in lower mammals, but becomes well marked in the primates and especially in man. It is supplied with associating fibres joining it to the last area, and these fibres become medullated at a comparatively late date.

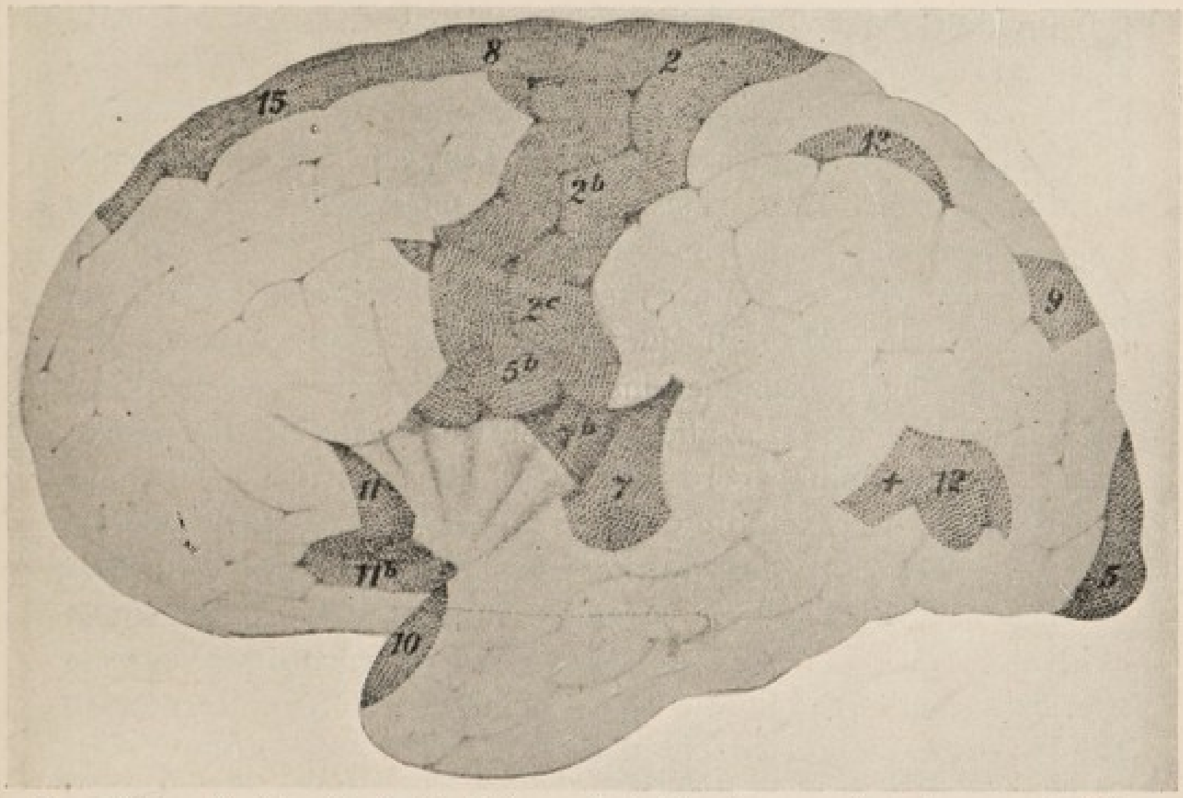


FIG. 100B.—To show Flechsig's Primary Projection Areas on the outer aspect of the Cerebral Cortex (*see* text). (HOWELL.)

It would seem as if this were the region in which the simple visual sensations become associated with the stored passed experiences so as to give rise to the perception of the significance of these sensations. It has been termed the **visuo-psychic area** of the cortex (fig. 101).

The visuo-sensory area is united by a strong band through the middle cerebral peduncle with the cerebellum (see p. 186), and from it a strong band of fibres passes to an area in the frontal region, concerned with the movements of the eyes, and also connected with the cerebellum through the peduncle.

While there is good evidence that a special localised area of the cortex is connected with the reception of stimuli from the eyes, the evidence of the existence of similar areas or centres connected with the other organs of special sense is not so satisfactory.

Auditory Centre. — Ferrier, by removing the superior temporo-sphenoidal lobe in the monkey, produced no motor disturbance, but found evidence of loss of hearing in the opposite ear. When the region was stimulated he found that the monkey pricked up its ears, and looked to the opposite side, and he considered that these observations prove the existence of a special localised mechanism for the reception of stimuli from the ear. Schäfer has removed these convolutions from both sides in the monkey, with aseptic precautions, and kept the animal alive. He failed to find evidence of loss of auditory sensations. Stimulation of the ear in such animals still caused the usual muscular response. But since lower connections exist between the auditory nuclei in the medulla and the centres for muscular movement in the spinal cord (fig. 98), this observation cannot be accepted as excluding the relationship of the superior temporo-sphenoidal convolution to hearing. The existence of such a relationship is strongly supported by pathological evidence. Cases of epilepsy have been recorded, in which the first symptom of the fit was the hearing of sounds, and in which the lesion was found in this lobe.

The limits of this centre are defined by a characteristic cell distribution (fig. 101), and around it is an area with a somewhat different cell arrangement, which is probably the **psycho-auditory** region (fig. 101)—the region in which the changes in the central region connected with the production of simple sensation are associated with the stored passed impressions to enable the nature of the sensation to be comprehended.

The central sensory area is early supplied by medullated fibres (fig. 100B).

Taste and Smell.—The intimate relationship of these senses renders it probable that their centres are closely associated in the cortex.

A study of the development of the olfactory mechanism throughout the mammalian series throws considerable light upon the position of the cortical centre. Many mammals depend very largely upon the sense of smell in their relationship with the external, while others, *e.g.* man, use it less, and the cetacea do not use it at all. In the first group, the osmatic mammals, the olfactory bulbs and tracts are enormously developed (fig. 97).

Each bulb terminates behind in three roots, the inmost sending fibres across to the opposite side (fig. 51, IV.), the others sending fibres to a part of the cortex at the base of brain just outside the olfactory tracts (fig. 51, III.). In man and apes, from the development of the temporo-sphenoidal lobe this region gets carried outwards and is represented by a swelling, the lobus pyriformis, on the inner aspect under the uncus (fig. 101). The cortex in the region indicated in the figure has a peculiar arrangement of cells. The medullated fibres to this area are early developed (fig. 100A, 4*a*).

Ferrier states that removal of the hippocampal convolution, including the lobus pyriformis in monkeys, leads to loss of taste and smell, and that stimulation causes torsion of the nostrils and lips, as if sensations of smell or taste were being experienced.

Touch.—Ferrier thought that removal of the hippocampal convolution caused loss of tactile sense, while Schäfer describes the gyrus fornicatus as the centre for this sense. It has been objected that in removing this lobe the fibres going to the areas on the outside of the cortex are apt to be injured. According to the observations of Mott, when the cortex round the fissure of Rolando—in which the mechanism for causing the various combinations of muscular movements is situated—is removed in the monkey, clips may be attached to the skin on the opposite side of the body without attracting attention, while if they are placed on the same side they are at once removed. He therefore regards the Rolandic area of the brain as connected with the reception of tactile impressions.

This view is strongly supported by the evidence of morphology. The ascending parietal convolution is early supplied by medullated fibres coming from the thalamus (fig. 100B 2), and in it a type of cell distribution similar to that in the other sensory areas exists (fig. 101). Further, in this region

Campbell has described degenerative changes as the result of extensive disease of the posterior nerve roots.

As already indicated, this centre must act as a chart of the surface of the body, stimulation of any definite part of the body leading to changes in the definite part of the centre, and these changes are accompanied by sensations referred to the part stimulated.

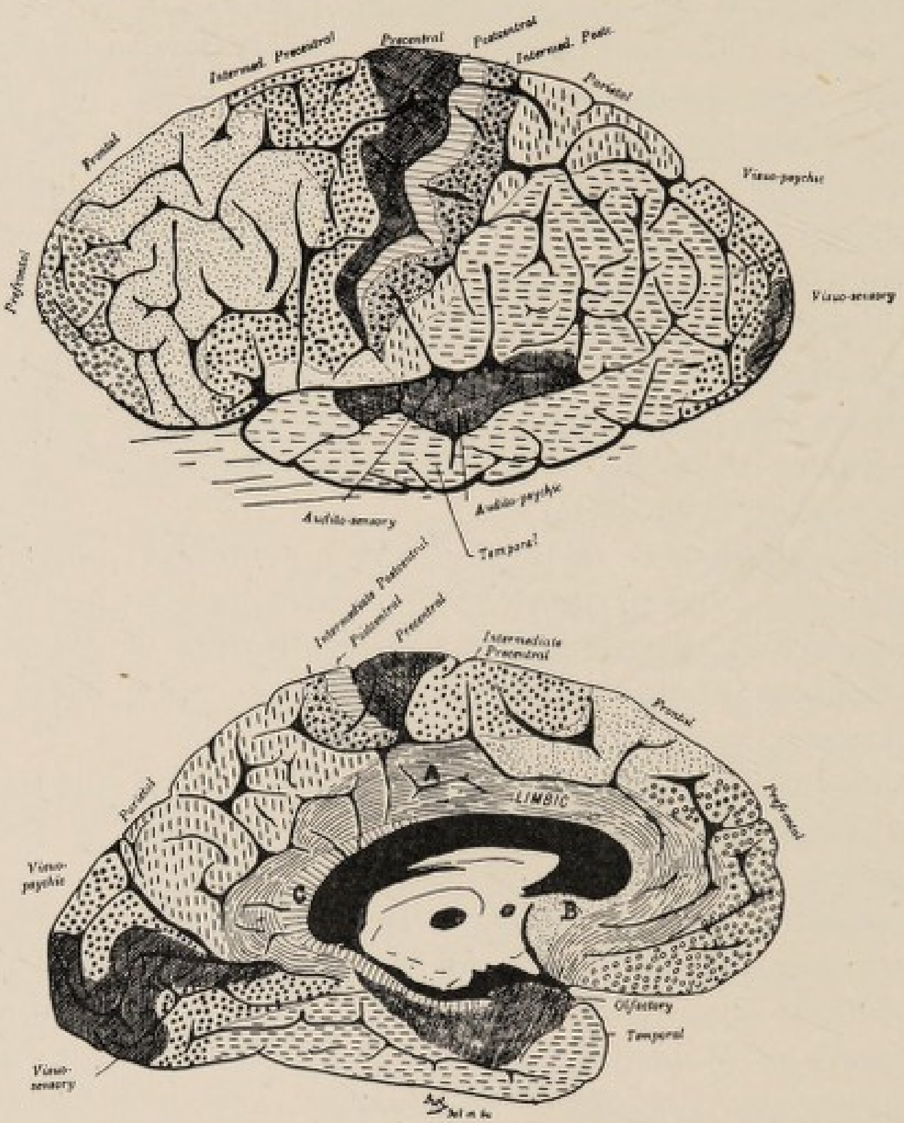


FIG. 101.—To show the mapping out of the Cerebral Cortex on its outer and inner aspects into areas by the character and distribution of the cells and fibres. (CAMPBELL.)

We know nothing of the locality of centres connected with the **thermal** and **muscular** senses.

B. **Storing and Associating Mechanism.**—The existence of a special part or parts of the brain connected with the storing of impressions, so that they may be associated with present sensations, is indicated by the following considerations:—It is this association of present stimuli with past sensations which is the basis of intellectual life, and in man, where apparently the intellectual functions are most highly developed, the frontal and parietal lobes of the brain are much larger than in the lower animals. So far stimulation of these lobes has failed to give indication of resulting sensations or to produce muscular movements. They may be extensively injured without loss of sensation and without paralysis, and hence it has been concluded that the storing and associating functions must be chiefly located in them. Further, in these regions the nerve fibres acquire their medullary sheath at a very late date.

C. **Discharging Mechanism.**—(*a*) The position of the discharging mechanism for cerebral action has been definitely localised, by pathological and experimental observation, in the cerebral convolutions round, or probably chiefly in front of, the fissure of Rolando or sulcus centralis (fig. 99, p. 192). Destructive lesions of this area on one side cause a loss of the so-called voluntary action of groups of muscles on the opposite side of the body. The cerebral arc is stimulated and acts along certain lines—possibly with the accompaniment of changes in consciousness and a sensation of decision as to the line of action to be taken and a desire to accomplish it—but this so-called *volition* is not accompanied by the appropriate muscular action. From the frequent involvement of the so-called volition in these actions, and from the fact that it is the metaphysical changes which figure in our consciousness rather than the physical changes which are their basis, we are accustomed to assume that the movements produced are the result of volition, and to speak of them as voluntary movements, and of the brain mechanism producing them as **voluntary centres.** There is no harm in doing so, if we remember that these centres can and do act without the involvement of consciousness, and, therefore, without volition; and that their action generally implies the previous action of parts of the receiving and associating mechanism of the cerebrum.

But certain lesions may directly stimulate these centres, causing them to act without the previous action of the other cerebral mechanisms. This is seen in Jacksonian epilepsy, where, as the result of a spicule of bone or a thickened bit of membrane, one part of the cortex is from time to time excited, and by its action produces movement of certain groups of muscles.

Experimental observations have fully confirmed and extended the conclusions arrived at from such pathological evidence.

If parts of these convolutions be excised in the monkey, the animal loses the power of voluntary movement of certain groups of muscles, while if they are stimulated by electricity these groups of muscles respond.

These convolutions, just in front of the fissure of Rolando, may be considered as a map of the various muscular combinations throughout the body, the map being mounted so that the lower part represents the face, the middle part the arm, and the upper part the leg. Each large division is filled in so that all the various combinations of muscular movement are represented (figs. 99 and 101). It must be remembered that these centres do not send nerves to single muscles, but act upon groups to produce definite combined movements, through the lower spinal centres.

(*b*) The action of these centres involves not only stimulation of certain muscles, but the inhibition of others. This is very clearly shown as regards the eye movements. In the monkey the resting position of the eyes is straight forward, with the optic axes parallel. If all the nerves to the ocular muscles be cut this position is assumed, and if the position of the eye be passively altered, upon removing the displacing force it springs back to this position. If the III. or IV. nerve of the left side be cut so that the external rectus alone is unparalysed, then, exciting a part of the cortex which causes movements of the two eyes to the opposite side, produces not only a movement of the right eye in that direction, but a movement of the left eye to the right as far as the middle line—the position of rest—showing that the VI. nerve has been inhibited.

Stimulation of the cortex causes flexion more readily than extension, apparently because the inhibitory mechanism for the extensors is better developed than that for the flexors. Sherrington finds that under the influence of strychnine or of tetanus toxin this condition is reversed, and that stimuli which in normal conditions will cause flexion now cause powerful extension, and hence co-ordinated movement is impossible.

(*c*) In these motor areas the lesion must be extensive to cause complete paralysis of any group of muscles. A limited lesion may simply cause a loss of the finer movements. Thus, a monkey with part of the middle portion of the Rolandic areas removed may be able to move its arm and hand, but may be quite unable to pick up objects from the floor of its cage.

(*d*) The limits of these areas may be mapped out by the character and distribution of the cells. The great feature is the presence of very large pyramidal cells, the cells of Betz, in the sixth layer of the cortex (fig. 95). These are confined to the ascending frontal lobes. But in front of this is a region stimulation of which gives rise to movements, and in which the cell arrangement is much the same except that the cells of Betz are absent. Well out in the frontal region is a patch, stimulation of which leads to movements of the eyes, and this region is directly connected by a strong band of fibres with the occipital lobe and with the cerebellum. It is present only in animals which employ binocular vision. It has been suggested that this intermedio-precentral region is specially connected with the finer and more highly co-ordinated muscular movements, such as those of the eyes and of the mouth in speech.

PART II

NUTRITION OF THE TISSUES

SECTION V

FLUIDS BATHING THE TISSUES

BLOOD AND LYMPH

THE **blood** carries the necessary nourishment to the tissues, and receives their waste products. But it is enclosed in a closed system of vessels, and does not come into direct relationship with the cells. Outside the blood vessels, and bathing the cells, is the **lymph** which plays the part of middleman between the blood and the tissues, receiving nourishment from the former for the latter, and passing the waste from the latter into the former.

A. BLOOD

The various physical, chemical, and histological characters of blood must be practically investigated.

I. General Characters

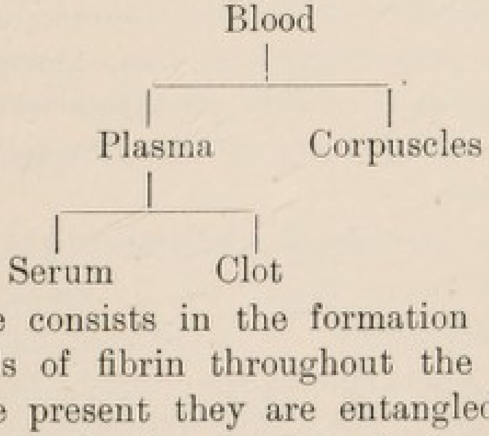
Colour.—Blood changes its colour from purple to cinnabar red on shaking with air, showing that the pigment of the blood may exist in two conditions. **Elements of Blood.**—Microscopic examination shows that blood is composed of a clear fluid (Liquor Sanguinis or Plasma) in which float myriads of small disc-like yellowish-red cells (Erythrocytes), and a smaller number of greyish cells (Leucocytes), and certain more minute grey particles (Blood Platelets). **The Opacity of Blood** is due to the erythrocytes, and when the pigment is dissolved out of them by water, and they are rendered transparent, the blood as a whole becomes transparent and is said to be "laked." The **Specific Gravity** in the horse is about 1060. It may be estimated by finding the specific gravity of a sodium sulphate solution in which a drop of blood neither sinks nor floats. (*Chemical Physiology.*)

Taste and Smell are characteristic, and must be experienced. **Reaction.**—Blood is alkaline, and the degree of alkalinity is very constant in health. It is more alkaline in herbivorous than in carnivorous animals. It is increased during digestion and diminished after muscular exercise. (*Chemical Physiology.*)

The cells of the blood constitute about 33 per cent. of its weight, and the total solids of the blood are about 20 per cent.

Clotting or Coagulation.—In the course of about three minutes the blood of the dog when shed becomes a solid jelly. In the blood of the **horse** the process is much slower and the blood cells may sink before clotting occurs, thus leaving the upper part of the clot colourless. The process starts from the sides of the vessel, and spreads throughout the blood until, when clotting is complete, the vessel may be inverted without the blood falling out. In a short time, drops of clear fluid appear upon the surface of the clot, and in a few hours these have accumulated to a considerable extent, while the clot has contracted and drawn away from the sides of the vessel, until it finally floats in the clear fluid—the **Serum.** If clotting occurs slowly, as it does in the horse, the erythrocytes subside, leaving a layer of clear plasma above, which, when coagulation takes place, forms a "buffy layer" in the upper part of the clot. Clotting is due to changes in the plasma, since this fluid will coagulate in the absence of corpuscles.

The change may be represented thus :—



The change consists in the formation of a series of fine elastic threads of fibrin throughout the plasma, and if red corpuscles are present they are entangled in the meshes of the network and give the clot its red colour.

These threads may be readily collected in mass upon a stick with which the blood is whipped as it is shed. The red fluid blood which is left, consisting of blood cells and serum, is said to be *defibrinated.*

Fibrin is a protein substance. It is slowly dissolved in solutions of neutral salts. It is coagulated by heat, and is precipitated when an excess of a neutral salt is added. It is therefore a globulin.

The plasma before clotting and the serum squeezed out from the clot both contain in the same proportion an albumin (**serum albumin**) and a globulin, or series of globulins which may be classed together as **serum globulin.** But the plasma contains a small quantity—about 0·4 per cent.—of another globulin (**fibrinogen**) which coagulates at a low temperature, and which is absent from serum. It is this which undergoes the change from the soluble form to the insoluble form in coagulation. If, by taking advantage of the fact that it is more easily precipitated by sodium chloride than the other proteins, it is separated from them, it may still be made to clot. (*Chemical Physiology.*)

The substance which usually causes clotting appears to be an enzyme, which is formed by the action of calcium salts or ions on a pro-enzyme set free in the blood. The enzyme may be called **thrombin**, and its precursor **prothrombin**. Oxalates, when added to blood, precipitate the soluble calcium salts, and prevent the formation of thrombin, and thus prevent coagulation. (*Chemical Physiology.*)

It is not yet quite clear what brings about this change of prothrombin into thrombin. Calcium salts or calcium ions and prothrombin may exist together without thrombin being formed, and it has been suggested that another enzyme is required to activate the thrombin—a **thrombokinase** as it has been called. This may be liberated from the cellular elements of the blood and tissues.

The steps in the process of clotting might therefore be represented as follows:—

$$\begin{tikzcd}
 & \text{Thrombokinase} \arrow[dl] \arrow[dr] & \\
\text{Prothrombin} \arrow[dr] & & \text{Calcium Salts} \arrow[dl] \\
 & \text{Thrombin} \arrow[r] & \text{Fibrinogen} \arrow[d] \\
 & & \text{Fibrin}
\end{tikzcd}$$

Many **circumstances influence the rapidity of clotting.** Temperature has a marked effect; a low temperature retarding it, a slight rise of temperature above the normal of the particular animal accelerating it. If a trace of a neutral salt be added to blood, coagulation is accelerated; but, if blood be mixed with strong solutions of salt, coagulation is prevented because the formation of thrombin is checked. Calcium salts have a marked and important action, and if they are precipitated by the addition of oxalate of soda, blood will not clot, apparently because thrombin cannot be formed.

The injection into the blood vessels of a living animal of *commercial peptones*, which chiefly consist of proteoses, or of *hirudin*, an extract *of the head of the medicinal leech*, retards coagulation after the blood is shed. They appear to cause the development in the liver of some body of the nature of an anti-thrombin which checks coagulation, and if the liver be excluded from the circulation this is not developed

Why is it that blood **does not coagulate in the vessels and does coagulate when shed?** Such a general statement is not absolutely correct, for blood may be made to coagulate in the vessels of a living animal in various ways. If inflammation is induced in the course of a vessel, coagulation at once occurs. If the inner coat of a vessel be torn, as by a ligature, or if any roughness occurs on the inner wall of a vessel, coagulation is apt to be set up. Again, various substances injected into the blood stream may cause the blood to coagulate, and thus rapidly kill the animal. Among such substances are extracts of various organs—thymus, testis, and lymph glands—which yield thrombokinase, and snake venom which seems to contain active thrombin. The injection of pure thrombin does not usually cause clotting, because an anti-thrombin is developed.

Nor does blood necessarily coagulate when shed. If it is received into castor oil, or into a vessel anointed with vaseline and filled with paraffin oil, it will remain fluid for a considerable time. Apparently some roughness in the wall of the blood vessel or of the vessel in which the blood is received is required to start the process, acting as a focus from which it can spread outwards.

The **advantages of coagulation** of blood are manifest. By means of it wounds in blood vessels are sealed and hæmorrhage stopped.

Although an important and very prominent change in the blood, clotting is really produced by change in one constituent of the plasma, which is present in very small quantities.

II. Plasma and Serum

These may be considered together, since serum is merely plasma *minus* fibrinogen. As serum is so much easier to procure, it is generally employed for analysis.

Both are straw-coloured fluids, the colour being due to a yellow lipochrome. Sometimes they are clear and transparent, but after a fatty diet they become milky. They are alkaline in reaction, and have a specific gravity of about 1025. They contain about 90 per cent. of water and 10 per cent. of solids. The chief solids are the proteins—**serum albumin** and **serum globulin** (with, in the plasma, the addition of **fibrinogen**). The proportion of the two former proteins to one another varies considerably in different animals, but in the same animal at different times the variations are small. The globulin probably consists of at least two bodies—**euglobulin** precipitated by weak acid, and **pseudoglobulin** not so precipitated. The amount of albumin is generally greater when the body is well nourished. In most animals, they together form about 7 per cent. of the serum.

The other organic constituents of the serum are in much smaller amounts, and may be divided into—

1. *Substances to be used by the tissues.*

Glucose is the most important of these. It occurs only in small amounts—about 1 to 2 per mille. Part of it is free, but part is probably combined in organic combinations such as jecorin. It is probably in larger amount in blood going to muscles than in blood coming from muscles, and this difference seems to be specially well marked when the muscles are active.

Fats occur in very varying amounts, depending upon the amount taken in the food.

2. *Substances given off by the tissues.*

The chief of these is **urea**, which occurs constantly in very small amounts in the serum—about ·05 per cent. We shall afterwards see that it is derived from the liver, and that it is excreted in the urine by the kidneys.

Creatin (p. 40), with **uric acid** (p. 427), and some allied bodies appear to be normally present in traces, and their amount may be increased in diseased conditions.

Of the inorganic constituents of the serum the most abundant is **chloride of sodium**, but in addition **sodium carbonate** and **alkaline sodium phosphate** are also present. Calcium, potassium, and magnesium occur in very small amounts.

III. Cells of Blood.

1. **Leucocytes—White Cells.**—These are much less numerous than the red cells, and their number varies enormously in normal conditions. On an average there is one to every 400 or 500 red cells.

They are soft, extensile, elastic, and sticky, and each contains a nucleus and a well-developed double centrosome. In size they vary considerably, some being much larger than the red cells, some slightly smaller. The character of the nucleus varies greatly, and from this and from variations in the protoplasm, they may be divided into four classes.

1*st*. *Lymphocytes.*—Cells with a clear protoplasm and a more or less circular nucleus. Some are very small, while others are larger. They constitute about 20 to 25 per cent. of the leucocytes (fig. 102, *b* and *c*).

2*nd*. *Polymorpho-nuclear leucocytes*, with a much-distorted and lobated irregular nucleus and a finely granular protoplasm, whose granules stain with acid and neutral stains. These constitute about 70 to 75 per cent. of the leucocytes.

3*rd*. *Eosinophil or oxyphil leucocytes*, with a lobated nucleus like the last, but with large granules in the protoplasm which stain deeply with acid stains. From 1 to 4 per cent. of the leucocytes are of this variety.

4*th*. *Basophil leucocytes*, practically absent from normal blood, with a lobated nucleus and granules in the protoplasm, staining with basic stains.

Myelocytes are large leucocytes with a large circular or oval nucleus and a finely granular protoplasm. They are not normal constituents of the blood, but appear when the activity of the bone marrow is increased in certain pathological conditions.

These various forms have certain properties—(*a*) **Amœboid movement.** They can, under suitable conditions, undergo certain changes in shape, as may be readily seen in the blood of the frog or other cold-blooded animal. The motion may consist simply of the pushing out and withdrawal of one or more processes (pseudopodia), or, after a process is extended, the whole corpuscle may follow it and thus change its place, or the corpuscle may simply retract itself into a spherical mass. As a result of these movements the corpuscles, in certain conditions, creep out of the blood vessels and wander into the tissues (*Diapedesis*).

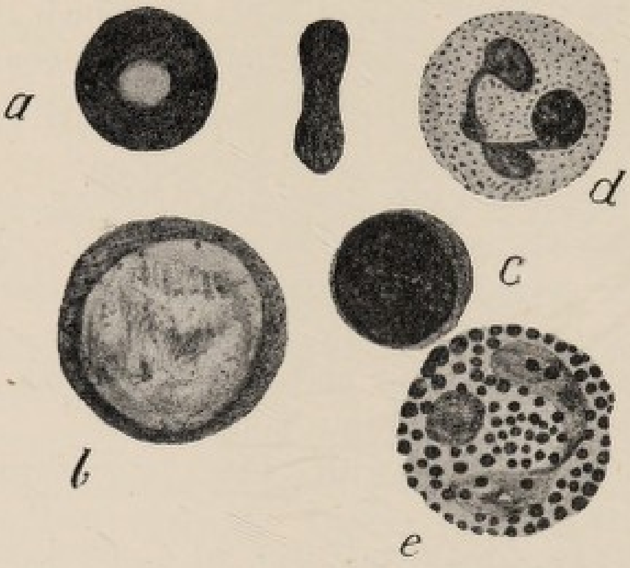


FIG. 102.—Cells of the Blood. *a*, erythrocytes ; *b*, large, and *c*, small lymphocyte ; *d*, polymorpho-nuclear leucocyte ; *e*, eosinophil leucocyte.

(*b*) **Phagocyte action.**—The finely granular leucocytes and the lymphocytes have further the power of taking foreign matter into their interior, and of thus digesting it. By this devouring action, useless and effete tissues are removed and dead micro-organisms in the body are taken up and got rid of. This scavenger action of the leucocytes is of vast importance in pathology.

Chemistry of Leucocytes.—The nucleus is chiefly made up of nuclein, and in the protoplasm a nucleo-protein, along with two globulins and a small amount of an albumin, are found. Along with these protein substances glycogen and a small amount of fat are present, while the chief inorganic constituents are potassium salts.

2. **Blood Platelets.**—These are small circular or oval discoid bodies, about one-third the diameter of a red blood corpuscle. Some observers have stated that they contain a central nucleus. They are very sticky and mass together when blood is shed and adhere to a thread passed through blood or to any rough point in the lining of the heart or vessels. They there form clumps, and from these clumps fibrin threads are seen to shoot out. They thus appear to play an active part in clotting. They are present in the blood of mammals only. Their source is not definitely known, but it has been suggested that they are the extruded nuclei of developing erythrocytes.

3. **Erythrocytes—Red Cells.**—All mammals except the camels have circular, biconcave, discoid erythrocytes, which, when the blood is shed, tend to run together like piles of coins. The camels have elliptical biconvex corpuscles. A nucleus is not present in the fully-developed mammalian erythrocyte. In birds, reptiles, amphibia and fishes, the corpuscles are elliptical biconvex bodies, with a well-marked central nucleus. The **size** of the erythrocytes is fairly constant in each species of animal. In the horse they are on an average 6 to 6·5 micro-millimetres in diameter. The **number** of red cells in health is about 7,000,000 per cubic millimetre in the horse; but in disease it is often decreased.

The number of corpuscles per cubic millimetre is estimated by the Hæmocytometer. This consists of (1) a pipette by which the blood may be diluted to a definite extent with normal salt solution, and (2) a cell of definite depth ruled in squares, each containing above it a definite small volume of blood so that the number of corpuscles in that volume may be counted under the microscope. (*Practical Physiology.*)

The pale yellow **colour** of the individual corpuscles is due to a pigment held in a fine sponge like stroma which seems to form a capsule round the cell. This pigment may be dissolved out by various agents, and the action is termed *Hæmolysis.* It may be brought about in different ways—1*st.*

By placing the erythrocytes in a fluid of lower osmotic equivalent, *i.e.* of lower molecular concentration, than the blood plasma and corpuscles. A solution of 0·9 per cent. of sodium chloride has the same osmotic equivalent as the plasma and preserves the corpuscles unaltered; in more dilute fluid the corpuscles tend to swell up by endosmosis and the pigment is dissolved out. Erythrocytes may therefore be used as a means of determining the osmotic equivalent—the molecular concentration of a fluid. *2nd.* By the action of substances which dissolve some constituent of the stroma, *e.g.* salts of the bile acids (see p. 376), chloroform, ether, etc. *3rd.* By Hæmolysins. The serum of one animal contains a substance, destroyed by heating to 55° C., which is hæmolytic to the blood of animals of other species, *e.g.* the serum of eels' blood contains a powerful hæmolysin for rabbits' erythrocytes, and the serum of the dog a less powerful one. Further, by injecting the blood or the erythrocytes of one species of animal into another species, a hæmolysin is developed which has a specific action on the erythrocytes of the first species.

Chemistry.—The *stroma* of the erythrocytes is made up of a globulin-like substance, in connection with which lecithin and cholesterin occur in considerable quantities. Potassium is the base most abundantly present.

The *pigment* is **Hæmoglobin.** It constitutes no less than 90 per cent. of the solids of the corpuscles. In many animals, when dissolved from the corpuscles, it crystallises very readily. The crystals prepared from the human blood are rhombic plates. When exposed to air they are of a bright red colour, but if placed in the receiver of an air-pump at the ordinary temperature they become of a purplish tint. The same thing occurs if the hæmoglobin is in solution, or if it is still in the corpuscles. The addition of any reducing agent such as ammonium sulphide or a ferrous salt also causes a similar change. This is due to the fact that *hæmoglobin has an affinity for oxygen,* which it takes up from the air, forming a definite compound of a bright red colour in which one molecule of hæmoglobin links with a molecule of oxygen, HbO_2, and is known as **oxyhæmoglobin.**

Hæmoglobin is closely allied to the proteins, but differs from them in containing 0·42 per cent. of iron.

When light from the sun is allowed to pass through solutions of blood pigments, certain parts of the solar spectrum are absorbed, and when the spectrum is examined dark bands—the absorption bands—are seen. In a weak solution of **oxyhæmoglobin** a dark band is seen in the green and another in the yellow part of the spectrum between Frauenhofer's lines D and E, while the violet end of the spectrum is absorbed (fig. 103). These bands may be broadened or narrowed by strengthening or weakening the solution. When the oxygen is taken away and the purple **reduced hæmoglobin** is formed, a single broad band between D and E takes the place of the two bands (fig. 103). (*Chemical Physiology.*)

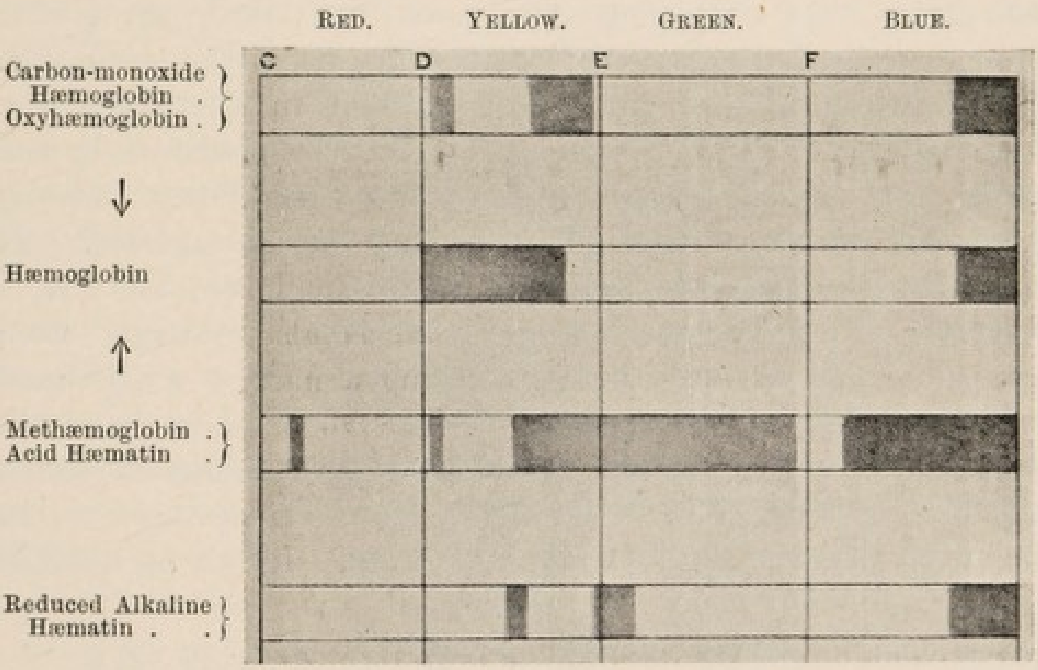
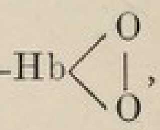
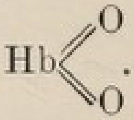


FIG. 103.—Spectra of the more important Blood Pigments and their more important derivatives. (The Spectrum of Acid Hæmatin is not *identical* with that of Methæmoglobin.)

The property of taking oxygen from the air and of again giving it up at a moderate temperature and under a low pressure of oxygen is the great function of the blood pigment in the body. The hæmoglobin plays the part of a middleman between the air and the tissues, taking oxygen from the one and handing it on to the others. (*Chemical Physiology.*)

Hæmoglobin constitutes about 13 or 14 per cent. of the blood, but in various diseases its amount is decreased. The best method of estimating its amount is by Haldane's Hæmoglobinometer. This consists of two tubes of uniform calibre, one filled with a 1 per cent. solution of normal blood saturated with CO, and another in which 20 cmm. of blood to be examined, measured in a pipette, is placed in water, mixed with coal gas to saturate with CO, and then diluted till it has the same tint as the standard tube. The percentage of hæmoglobin in terms of the normal is indicated by the mark on the tube at which the fluid stands. (*Chemical Physiology.*)

Methæmoglobin. — Hæmoglobin forms another compound with oxygen—methæmoglobin. The amount of oxygen is the same, but methæmoglobin must be acted on by the strongest reducing agents before it will part with its oxygen. When, therefore, this pigment is formed in the body, the tissues die from want of oxygen. It may be produced by the action of various substances on oxyhæmoglobin. Among these are ferricyanides, nitrites, and permanganates. It crystallises in the same form as oxyhæmoglobin, but has a chocolate brown colour. Its spectrum is also different from hæmoglobin or oxyhæmoglobin, showing a narrow sharp band in the red part of the spectrum, with two or more bands in other parts according to the reaction of the solution in which it is dissolved (fig. 103). It is of importance since it occurs in the urine in some pathological conditions. In all probability the molecule of oxyhæmoglobin has the formula— $\mathrm{Hb}\left\langle\begin{array}{c}\mathrm{O}\\ |\\ \mathrm{O}\end{array}\right.$, while in methæmoglobin the atoms are arranged  $\mathrm{Hb}\begin{array}{l}\diagup\!\!\!\diagup\mathrm{O}\\ \diagdown\!\!\!\diagdown\mathrm{O}\end{array}$.

Hæmoglobin also combines with certain other gases. Among these is **Carbon monoxide.** For this gas hæmoglobin has a greater affinity than for oxygen, so that when carbon monoxide hæmoglobin is once formed in the body, the blood has little power of taking up oxygen, and the animal dies. This gas is evolved freely in the fumes from burning charcoal, is present in coal gas, and is found in the air of coal mines after explosions. Carbon monoxide hæmoglobin forms crystals like oxyhæmoglobin, and has a bright *pinkish* red colour, without the yellow tinge of oxyhæmoglobin. Since after death it does not give up its carbon monoxide and become changed to purple hæmoglobin, the bodies of those poisoned with the gas maintain the florid colour of life. Its spectrum is very like that of oxyhæmoglobin, the bands being slightly more to the blue end of the spectrum (fig. 103).

It may be at once distinguished by the fact that when gently warmed with ammonium sulphide it does not yield reduced hæmoglobin. (*Chemical Physiology.*)

Decomposition of Hæmoglobin.—Hæmoglobin is a somewhat unstable body, and, in the presence of acids and alkalies, splits up into about 96 per cent. of a colourless protein **globin** belonging to the globulin group, and about 4 per cent. of a substance of a brownish colour called **hæmatin.**

The spectrum and properties of this substance are different in acid and alkaline media. In acid media it has a spectrum closely resembling methæmoglobin, but it can at once be distinguished by the fact that it is not changed by reducing agents. In medicine it is sometimes important to distinguish between these pigments since both may appear in the urine. Hæmatin in alkaline solution can take up and give off oxygen in the same way as hæmoglobin does. Reduced alkaline hæmatin or **hæmochromogen** has a very definite spectrum (fig. 103), and its preparation affords a ready means of detecting old blood stains. Hæmatin contains the iron of the hæmoglobin, and it is this pigmented iron-containing part of the molecule which has the affinity for oxygen. Apparently it is the presence of iron which gives it this property, because, if the iron be removed by means of sulphuric acid, a purple-coloured substance, *iron-free hæmatin*, **hæmatoporphyrin**, is formed, which has no affinity for oxygen. This pigment occurs in the urine in some pathological conditions. (*Chemical Physiology.*)

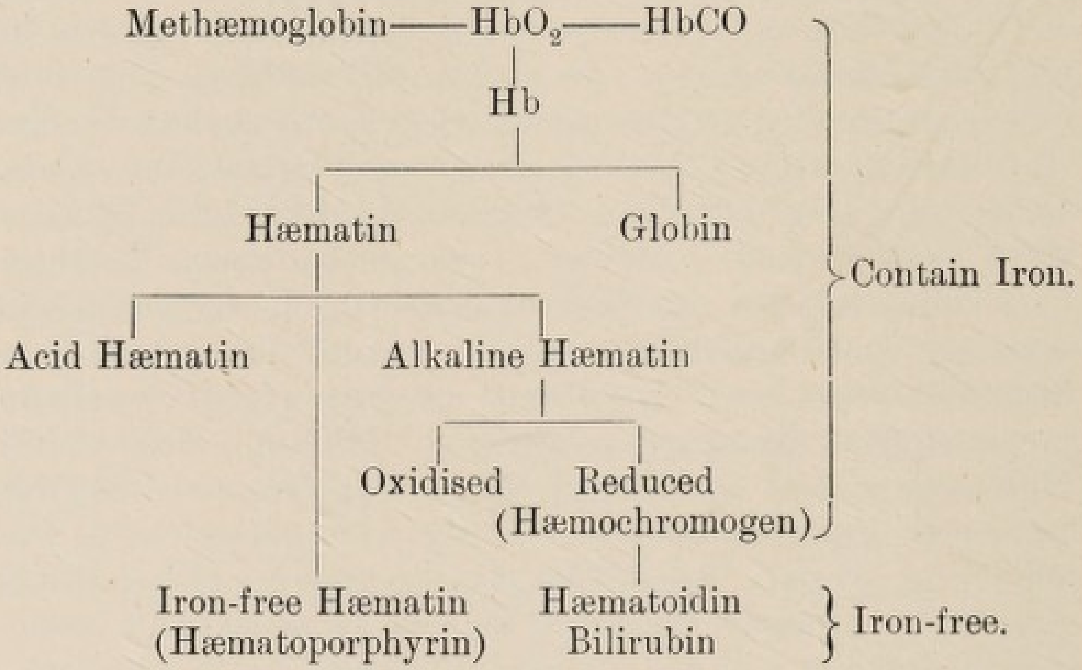
One point of great interest in the chemistry of hæmatin and its derivatives is that they, like the green chlorophyl of plants, yield upon decomposition bodies belonging to the pyrrhol group (see p. 9).

In the liver hæmoglobin is broken down to form **bilirubin** and the other bile pigments. These are iron-free, and, like iron-free hæmatin, do not take up and give off oxygen. But not only is this iron-free pigment formed from hæmoglobin in the liver, but the cells of any part of the body have the faculty of changing hæmoglobin in blood extravasations into a pigment known as **hæmatoidin**, which is really the same as bilirubin.

Hæmin—the hydrochloride of hæmatin—is formed when blood is heated with sodium chloride and glacial acetic acid. It crystallises in small steel-black rhombic crystals, and its formation is sometimes used as a test of blood stains. (*Chemical Physiology.*)

The following table shows the relationship of these pigments to one another:—

RELATIONSHIP OF HB AND ITS DERIVATIVES.



IV. Gases of the Blood

The muscles and other active tissues are constantly consuming oxygen and constantly giving off carbon dioxide. The oxygen must be brought to the tissues by the blood, and the carbon dioxide carried away by the same medium.

Various methods of carrying out the examination of the gases of the blood have been devised, and many different gas pumps have been invented in which the gases may be collected in the Torricellian vacuum over mercury. Haldane and Barcroft have devised a convenient method, which depends upon the fact that the oxygen can be driven off from blood treated with dilute ammonia by the addition of potassium ferricyanide, and that the carbon dioxide is liberated by adding an acid. The amount of gas is estimated by measuring the increased pressure in the tube in which the gas has been given off.

About 60 c.c. of gas measured at 0° C. and 760 mm. pressure can be extracted from 100 c.c. of blood. The proportion of the gases varies in arterial and in venous blood.

AMOUNT OF GASES PER HUNDRED VOLUMES OF BLOOD

	Arterial Blood.	Venous Blood.
Oxygen . .	20	12
Carbon dioxide .	40	46

There are two ways in which gases may be held in such a fluid as the blood—

1*st.* In simple solution.
2*nd.* In chemical combination.

Oxygen.—At the temperature of the body the blood can hold in solution less than 1 per cent. of oxygen. Now the amount of oxygen actually present is about 20 per cent. So that by far the greater quantity of the gas is not in solution. We have already seen that it is in loose chemical union with hæmoglobin.

Carbon Dioxide.—In the animal body the blood can dissolve about 2½ per cent. of carbon dioxide. But it may contain as much as 46 per cent., and this is uniformly distributed between plasma and corpuscles. Hence the greater part of the gas must be in chemical combination. Analysis of the ash of the plasma shows that the **sodium** is more than sufficient to combine with the chlorine and phosphoric acid, and is thus available to take up carbon dioxide, as the carbonate Na_2CO_3 and the bicarbonate $NaHCO_3$. Sodium carbonate and basic sodium phosphate are therefore present together in the plasma.

If carbon dioxide is passed into a solution of sodium phosphate it appropriates a certain amount of the sodium, changing Na_2PO_4 to $NaHPO_4$. This is what happens in the tissues where CO_2 is abundant. In the lungs, where the blood is exposed to an atmosphere poor in CO_2, the P_2O_5 again seizes on the Na, turning out the CO_2.

But the proteins of the blood also act in the same way as weak acids, being turned out of their combination with bases by the mass action of CO_2, and thus acting as carriers of CO_2.

In the corpuscles the hæmoglobin acts as an acid. When the amount of CO_2 is great, hæmoglobin is turned out of its combination with bases. But when the pressure of CO_2 is low the hæmoglobin turns it out. For this reason it is possible to remove all the CO_2 from whole blood in an air pump, but not possible to remove it from blood plasma. In fact, the carriage of carbon dioxide and its excretion are mainly the result of a struggle between that gas on the one hand and the proteins and phosphoric acid on the other, for the bases of the plasma.

Nitrogen.—The amount of nitrogen in the blood is not in excess of what can be held in solution, and we may therefore infer that it is simply dissolved in the blood plasma.

V. Source of the Blood Constituents

A. Of the Plasma.—The **water** of the blood is derived almost entirely from the water ingested.

The source of the **proteins** has not been fully investigated. Undoubtedly they are partly derived, somewhat indirectly as we shall afterwards see, from the proteins of the food. Very probably, too, they are in part derived from the tissues. But the significance of the two proteins, albumin and globulin, and of their variations has not yet been elucidated.

The **glucose** is derived from the carbohydrates and possibly from the proteins of the food, and during starvation it is constantly produced in the liver and poured into the blood (p. 395).

The **fats** are derived from the fats and carbohydrates and possibly from the proteins of the food.

The **urea** and other waste constituents are derived from the various tissues.

B. Of the Cells.—**I. Leucocytes.**—In the embryo these are first developed from the mesoblast cells generally. In extra-uterine life they are formed in the lymph tissue and in the red marrow of bone.

1. **Lymph Tissue** (see p. 30) is very widely distributed in

the body, occurring either in patches of varying shape and size, or as regular organs, the **lymphatic glands** (fig. 104). These are placed on the course of lymphatic vessels, and consist of a sponge-work of fibrous tissue, in the interstices of which are set the patches of lymph tissue or *germ centres*, each surrounded by a more open network, the sinus, through which the lymph flows, carrying away the lymphocytes, which are the characteristic elements produced, from the germ centres. Round some of the lymphatic glands of certain animals large blood spaces or sinuses are seen, and these glands are called **hæmolymph glands** (fig. 106). They are intermediate between lymphatic glands and the spleen. When erythrocytes are destroyed by hæmolytic agents the pigment and the iron derived from the hæmoglobin are often found abundantly in the cells in the sinuses of lymph and hæmolymph glands.

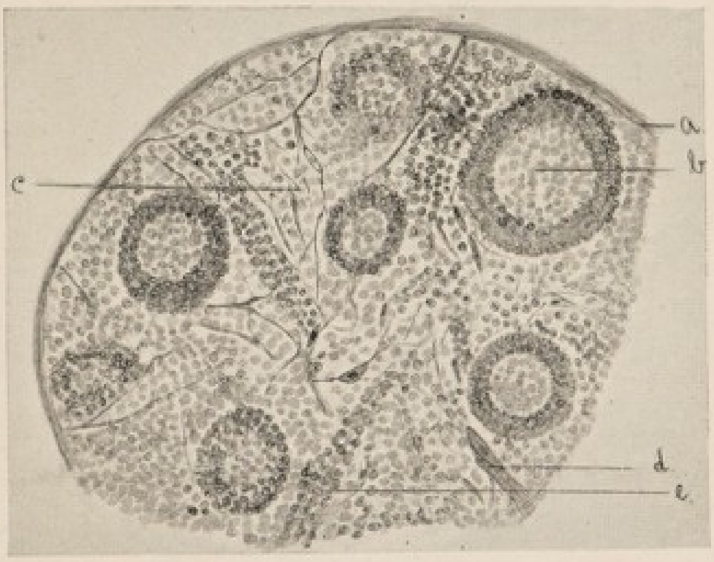


FIG. 104.—Section of a Lymph Gland. *a*, capsule ; *b*, germ centres of cortex ; *c*, sinuses ; *d*, trabecula ; *e*, germ centres of medulla.

2. **Bone Marrow.**—The structure of bone marrow is considered below, but it may be stated here that young leucocytes or leucoblasts, in the condition of mitosis, are abundant, and that they pass away in the blood stream. They are of all varieties. In certain pathological conditions the formation of these cells is increased and a leucocytosis results (fig. 105).

II. **Erythrocytes.**—In the embryo these cells seem to be formed by a process of budding from the mesoblast cells, which become vacuolated to form the primitive blood vessels. Later they develop in the liver and spleen, but after birth they are formed in the **red marrow of bone** (fig. 105). Marrow consists of a fine fibrous tissue with large blood capillaries or sinuses running in it. In the fibrous tissues are numerous *fat cells* (clear spaces *b* in fig. 105) and generally a considerable number of multi-nucleated *giant cells* or myelocytes (*d*). In addition to these are the young leucocytes, *leucoblasts* (*a.g.h.*), and lastly young nucleated red cells, the *erythroblasts* (*c.f.*). After hæmorrhage, the formation of these becomes unusually active, and may implicate parts of the marrow not generally concerned in the process, and hence the red marrow may spread from the ends of the long bones, where it is usually situated, towards the middle of the shaft. The nuclei of the erythroblasts atrophy or are shed and the cells escape into the blood stream. The red marrow has the power of retaining the iron of disintegrated erythrocytes, which are often found enclosed in large modified leucocytes or phagocytes. The iron is often very abundant after a destruction of erythrocytes.

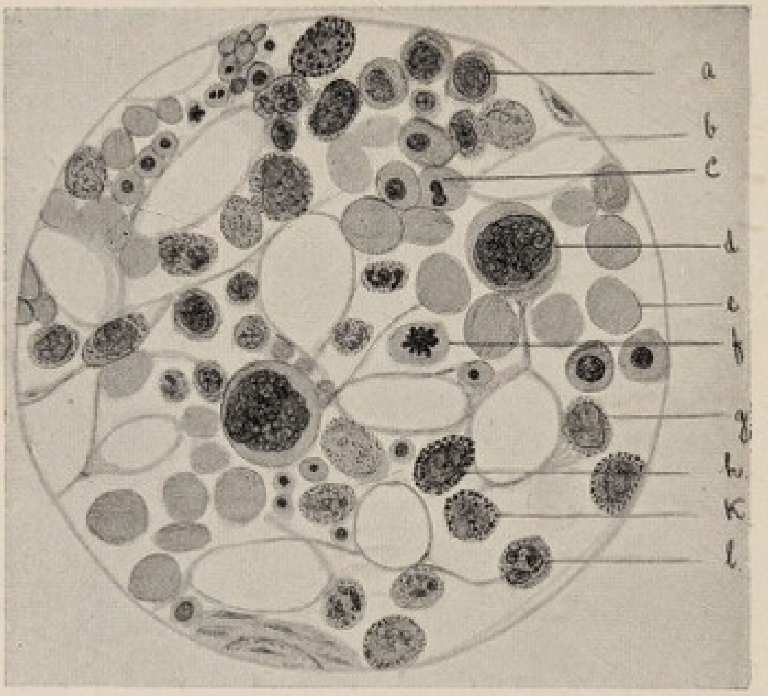


Fig. 105.—Section of Red Marrow of Bone. *a*, lymphocyte; *b*, fat cell; *c*, erythroblast; *d*, giant cell; *e*, erythrocyte; *f*, erythroblast in mitosis; *g*, neutrophil myelocyte; *h*, eosinophil myelocyte; *k*, eosinophil leucocyte; *l*, polymorpho-nuclear leucocyte.

VI. Total Amount of Blood in the Body

This was formerly determined by bleeding an animal, measuring the amount of blood shed, and determining the amount of hæmoglobin contained in it; then washing out the blood vessels, and after measuring the amount of fluid used, determining the amount of hæmoglobin in it to ascertain the amount of blood it represented. By this method the amount of blood was found to be about $\frac{1}{13}$ of the body weight in man.

Haldane and Lorrain Smith have devised a method which can be applied to the living animal. It depends upon the fact that, after an animal or person has inhaled carbon monoxide, it is possible to determine to what proportion the gas has replaced oxygen in the oxyhæmoglobin. If then an individual breathes a given volume of carbon monoxide, and if a measured specimen of blood is found to contain a definite percentage of the gas, the rest of the gas must be equally distributed through the blood, and thus the amount of blood may be deduced.

By this method they conclude that the blood is about $\frac{1}{20}$ of the weight of the body in the human subject.

VII. Distribution of the Blood

Roughly speaking, the blood is distributed somewhat as follows:—

Heart, lungs, large vessels	$\frac{1}{4}$
Muscles	$\frac{1}{4}$
Liver	$\frac{1}{4}$
Other organs	$\frac{1}{4}$

VIII. Fate of the Blood Constituents

The **water** of the blood, constantly renewed from outside, is constantly got rid of by the kidneys, skin, lungs, and bowels.

About the fate of the **proteins** we know nothing. They are probably used in the construction of the tissues, but experimental evidence of this is wanting.

The **glucose** and **fat** are undoubtedly used up in the tissues.

The **urea** and waste products are excreted by the kidneys.

The fate of the salts is not fully worked out. The chlorides are partly excreted by the kidneys and are partly split up to form the hydrochloric acid required for stomach digestion. The phosphates and sulphates are excreted in the urine, but whether they are also used in the tissues is not known.

The **leucocytes** break down in the body—but when and how we do not know. We shall afterwards find that they are greatly increased in number after a meal of proteins, and, since the increase is transitory, lasting only for a few hours, they are probably rapidly broken down, possibly to feed the tissues. It would thus seem that a leucocyte may live for only a short time in the blood.

The **erythrocytes** also break down. How long they live is not known. It is found, after injecting blood, that the original number of corpuscles is not reached for about a fortnight, and hence it has been concluded that the corpuscles live for that period. The experiment, however, is far from conclusive, and must be accepted with reservation.

Organs connected with Hæmolysis.—The process of breaking down of old erythrocytes and eliminating their pigment is often called the process of **hæmolysis**. Certain organs appear to be specially connected with it, but the precise part played by each of them is not very clearly understood.

That the **liver** acts in this way is indicated, first, by the fact that the blood passing from the organ during digestion contains fewer erythrocytes than the blood going to it; second, by the formation in the liver cells of bile pigments, which are derivatives of hæmoglobin; third, by the presence of pigment and of iron in simple combinations in the liver cells under certain conditions. It is possible that the reabsorbed salts of the bile acids in the portal blood dissolve the pigment out of the old erythrocytes, and that the liver cells may then act upon the liberated pigment. Under ordinary conditions the liver does not store much iron.

The **spleen** is generally said to have a similar action. This organ is composed of a fibrous capsule containing non-striped muscle and a sponge-work of fibrous and muscular trabeculæ, in the interstices of which is the spleen pulp. The branches of the splenic artery run in the trabeculæ, and twigs pass out from these trabeculæ, and are covered with masses of lymph tissue forming the Malpighian corpuscles. Beyond these, the vessels open into a series of complex sinuses lined by endothelial cells of large size, from which the blood is collected into channels, the venous sinuses, which carry it back to branches of the splenic vein in the trabeculæ. The pulp is thus comparable with the blood sinuses of the hæmolymph glands, and the spleen may be considered as being a still further development of the hæmolymph gland (fig. 106).

So far no decrease in the number of erythrocytes in the blood leaving the spleen has been recorded. In the cells of the spleen pulp and chiefly in the endothelial cells yellow pigment and simple iron compounds are frequently found, indicating that hæmoglobin is being broken down. But the idea that the spleen plays an important part in the actual destruction of erythrocytes seems to be negatived by the fact that, when blood is injected, the cells are broken down no faster in an animal with the spleen intact than in an animal from which the spleen has been removed. While the spleen appears to have no action in killing and destroying erythrocytes, its cells, like those of the sinuses of the **Lymph Glands and Hæmolymph Glands**, have the power of taking up dead and disintegrating erythrocytes and storing the iron for future use in the body. These organs may, in fact, be regarded as the graves of the dead erythrocytes.

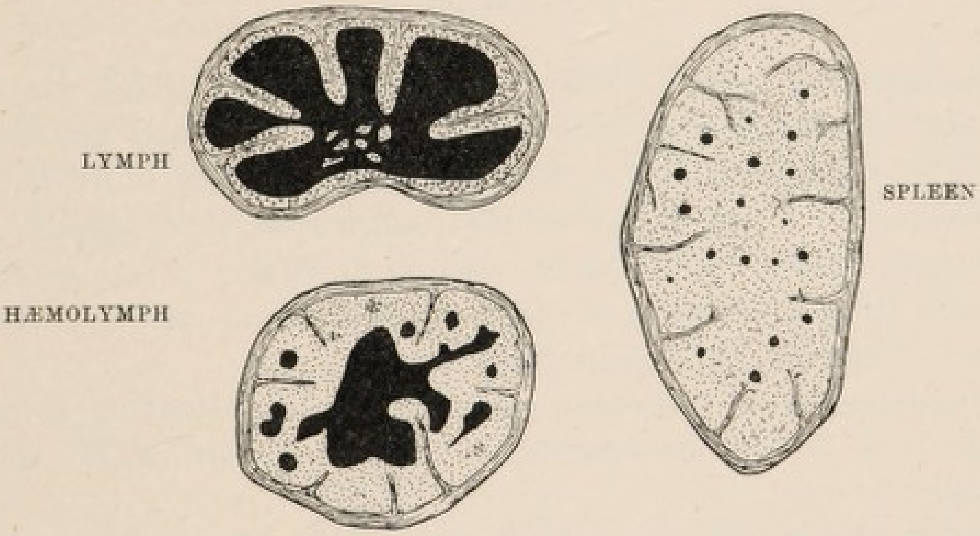


Fig. 106.—To show the relationship of the Spleen to Lymph Glands and Hæmolymph Glands. The black indicates lymphoid tissue; the coarsely spotted part, lymph sinuses, and the finely dotted part, blood sinuses. (Lewis.)

The non-striped muscle in the framework of the spleen undergoes rhythmic contraction and relaxation, and the organ thus contracts and expands at regular intervals of about a minute.

These movements may be recorded by enclosing the organ in an oncometer, a closed capsule connected with some form of recording apparatus.

The movements are controlled by fibres leaving the spinal cord chiefly in the 6th, 7th, and 8th dorsal nerves of both sides. Strong stimulation of these causes contraction.

B. LYMPH

Characters of Lymph.—The lymph is the fluid which plays the part of middleman between the blood and the tissues. It fills all the spaces in the tissues and bathes the individual cell elements. These spaces in the tissues open into vessels—the lymph vessels—in which the lymph flows and is conducted through lymph glands and back to the blood through the thoracic duct (see fig. 107, p. 225).

Lymph varies in character according to the situation from which it is taken and according to the condition of the animal.

Lymph taken from the lymph spaces—*e.g.* the pericardium, pleura, or peritoneum—is a clear straw-coloured fluid. It has little or no tendency to coagulate. Microscopic examination shows that it contains few or no cells—any cells which may exist being lymphocytes. In reaction it is alkaline. The specific gravity varies according to its source, being lowest when from the limbs and highest when from the liver.

Apparently the cause of the non-coagulation of such lymph is the absence of cells from which thrombokinase may be set free. If blood or white corpuscles be added to it, a loose coagulum forms.

If the lymph be taken from lymphatic vessels after these have passed through lymphatic glands, it is found to contain a number of lymphocytes, and it coagulates readily.

Chemically, lymph resembles blood plasma in which the proteins are in smaller amount, but the inorganic salts in the same proportion as in the blood. The amount of solids varies in lymph from different organs.

Lymph of	Proteins.
Limbs	2–3 per cent.
Intestines	4–6 ,,
Liver	6–8 ,,

In the lymphatics coming from the alimentary canal during starvation, the lymph has the characters above described. But after a meal it has a milky appearance and is called **chyle.** This milky appearance is due to the presence of fats in a very fine state of division, forming what is called the molecular basis of the chyle.

Lymph in various diseases tends to accumulate as serous effusions in the large lymph spaces—*e.g.* the pleura, peritoneum, pericardium—and these effusions behave differently as regards coagulation. The following table helps to explain this (S.A. is Serum Albumin, S.G. Serum Globulin):—

COAGULABILITY OF LYMPH, SERUM, AND EFFUSIONS.

Plasma and Lymph.	Serous Effusion.			Serum.
	Coag.	Coag. with Thrombin.	Uncoag.	Uncoag.
S. A.	S. A.	S. A.	S. A.	S. A.
S. G.	S. G.	S. G.	S. G.	S. G.
Fibrinogen.	Fibrinogen.	Fibrinogen.	...	...
Thrombin.	Thrombin.	...	...	Thrombin.

2. **Formation of Lymph.**—Lymph is derived partly from the blood and partly from the tissues. The formation of **lymph from the blood** depends upon the permeability of the walls of the capillaries and the pressure of blood in the blood vessels. Thus, although the pressure in the blood vessels of the limbs is much higher than the pressure in the vessels of the liver, hardly any lymph is usually produced in the former, while very large quantities are produced in the latter—apparently because of the small permeability of the limb capillaries and the great permeability of the hepatic capillaries. The permeability may be increased by anything which

injures the capillary wall. Thus the injection of hot water or of proteoses at once leads to an increased flow of lymph.

While the permeability of the vessel wall is the most important factor controlling lymph formation, any increase of the intra-vascular pressure of a region increases the flow of lymph, and for this reason any obstruction to the free flow of blood from a part leads to increased lymph production from that area.

That lymph is also formed **from the tissues** is indicated by the fact that the injection of substances of high osmotic equivalent into the blood—such as sugar or sodium sulphate—leads, by a process of osmosis, to a flow of fluid into the blood, so that it becomes diluted, and also to an increased formation of and flow of lymph, and this increase of water in both can be explained only by its withdrawal from the tissues.

THE CIRCULATION

I. GENERAL ARRANGEMENT

THE arrangement by which the blood and lymph are distributed to the tissues may be compared to a great irrigation system.

It consists of a central force pump—the *systemic heart* (fig. 107, *S.H.*)—from which pass a series of conducting tubes—the *arteries*—leading off to every part of the body, and ending in

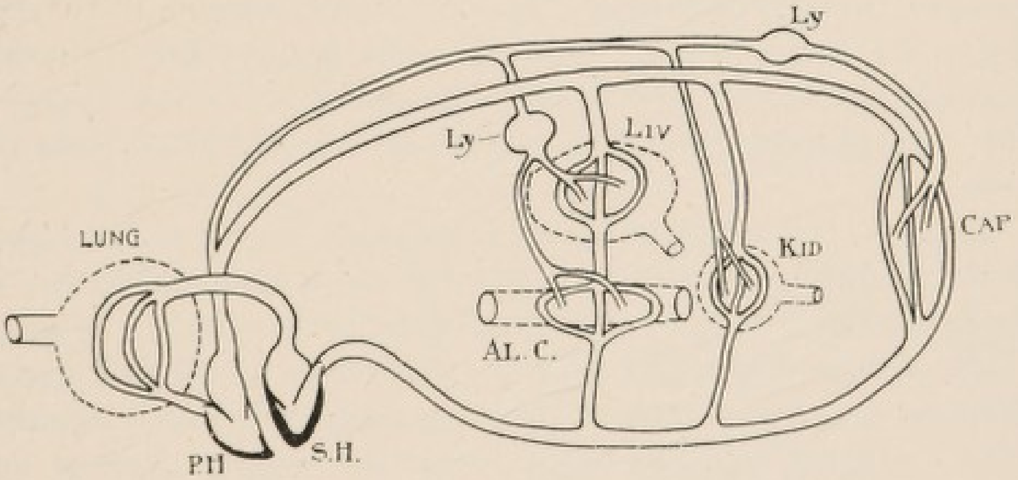


FIG. 107.—Scheme of the Circulation. *S.H.*, systemic heart sending blood to the capillaries in the tissues, *Cap.* The blood brought back by veins and the exuded lymph by lymphatics, *Ly.*, passing through glands; blood sent to the alimentary canal, *Al.C.*, and from that to the liver, *Liv.*; blood also sent to the kidneys, *Kid.*; the blood before again being sent to the body is passed through the lungs by the pulmonic heart, *P.H.*

innumerable fine irrigation channels—the *capillaries* (*Cap.*)—in the substance of the tissues. From these, a considerable proportion of the blood constituents is passed into the spaces between the cells as lymph. From these spaces the fluid is either passed back into the capillaries, or is conducted away in a series of *lymph vessels*, which carry it through *lymph glands*

(*Ly.*), from which it gains certain necessary constituents, and finally bring it back to the central pump.

The fluid, which has not passed out of the capillaries into the tissues, has been deprived of many of its constituents, and this withdrawal of nutrient material by the tissues is made good by a certain quantity of the blood being sent through the walls of the stomach and intestine (*Al.C.*), in which the nutrient material of the food is taken up and added to the blood returning to the heart. At the same time, the waste materials added to the blood by the tissues are partly got rid of by a certain quantity of the blood being sent through the liver and kidneys (*Liv.* and *Kid.*).

The blood is then poured back, not at once into the great pump which sends it through the body, but into a subsidiary pump—the *pulmonic heart* (*P.H.*)—by which it is pumped through the lungs, there to obtain a fresh supply of oxygen, and to get rid of the carbon dioxide excreted into it by the tissues. Finally the blood, with its fresh supply of oxygen from the lungs, and of nourishing substances from the alimentary canal, is poured into the great systemic pump—the left side of the heart—again to be distributed to the tissues.

Thus the circulation is arranged so that the blood, exhausted of its nourishing material by the tissues, is replenished in the body before being again supplied to the tissues.

The **sectional area** of this irrigation system varies enormously. The aorta leaving the heart has a comparatively small channel. If all the arteries of the size of the radial were cut across and put together, their sectional area would be many times the sectional area of the aorta. And, if all the capillary vessels were cut across and placed together, the sectional area would be about 700 times that of the aorta.

From the capillaries, the sectional area of the veins and lymphatics steadily diminishes as the smaller branches join with one another to form the larger veins and lymphatics; but, even at the entrance to the heart, the sectional area of the returning tubes, the veins, is about twice as great as that of the aorta (fig. 132, p. 288).

The circulatory system may thus be compared to a stream which flows from a narrow deep channel, the aorta, into a gradually broadening bed, the greatest breadth of the channel being reached in the capillaries. From this point the channel gradually narrows until the heart is reached.

Hence the blood stream is very rapid in the arteries where the channel is narrow, and very sluggish in the capillaries where the channel is wide, so that in them plenty of time is allowed for exchanges between the blood and the tissues.

II. THE CENTRAL PUMP—THE HEART

A. Structure

A very simple form of heart exists in the ascidians. At one point on a large vessel there is a thickening in the wall composed of non-striped muscular fibres. A contraction is seen to pass from one end of this to the other at frequent regular intervals, thus forcing the fluid through the vessels. The embryonic heart in man has a similar structure.

In the snail and cuttle-fish, in addition to the contracting muscular thickening, there is also a thin-walled receiving chamber into which the blood flows before it is expelled onwards. The heart is thus composed of two chambers.

1*st*. A receiving chamber—the **auricle.**

2*nd*. An expelling chamber—the **ventricle.**

In fish the heart has a similar structure. But in lung-bearing animals a more complex arrangement is required, and a double heart is found, one concerned with the propulsion of blood to the system generally, and hence called the **systemic heart**; one propelling blood to the lungs, and hence called the **pulmonic heart.** In mammals, the former chamber is on the left side, the latter on the right. Each consists of a receiving and expelling chamber—an auricle and a ventricle.

The walls of these chambers are essentially muscular; but this muscular layer, or myocardium, lies between two fibrous layers, the **pericardium** and the **endocardium.**

The **musculature** of the auricles is separate from that of the ventricles, but some fibres more like ordinary visceral fibres than cardiac muscle extend from one to the other. This band of His' plays a most important part in conducting contraction started in the auricles to the ventricles. If the heart be boiled, the auricles, the aorta and the pulmonary artery may be separated from the ventricles. This is because boiling converts fibrous tissue to gelatine and dissolves it, and it is by white fibrous tissue that the auricles and great arteries are attached to the ventricles. This tissue is arranged in three **rings,** one encircling the opening between the right auricle and ventricle, and crescentic in shape; one, more circular in shape, encircling in common the left auriculo-ventricular and the aortic orifice, and one encircling the pulmonary opening. The auricles are attached to the auriculo ventricular rings above, the ventricles are attached below, while the valves of the heart are also connected with them.

The muscular fibres of the **auricles** are arranged in two badly-defined layers—

1*st.* An outer layer runs horizontally round both auricles.

2*nd.* An inner layer arches over each auricle, and is connected with the auriculo-ventricular rings.

Contraction of the first layer diminishes the capacity of the auricles from side to side. Contraction of the second pulls the auricles downwards towards the ventricles, and thus diminishes their capacity from above downwards.

The peculiar striped muscle fibres of the auricular wall extend for some distance along the great veins which open into these chambers.

The **left ventricle** forms the cylindrical core to the heart, and the right ventricle is attached along one side of it. The septum between the ventricles is essentially the right wall of the left ventricle, and it bulges into the right ventricle with a double convexity from above downwards and from before backwards (figs. 108 and 110).

The muscle fibres of the **ventricles** are arranged essentially in three layers—

1*st.* The outmost layer takes origin from the auriculo-ventricular rings, and passes downwards and to the left till it reaches the apex of the heart. Here it turns inwards, forming a sort of vortex, and becomes continuous with the inmost layer.

2*nd.* The middle layer is composed of fibres running horizontally round each ventricle. It is the thickest layer of the heart, and in contracting it pulls the walls of the ventricles towards the septum ventriculi.

3rd. The inmost layer is continuous with the outmost layer, as it turns in at the apex. It may be considered as composed of two parts—

(*a*) A layer of fibres running longitudinally along the inside of each ventricle from the apex upwards to the auriculo-ventricular ring. These fibres are raised into fleshy columns, the **columnæ carneæ.**

(*b*) A set of fibres, constituting the **papillary muscles** (fig. 109, *P.M.*), which, taking origin from the apical part of the ventricles, extend freely upwards to terminate in a series of tendinous cords (the **chordæ tendineæ**), which are inserted partly into the auriculo-ventricular valves, presently to be described, and partly into the auriculo-ventricular rings. The papillary muscles are merely specially modified columnæ carneæ. In many cases, actual muscular processes extend from the apex of the papillary muscles to the auriculo-ventricular ring.

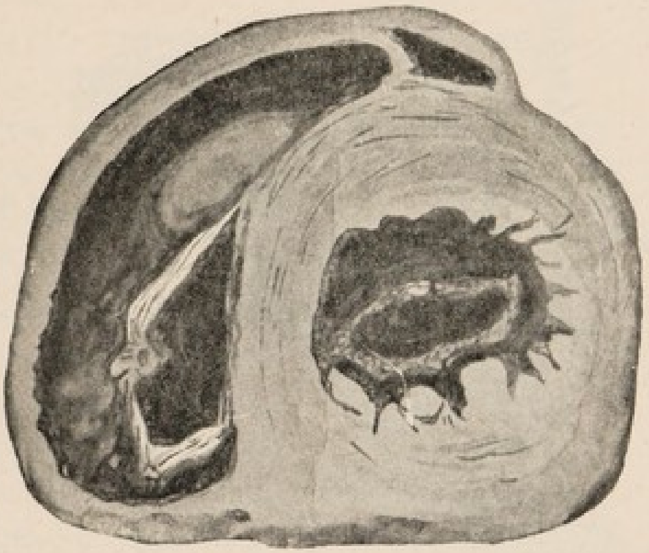


Fig. 108.—Cross Section through the Ventricles of the Heart looking towards Auricles, to show the right Ventricle placed on the Central Core of the left Ventricle. The cusps of the Auriculo-ventricular Valves are also shown.

In the *left ventricle* there are two papillary muscles, or groups of papillary muscles, one in connection with the anterior wall of the ventricle, and one in connection with the posterior wall.

In the *right ventricle* there are—1*st*. One or more small horizontally running papillary muscles just under the pulmonary orifice, their apices pointing backwards—(fig. 109, *S.P.M.*).

2*nd*. A large papillary muscle taking origin from the mass of fleshy columns at the apex of the ventricle (*A.P.M.*).

3*rd*. One or more papillary muscles of varying size arising from the posterior part of the apical portion of the ventricle (*P.P.M.*).

4*th*. A number of small septal papillary muscles arising from the septum.

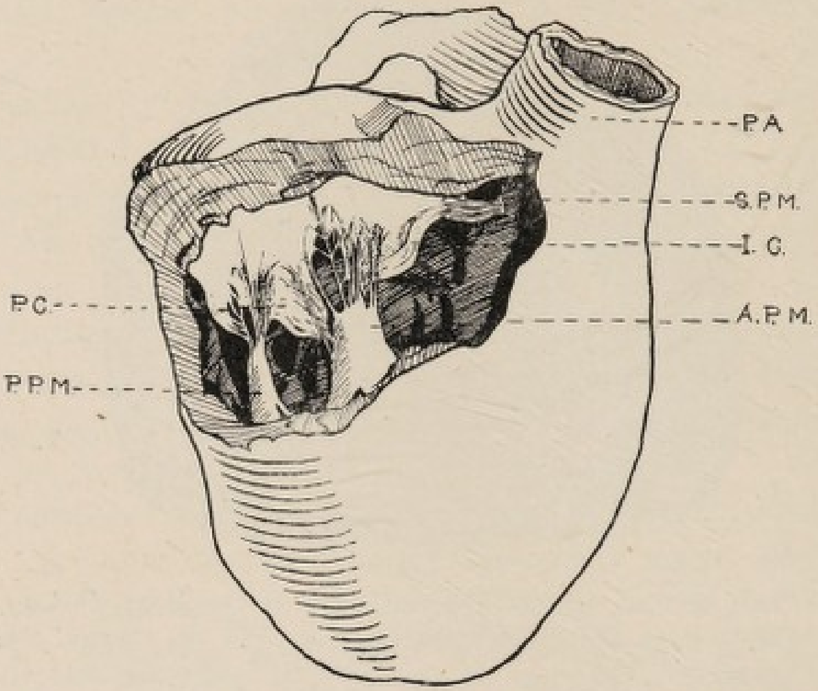


FIG. 109.—The Right Ventricle and Tricuspid Valve to show the relationship of the Papillary Muscles and Chordæ Tendineæ to the Cusps of the Valve. (See text.)

The distribution of the chordæ from these muscles will be considered in connection with the auriculo-ventricular valves.

In contraction, the outmost and inmost layers of the ventricles tend to approximate the apex to the base of the ventricles, but this is resisted by the contracting middle layer. The apex tends to be tilted towards the right, the papillary muscles shorten, the columnæ carneæ by their shortening and thickening encroach upon the ventricular cavity, and help to abolish it, while the auriculo-ventricular rings are drawn downwards and inwards towards the septum.

The **endocardium** forms a continuous fibrous layer, lined by endothelium, extending from the vessels over the inner aspect of auricles and ventricles. At certain points flaps of this endocardium are developed to form the valves of the heart.

In the heart, valves are situated at the entrance to and at the exit from the expelling cavities. There is thus on each side of the heart a valve between the auricles and ventricles, and a valve between the ventricles and the great arteries.

Auriculo-ventricular Valves.—On each side of the heart the auriculo-ventricular valve is formed by flaps of endocardium, which hang downwards from the auriculo-ventricular ring like a funnel into the ventricular cavity, and which are attached to the apices of the papillary muscles by the chordæ tendineæ (figs. 109 and 110).

On the left side of the heart there are two main cusps, forming the **mitral valves** (fig. 110)—

1*st*. An anterior or right cusp, which takes origin from, and is continuous with, the right posterior wall of the aorta. It hangs down into the ventricle between the aortic and auriculo-ventricular orifices, thus dividing the ventricle into two parts, an aortic and an auricular part. This cusp is very strong, and in many animals bone is developed in it towards its base. It is composed of dense fibrous tissue, is smooth on both sides, and the chordæ are inserted chiefly along its edges.

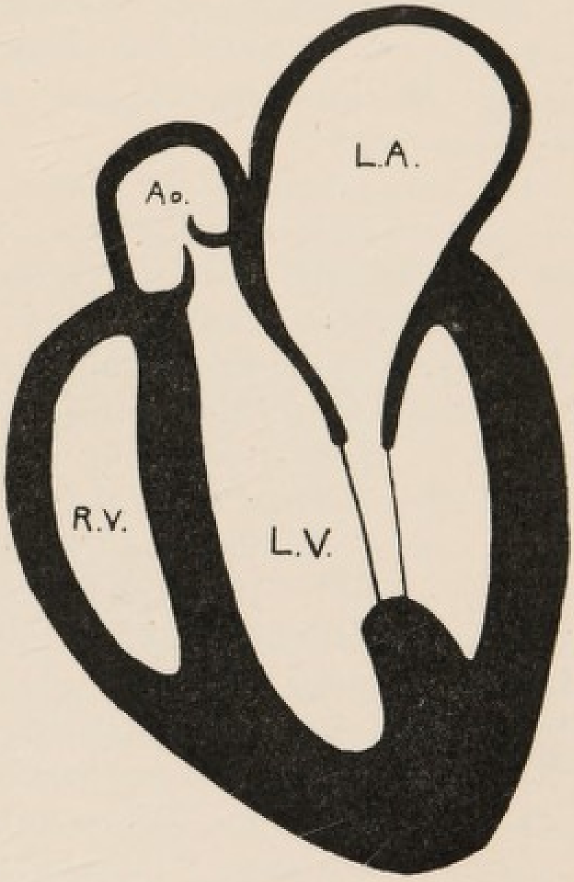


FIG. 110.—Vertical Mesial Section through Heart to show Aortic and Mitral Valves. R. V., right ventricle ; L. V., left ventricle with papillary muscle ; L. A., left auricle ; Ao., aorta with anterior cusp on top of septum.

2*nd*. The posterior or left cusp takes origin from the back part of the auriculo-ventricular ring, and hangs in the ventricle in its relaxed state against the posterior and left wall. It is smaller and less strongly made than the anterior cusp. The chordæ tendineæ are not only inserted into its edge, but run up along its posterior aspect to be inserted into the auriculo-ventricular ring, and they thus give the posterior aspect of the cusp a rough ridged appearance.

When the papillary muscles contract, the cusps are drawn together. The edge of each cusp thins out to form a delicate border, which, when the cusps are approximated, completely seals the aperture.

On the right side of the heart the auriculo-ventricular orifice is separate from the pulmonary opening, and the three cusps of the **tricuspid valve** are developed in connection with the crescentic opening from the auricle (fig. 108). One rises from the ring above the septum, and hangs down into the ventricle upon the surface of the septum. This cusp is small, thin, and delicate. It is attached by its lower border to the septal papillary muscles. The chief or infundibular cusp (fig. 109, *I.C.*) rises from the front part of the ring between the pulmonary infundibulum and the auriculo-ventricular opening. It is connected by its anterior border with the horizontal fibres from the superior papillary muscles, and by its lower and inferior border with the chordæ from the anterior papillary muscle. When these two sets of papillary muscles contract, this cusp is drawn flat against the bulging septum.

The posterior cusp (*P.C.*) takes origin from the posterior and outer part of the ring, and hangs down into the posterior part of the ventricle. It is connected by its anterior margin with the anterior papillary muscle and by its posterior margin with the posterior papillary muscle. Contraction of these muscles therefore approximate its anterior edge to the infundibular cusp, its posterior edge to the septal cusp, and pull it towards the septum.

In both the infundibular and posterior cusps many of the chordæ pass up to be inserted into the auriculo-ventricular ring.

Semilunar Valves.—The valves, situated at the opening of the ventricles into the great arteries, are also formed as special developments of the endocardium.

Each is composed of three half-moon-shaped membranous pouches attached along their curved margin to the walls of the artery and upper part of the ventricle, and with their concavities directed away from the ventricle. In the centre of the free margin is a fibrous thickened nodule, the corpus Arantii, from which a very thin piece of membrane, the lunule, extends to the attached margin of the edges. A pouch, the sinus of Valsalva, lies behind each cusp.

The arrangements of these various cusps is of importance in connection with their action (fig. 110).

Aortic Valve.—The anterior cusp is largest, and lies somewhat deeper in the heart than the others. At each side it is attached to the aortic wall, but below it is attached to the upper part of the septum ventriculi, so that the base of the sinus of Valsalva is formed by the upper part of the septum. At a somewhat higher level is a cusp which is partly attached to the upper part of the septum, partly to the posterior wall of the aorta, where this becomes continuous with the anterior cusp of the mitral. The third cusp is still higher, and is attached to the aortic wall, where it becomes continuous with the anterior cusp of the mitral.

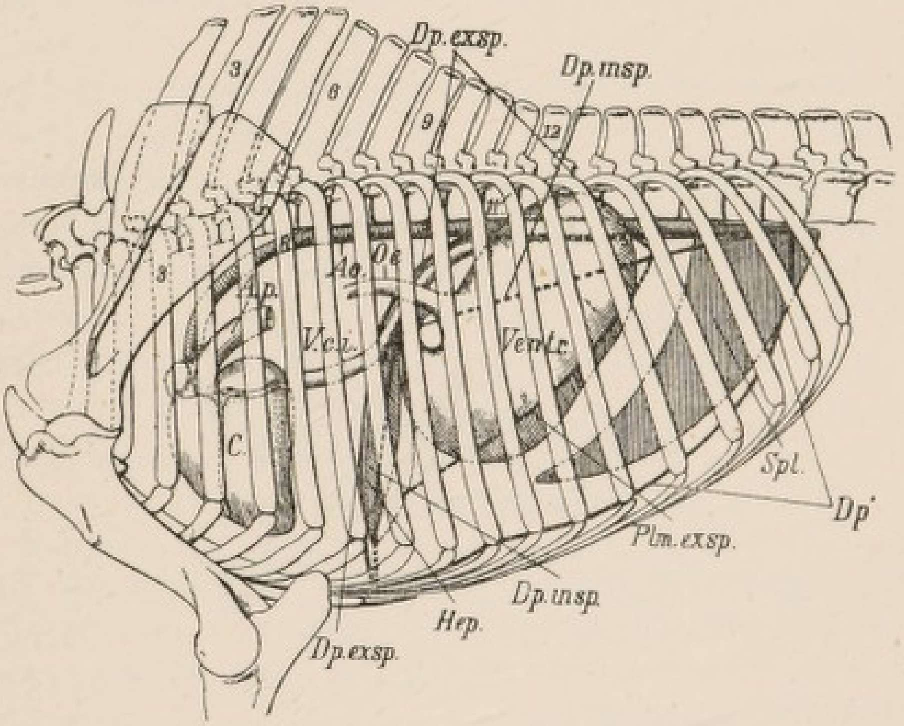


FIG. 111.—Relations of the Thoracic Viscera in the Horse. *C.*, heart; *Dp.*, the diaphragm; *exsp.*, in expiration; *insp.*, in inspiration. (*From* ELLENBERGER.)

Pulmonary Valve.—The posterior cusp is mounted on the top of the septum ventriculi, and is at a somewhat lower level than the other two.

Thus, in each valve, the cusp placed lowest is mounted on a muscular cushion, the use of which will afterwards be considered.

Attachments and Relations of the Heart (fig. 111).—In the horse the heart hangs downwards from the vertebral column, and the apex is in relation to the posterior end of the sternum and a little to the left.

Behind the heart is in relation to the tendon of the diaphragm.

All round it are the lungs, completely filling up the rest of the thorax.

The heart is enclosed in a strong fibrous bag, the **Pericardium**, which supports it and prevents over-distension. When fluid accumulates in this bag the auricles are pressed upon and the flow of blood into them is impeded.

B. Physiology of the Heart

The Cardiac Cycle

Each part of the heart undergoes contractions and relaxations at regular rhythmical intervals, *and the sequence of events from the occurrences of any one event to its recurrence constitutes the cardiac cycle.*

A. Frog.—In the frog a contraction, starting from the openings of the veins, suddenly involves the sinus venosus, causing it to become smaller and paler. This contraction is rapid and of short duration, and is followed by a relaxation, the cavity again regaining its former size and colour. As this relaxation begins, the two auricles are suddenly contracted and pulled downwards towards the ventricle, at the same time becoming paler, while the ventricle becomes more distended and of a deeper red. The rapid brief auricular contraction now gives place to relaxation, and, just as this begins, the ventricle is seen to become smaller and paler, and, if held in the finger, is felt to become firmer. This event takes place more slowly than the contraction of either sinus or auricles.

The chief change in the ventricle is a diminution in its lateral diameter, though it is also decreased in the antero-posterior and vertical directions. During ventricular contraction the bulbus is seen to be distended and to become of a darker colour. The ventricular contraction passes off suddenly, the ventricle again becoming larger and of a deep red colour. At this moment the bulbus aortæ contracts and becomes pale and then relaxes before the next ventricular contraction. (*Practical Physiology.*)

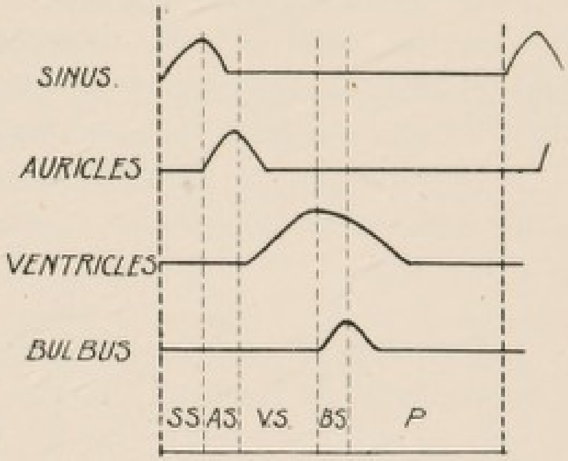


FIG. 112.—Scheme of the Cardiac Cycle in the Frog. *S.S.*, sinus systole ; *A.S.*, auricular systole ; *V.S.*, ventricular systole ; *B.S.*, bulbus systole ; *P.*, rest of all chambers.

Each chamber of the heart thus passes through two phases—a contraction phase, a **systole** of short duration, and a longer relaxation phase, the **diastole.** And the sequence of events in the frog's heart might be schematically represented as in fig. 112.

B. Mammal.—1. Rate of Recurrence.—The rate of recurrence of the cardiac cycle varies with the animal examined. In the adult horse it is about 36 to 40 per minute. Many factors modify the rate of the heart.

Rate of heart per minute in different animals:—

Horse	36 to 40
Ox	45 to 50
Sheep	70 to 80
Dog	90 to 100
Rabbit	120 to 150

1. *Period of Life.*—The following table shows the average rate of the heart at different ages:—

HORSE

New born	92 to 132 per minute.
Under 1 year	50 to 68 „
4 years	50 to 56 „

2. *Temperature of the Body.*—The pulse varies with the body temperature, being increased as the temperature rises.

3. *Muscular Exercise* increases the rate of the heart, first by driving the blood from the muscles into the great veins (p. 291), and second, by developing substances such as CO_2, which act directly upon the cardiac and respiratory mechanisms.

4. Stimulation of certain nerves—especially those of the abdomen—tends to cause a retardation in the rate of the heart (p. 256).

2. **Sequence of Events.**—The sequence of events making up the cardiac cycle is simpler in the mammal than in the frog.

The contraction starts in the great veins which enter the auricles, and spreads down along them to these chambers. This corresponds to the contraction of the sinus in the frog's heart. It is followed by a short sharp contraction of the auricles, which become smaller in all directions and seem to be pulled down towards the ventricles. The contraction of the auricles in mammals is not accompanied by so marked a dilatation of the ventricles as in the frog.

After the auricles have fully contracted, the contraction of the ventricles begins, and immediately the auricles relax and resume their original size.

The ventricular contraction develops suddenly, lasts for some time, and then suddenly passes off.

The contraction of the ventricles is followed by a period during which both auricles and ventricles remain relaxed. This is called the **pause** of the cardiac cycle.

The cardiac cycle in mammals may be represented as in fig. 113.

3. **Duration of the Phases.**—Ventricular systole lasts three times as long as auricular systole.

The duration of these two phases in relationship to the pause varies very greatly. Whatever may be the rate of the heart, the auricular and ventricular systoles do not vary, but in a rapidly acting heart the pause is short, in a slowly acting heart it is long.

4. **Changes in the Shape of the Chambers.**

1. *Auricles.*—These simply become smaller in all directions during systole.

2. *Ventricles.* — The changes in the diameters of the ventricles may be studied by fixing them in the various phases of contraction and measuring the alterations in the various diameters.

The shape in *diastole* may be investigated after death stiffening has passed off and has left the walls relaxed. The condition at the *end of systole* may be studied by rapidly excising *the heart* while it is still beating and plunging it in some hot solution to fix its contraction.

The condition *in the early stage of systole,* before the blood has left the ventricles, may be studied by applying a ligature round the great vessels and then plunging the heart in a hot solution to cause it to contract round the contained blood which cannot escape.

Measurements of hearts so fixed show that at the beginning of contraction the antero-posterior diameter is increased, while the lateral diameter is diminished. In contracting, the lateral walls appear to be pulled towards the septum—the increase in the antero-posterior diameter being largely due to the blood in the right ventricle pressing on and pushing forward the thin wall of the conus.

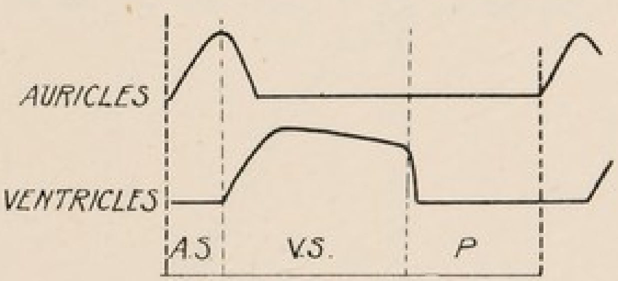


FIG. 113.—Scheme of the Cardiac Cycle in the Human Heart. *A.S.*, auricular systole ; *V.S.*, ventricular systole ; *P.*, pause.

As the ventricles drive out their blood, both antero-posterior and lateral diameters are diminished—but the diminution in the lateral direction is the more marked.

There is no great shortening in the long axis of the heart. Although the contraction of the longitudinal fibres tends to approximate base and apex, this is in part prevented by the contraction of the circular fibres.

5. **Changes in the Position of the Heart.**—During contraction the heart undergoes, or attempts to undergo, a change in

position. In the relaxed condition it hangs downwards and to the left from its plane of attachment, but when it becomes rigid in ventricular contraction it tends to take a position at right angles to its base—*Cor sese erigere*, as Harvey describes the movement. Since the apex and front wall are in contact with the chest, the result of this movement is to press the heart more forcibly against the chest wall. This gives rise to the **cardiac impulse** which is felt with each ventricular systole over the præcordium (fig. 111).

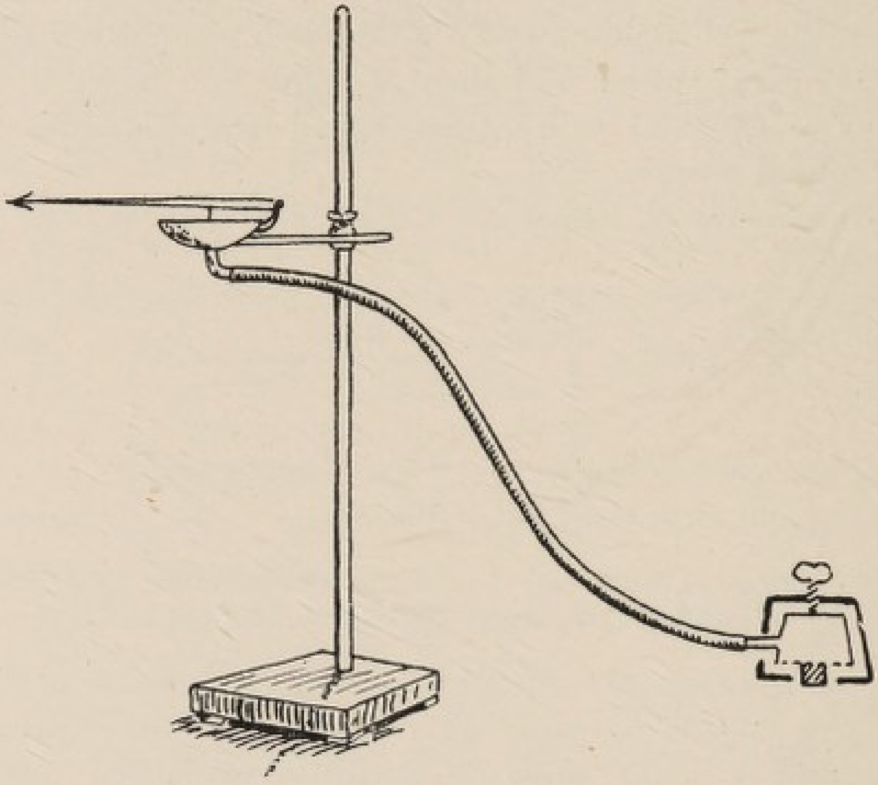


FIG. 114.—Cardiograph consisting of a Receiving Tambour, with a button on the Membrane which is placed upon the Cardiac Impulse, and a Recording Tambour connected with a Lever.

If the chest is opened and the animal placed on its back this elevation of the apex is readily seen. If the animal is placed on its belly, so that the heart when relaxed hangs forwards, the apex is tilted back during contraction.

The increased thickness of the heart from before backwards also assists, to some extent, in the production of the impulse.

In *character* it is felt as a forward impulse of the chest wall, which develops suddenly, persists for a short period, and then suddenly disappears.

The cardiac impulse may be recorded graphically by means of any of the various forms of **cardiograph**, one of the simplest consisting of a receiving and recording tambour connected by means of a tube (fig. 114). (*Practical Physiology.*)

The form of the trace varies according to the part of the heart upon which the button is placed, but it has the character shown in fig. 115 if the button is upon the cardiac impulse.

At the moment of ventricular systole the lever is suddenly thrown up to a certain level (*a* to *b*). From this point it suddenly falls slightly (*b* to *c*), but is maintained during the ventricular systole above the abscissa (*c* to *d*). At the end of the ventricular systole, as the heart falls away from the chest wall, the lever falls to its original level (*d* to *e*). In many tracings a small rise of the lever may be seen just before the great upstroke. This corresponds to the contraction of the auricles.

In various diseases of the heart the cardiogram is materially modified. Hence it is important to have a clear conception of the various parts of the trace.

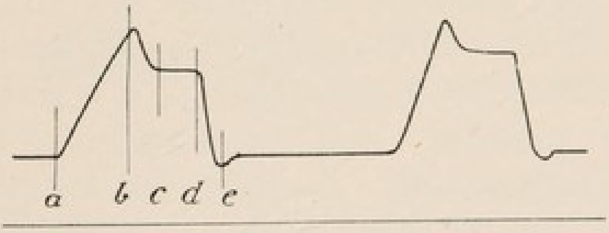


FIG. 115.—Cardiographic Trace. *a* to *d*, ventricular contraction.

The elucidation of the various parts of the cardiogram is only possible after careful study of the other changes in the heart during the cycle.

6. **Changes in the Intracardiac Pressure.**

These can be studied only in the lower animals.

The most common way of determining the pressure in a cavity is to connect it to a vertical tube and to see to what height the fluid in the cavity is raised. If such a method be applied to the ventricles of the heart, the blood in the tube undergoes such sudden and enormous changes in level that it is impossible to get accurate results.

The same objection applies to the method of connecting the heart with a U tube filled with mercury. When this is done the changes in pressure are so sudden and so extensive that the mercury cannot respond to them on account of its inertia.

Various means of obviating these difficulties have been devised. One of the best is to allow the changes of pressure to act upon a small elastic membrane tested against known pressures. A tube is thrust through the wall of the heart and connected with a tambour covered by a membrane to which a lever is attached.

A. Pressure in the Great Veins (small dotted line in fig. 116).—When the auricles contract, the flow of blood from the great veins into these chambers is arrested, and, as a result, the pressure in the veins rises. As the auricles relax the blood is sucked from the veins and the pressure falls, but, as the auricles fill up, it again rises. When the ventricles relax and suck blood from the auricles, blood again flows in from the great veins and the pressure falls, again to rise as the auricles and veins are both filled up, towards the end of the pause.

B. Pressure in the Auricles (dash line in fig. 116).—At the moment of auricular contraction there is a marked rise in the intra-auricular pressure. When the auricular systole stops, the pressure falls rapidly, reaching its lowest level when the ventricles are throwing their blood into the arteries. From this point the pressure in the auricles rises until the moment when the ventricles relax, when another fall in the pressure is observed. The pressure remains about constant from this point until the next auricular contraction.

C. Pressure in the Ventricles (continuous line in fig. 116).—The intra-ventricular pressure suddenly rises at the moment of ventricular systole to reach its maximum. From this it falls, but the fall is gradual, and is interrupted by a more or less well-marked period during which the pressure remains constant. As the ventricles relax the pressure suddenly falls to below zero, and then rises to a little above zero, at which it is maintained until the next ventricular systole. The diastolic expansion of the ventricle is in part due to the elasticity of the muscular wall, and in part to the filling of the coronary arteries which takes place only as the muscular fibres relax.

D. Pressure in the Arteries (dot-dash line in fig. 116).—The aortic pressure is high throughout. There is a sudden rise as the blood rushes out of the ventricles. The pressure then falls, but the fall is not steady. Often it is interrupted by a more or less marked increase corresponding to the later part of the ventricular contraction. At the moment of ventricular diastole, the fall is very sharp and is interrupted by a well-

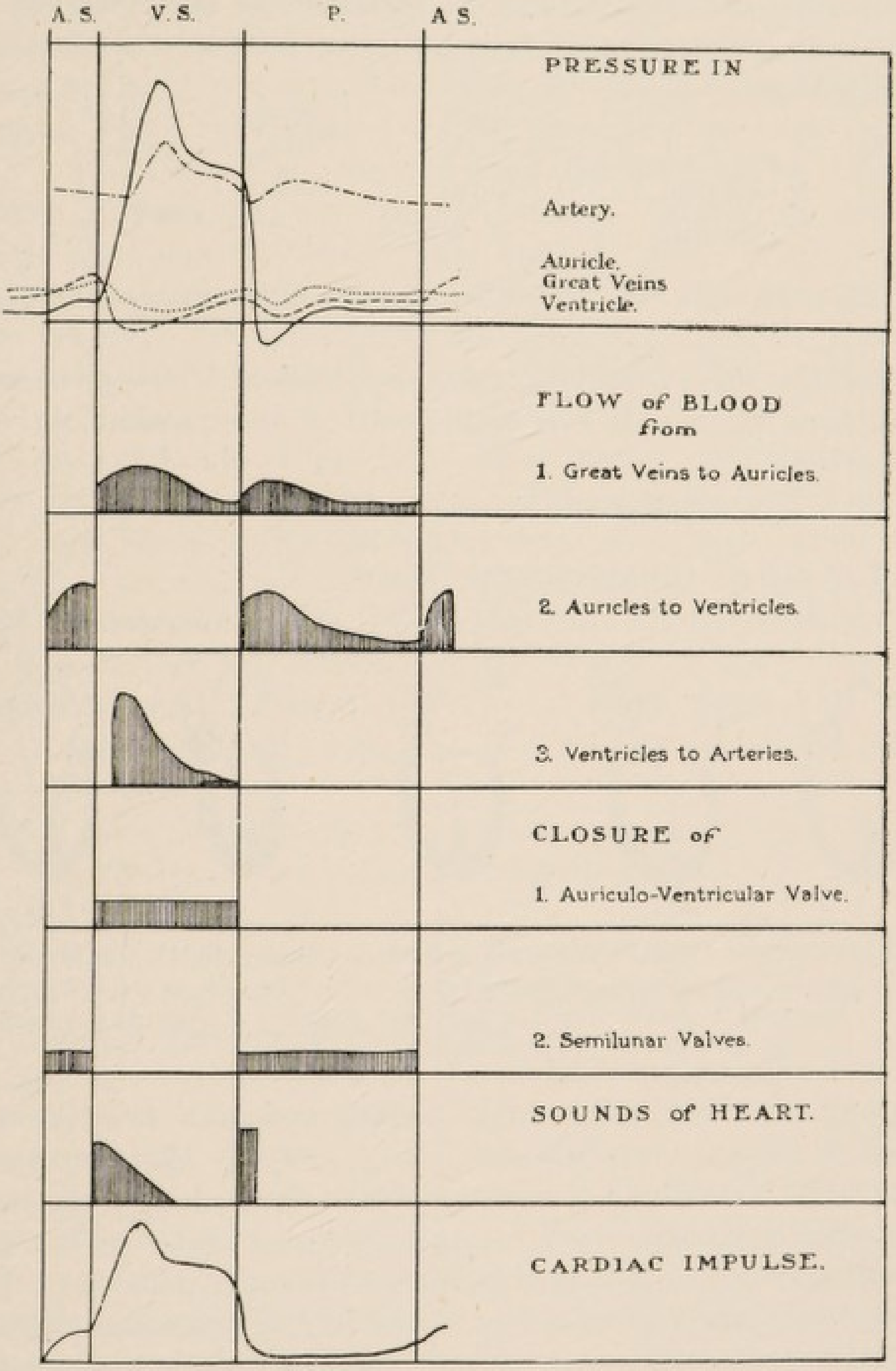


FIG. 116.—Diagram to show the relationship of the events in the Cardiac Cycle to one another. *A.S.*, auricular systole ; *V.S.*, ventricular systole ; *P.*, pause.

marked and sharp rise. Following this the fall is continuous till the next systolic elevation.

In the dog the extent of variation of the pressure in auricles and ventricles is roughly as follows—measured in millimetres of mercury—

	Left Ventricle.	Right Ventricle.	Right Auricle.
Maximum . .	+140	+60	+30
Minimum . .	− 30	−15	− 7

These changes in the pressure in the different chambers are due—

1*st.* To the alternate systole and diastole of the chambers, the first raising, the second lowering the pressure in the chambers.

2*nd.* To the action of the valves.

7. Action of the Valves of the Heart.

A. Auriculo-ventricular (fig. 117).—These valves have been already described as funnel-like prolongations of the auricles into the ventricles. They are firmly held down in the ventricular cavity by the chordæ tendineæ. When the ventricle contracts the papillary muscles pull the cusps of the valves together and thus occlude the opening between auricles and ventricles. The cusps are further pressed face to face by the increasing pressure in the ventricles, and they may become convex towards the auricles. They thus form a central core around and upon which the ventricles contract.

Fig. 117.—State of the various parts of the Heart throughout the Cardiac Cycle. 1, auricular systole; 2, beginning of ventricular systole (latent period); 3, period of outflow from the ventricle; 4, period of residual contraction; 5, beginning of ventricular diastole.

On the *left side* of the heart the strong anterior cusp of the mitral valve does not materially shift its position. It may be somewhat pulled backwards and to the left. The posterior cusp is pulled forwards against the anterior.

On the *right side* the infundibular cusp of the tricuspid valve is stretched between the superior and inferior papillary muscles, and is thus pulled towards the bulging septum, against which it is pressed by the increasing pressure inside the ventricles. The posterior cusp has its anterior margin pulled forward and its posterior margin backwards, and is thus also pulled toward the septum. The septal cusp remains against the septum. The greater the pressure in the ventricle the more firmly are these cusps pressed against one another and against the septum, and the more completely is the orifice between the auricle and the ventricle closed. On the right side of the heart other factors play an important part in occluding the orifice; the muscular fibres which surround the auriculo-ventricular opening contract, while the papillary muscles pull the auriculo-ventricular ring downwards and inwards through the chordæ which are inserted into it.

Nevertheless the occlusion of this orifice is apt to be incomplete when the right side of the heart becomes in the least over-distended, giving rise to a safety-valve action from the right ventricle.

The auriculo-ventricular valves are open during the whole of the cardiac cycle, except during the ventricular systole (fig. 116).

B. Semilunar Valves.—Before the ventricles contract these valves are closed and the various segments pressed together by the high pressure of blood in the aorta.

As the ventricles contract the pressure in them rises, until the intra-ventricular pressure becomes greater than the pressure in the arteries. Instantly the cusps of the valves are thrown back and remain thus until the blood is expelled. When the outflow of blood is completed, the cusps are again approximated by the pressure of blood in the arteries. As relaxation of the ventricles occurs, the intra-ventricular pressure becomes suddenly very low, and the high pressure of the blood in the arteries at once falls upon the upper surfaces of the cusps, which are thus forced downwards and together and thus completely prevent any back-flow of blood.

The prejudicial effect of too great pressure upon these cusps is obviated by the lower cusp being mounted on the top of the muscular septum upon which the pressure falls—the other cusps shutting down upon this one (fig. 110).

The Flow of Blood through the Heart

The circulation of blood through the heart depends upon these differences of pressure in the different chambers and upon the action of the valves.

A fluid always flows from a point of high pressure to a point of lower pressure. We may then consider the flow—

A. From Great Veins into Auricles.—This occurs when the pressure in the great veins is greater than the pressure in the auricles (fig. 116).

The pressure in the auricles is lowest at the moment of their diastole. At this time there is therefore a great flow of blood into them, but gradually this becomes less and less, until, when the ventricles dilate, another fall in the auricular pressure takes place and another rush of blood from the great veins occurs. Gradually this diminishes, and by the time that the auricles contract the flow from the great veins has stopped.

The contraction of the mouths of the great veins, which precedes the auricular systole, drives blood from the veins into the auricles, and, as these enter into contraction, no flow from the veins can occur and no back-flow from the auricles is possible (fig. 116).

B. From Auricles to Ventricles.—As the ventricles dilate, a very low pressure develops in them, and hence a great rush of blood occurs from the auricles. During the passive stage of ventricular diastole, the intra-ventricular pressure becomes nearly the same as the auricular, and the flow diminishes or may stop. When the auricles contract a higher pressure is developed, and a fresh flow of blood occurs into the ventricles. When the ventricles contract the auriculo-ventricular valves are closed, and all flow of blood from the auricles is stopped (fig. 116).

C. From Ventricles to Arteries.—When the ventricles begin to contract the intra-ventricular pressure is low, while the pressure in the arteries is high and keeps the semilunar valves shut. As ventricular systole goes on the intra-ventricular pressure rises, until after about 0·03 of a second it becomes higher than the arterial pressure (*Latent Period*). Immediately the semilunar valves are forced open and a rush of blood occurs from the ventricles (*Period of Overflow*). This usually lasts less than 0·2 second. If the ventricles are acting powerfully, and if the pressure in the arteries does not offer a great resistance to the entrance of blood, *the ventricles rapidly empty themselves* into the arteries, and the intra-ventricular pressure varies as shown in fig. 124, *b*, p. 267. If the heart, however, is not acting forcibly, or if the arterial pressure offers a great resistance to the entrance of blood, then *the outflow is slow and more continued* and in this case the trace of the intra-ventricular pressure is like fig. 124, *a*, with a well-marked *Period of Residual Contraction*. It is not so much the *absolute* force of the cardiac contraction or the *absolute* intra-arterial pressure which governs this, as the relationship of the one to the other. The heart may not be acting very forcibly, but still if the pressure in the arteries is low its action may be *relatively* strong.

The **Coronary Arteries**, unlike all the other arteries, are filled during ventricular diastole. During systole they are compressed by the contracting muscle of the heart, and it is only when the compression is removed in diastole that blood rushes into them. This helps to dilate the ventricles.

The interpretation of the various details of the **Cardiogram** is now rendered more easy. The ventricles, still full of blood, are suddenly pressed against the chest wall in systole. As the blood escapes into the arteries they press with less force, and hence the sudden slight downstroke (fig. 115, *b* to *c*). But, so long as the ventricles are contracted, the apex is kept tilted forward, and hence the horizontal plateau is maintained (*c* to *d*). The pressure of the apex disappears as the ventricles relax (*e*).

Sounds of the Heart

On listening in the region of the heart, a pair of sounds may be heard with each cardiac cycle, followed by a somewhat prolonged silence. These are known respectively as the First and Second Sounds of the Heart (fig. 116). (*Practical Physiology.*)

By placing a finger on the cardiac impulse while listening to these sounds it is easy to determine that the **first sound** occurs synchronously with the cardiac impulse—*i.e.* synchronously with the ventricular contraction.

It develops suddenly, and dies away more slowly. In character it is dull and rumbling, and may be imitated by pronouncing the syllable lūb. In pitch it is lower than the second sound.

The **second sound** is heard at the moment of ventricular diastole. Its exact time in the cardiac cycle has been determined by recording it on the cardiac tracing by means of a microphone. It develops suddenly and dies away suddenly. It is a clearer, sharper, and higher-pitched sound than the first. It may be imitated by pronouncing the syllable dŭpp.

According to the part of the chest upon which the ear is placed, these sounds vary in intensity. Over the apical region the first sound is louder and more accentuated; over the base the second sound is more distinctly heard.

The *Cause of the Second Sound* is simple. At the moment of ventricular diastole, when this sound develops, the only occurrence which is capable of producing a sound is the sudden stretching of the semilunar valves by the high arterial pressure above them and the low intra-ventricular pressure below them. The high arterial pressure comes on them suddenly like the blow of a drum-stick on a drum-head, and, by setting the valves in vibration, produces the sound.

Aortic and Pulmonary Areas.—The second sound has thus a dual origin—from the aortic valve and from the pulmonary valve; and it is possible by listening in suitable positions to distinguish the character of each of these.

The aortic valve is placed behind the sternum at the level of the lower border of the third costal cartilage. But it is deeply situated. The aorta, passing upwards and forwards, lies in close relationship to the chest wall at the junction of the right side of the sternum and the right second costal cartilage. The sound produced by the valve is conducted up the aorta, and may be heard best in this "aortic area."

On the other hand, the pulmonary valve lies in close relationship to the anterior chest wall—being covered only by the anterior border of the left lung—close to the edge of the sternum in the second left interspace. The pulmonary element of the second sound may best be heard here.

The *Cause of the First Sound* is by no means so simple. When it is heard, two changes are taking place in the heart, either of which would produce a sound.

1*st*. The muscular wall of the ventricles is contracting.

2*nd*. The stretching of the auriculo-ventricular valves.

1*st*. That the first factor plays an important part in the production of the first sound is proved by rapidly cutting out the heart of an animal, and while it is still beating—but without any blood passing through it to stretch the valves—listening to the organ with a stethoscope. With each beat the lūb sound is distinctly heard.

Apparently the wave of contraction, passing along the muscular fibres of the heart, sets up vibrations, and when these are conducted to the ear the external meatus picks out the vibration corresponding to its fundamental note, and thus produces the characters of the sound.

2*nd*. The auriculo-ventricular valves are being closed and subjected on the one side to the high ventricular pressure and on the other to the low auricular pressure. If the valves be destroyed or diseased the characters of the first sound are materially altered, or the sound may be entirely masked by a continuous musical sound—a murmur. Again, it has been maintained that a trained ear can pick out in the first sound the note corresponding to the valvular vibration.

The idea that the impulse of the heart against the chest wall plays a part in the production of this sound is based upon the fallacious idea that the heart "*hits*" the chest wall. All that it does is to press more firmly against it.

Mitral and Tricuspid Areas.—On account of the part played by the valves in the production of the first sound, it may be considered to be double in nature—partly due to the mitral valve, partly to the tricuspid. The mitral valve element may best be heard *not* over the area of the mitral valve—which lies very deep in the thorax—but over the apex of the heart, as at this situation the left ventricle, in which the valve lies, comes nearest to the thoracic wall and conducts the sound thither. The tricuspid element may be best heard over the area of the valve, and in listening to it it is usual to go to the right extremity of the area in order, as far as possible, to eliminate the mitral sound. The best situation to select is at the junction of the fifth right costal cartilage with the sternum.

Cardiac Murmurs.—When the valves are diseased and fail to act properly, certain continuous sounds called cardiac murmurs are heard.

These owe their origin to the fact that, while a current of fluid passing along a tube of fairly uniform calibre is not thrown into vibrations and therefore produces no sound, when any marked alterations in the lumen of the tube occur—either a sudden narrowing or a sudden expansion—the flow of fluid becomes vibratory, and, setting up vibrations in the solid tissues, produces a musical sound.

Such changes in the calibre of the heart are produced in two ways:—

1*st*. By a narrowing, either absolute or relative, of the orifices between the cavities—*stenosis*.

2*nd*. By a non-closure of the valves—*incompetence*.

Stenosis.—If one of the **auriculo-ventricular** orifices is narrowed, a murmur is heard during the period at which blood normally flows through this opening. A reference to fig. 116 at once shows that this occurs during the whole of ventricular diastole, and that the flow is most powerful during the first period of ventricular diastole and during auricular systole.

If the **aortic** or the **pulmonary** valve is narrowed the murmur will be heard (fig. 116) during ventricular systole.

The narrowing need not be absolute. A dilatation of the artery will make the orifice *relatively* narrow, and will produce the same result.

Incompetence.—If the **auriculo-ventricular** valves fail to close properly, then, during ventricular systole, blood will be driven back into the auricles, and a murmur will be heard during this period.

If the **aortic** or **pulmonary** valve fails to close, the blood will regurgitate into the ventricle from the arteries during ventricular diastole, and a murmur will be heard during this period.

By the position at which these murmurs are best heard the pathological condition producing them may be determined.

Work of the Heart

The heart in pumping blood through it is doing **work**, and the amount of work may be expressed in work units—*e.g.* kilogrammetres (see p. 60). The method employed to measure this in the **dog** is to determine, by means of the cardiometer, the amount of blood expelled at each systole, and to find the resistance against which it is expelled. This gives the factors for determining the work done at each systole, and it is easy to calculate the total work in any given period (fig. 118).

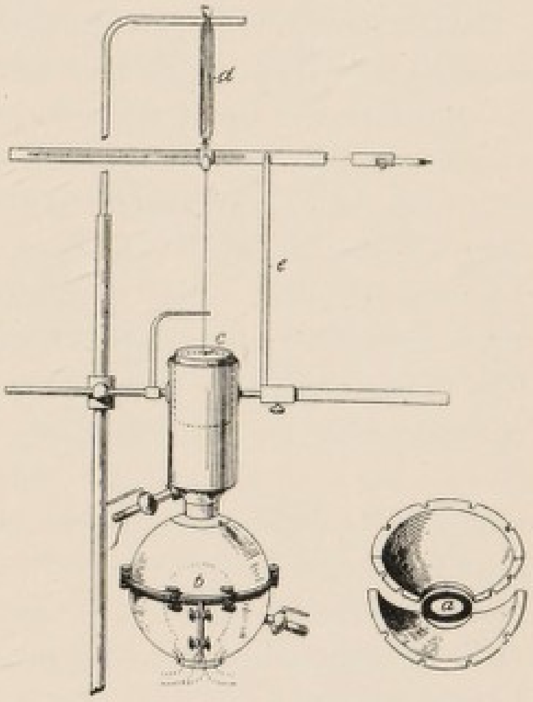


FIG. 118.—Roy's Cardiometer to measure the output of Blood from the Heart. *b*, heart in cardiometer chamber; *c*, piston recorder working on lever against rubber band, *d*.

Nature of Cardiac Contraction

The contraction of the ventricle lasts for a considerable period—0·3 seconds. Is it of the nature of a single contraction, or of a tetanus?

It is impossible to tetanise heart muscle, even by rapidly repeated induction shocks. A single stimulus applied to heart muscle produces a single prolonged contraction. Again, the mode of development of the currents of action does not indicate anything of the nature of a tetanus. With each beat of the ventricles the variation in the electric potential begins at the base and travels rapidly to the apex. This passage of the contraction wave along the fibres explains the great length of the ventricular systole as a whole. There can be no doubt that each contraction of heart muscle is of the nature of a muscle twitch. In this respect heart muscle resembles non-striped muscle.

It further resembles it in that the minimum stimulus is also a maximum stimulus—*i.e.* the smallest stimulus which will make the muscle contract makes it contract to the utmost.

But while this is the case the strength of stimulus necessary to call forth a contraction varies at different periods. To produce another contraction while the muscle is already in the period of contraction is difficult, but as it relaxes it reacts more and more readily to stimuli. In cardiac muscle, perhaps more than in any other, the staircase increase in the extent of contraction with a series of stimuli is manifested.

In cardiac muscle the *greater the resistance to contraction the stronger the force of contraction.* Hence when extra blood is poured into the heart from the veins, or when the outflow from the ventricles into the arteries is impeded, the increased strain put upon the heart muscle is met by increased contraction, and the additional work thrown upon the organ is effectually performed. Not only is this the case when temporary disturbances of the circulation occur, but when these disturbances are permanent, the heart adapts itself to them, and, if it has continuously to perform extra work, its muscular wall hypertrophies, just as the skeletal muscles grow by continual use. Of course, to allow such compensation to be established, the blood supply to the heart muscle must be sufficient, and hence, when the coronary arteries are diseased, heart failure rapidly ensues.

If the coronary arteries are clamped and then relaxed, a peculiar fibrillar contraction of the heart muscle occurs.

The maintenance of this rhythmic contraction and relaxation seems to depend greatly upon the presence of certain kations in the circulating blood. A due admixture of salts of sodium, potassium, and calcium is essential. For the frog's heart Ringer finds that the proportions which give the best results are—

NaCl	0·70 per cent.
KCl	0·03 ,,
CaCl	0·025 ,,

Since an excess of calcium salts leads to tonic contraction, and since an excess of sodium or of potassium leads to relaxation, it has been concluded that these two phases are determined by the presence of these ions.

How is the Rhythmic Contraction of the Heart maintained?

The mechanism is *in the heart itself*, for the excised heart continues to beat.

In considering what this mechanism is, it must be borne in mind that two distinct questions have to be investigated.

1*st*. How does the contraction, once started, pass in regular sequence from one part of the heart to the other?

2*nd*. What starts each rhythmic contraction?

1*st*. **Propagation of the Wave of Contraction.**—In the heart of many of the lower animals, and in the embryo of mammals, no nervous structures are to be found, and the rhythmic contraction is manifestly simply a function of the muscular fibres.

Even in the heart of animals with well-marked nerve cells in the walls of the heart, and with nerve fibres coursing among the muscular fibres, the conduction of the contraction is purely a function of the muscles. For if the heart of a frog be cut across and across, so that all nerve fibres are severed, the contraction passes along it. The rate at which the contraction travels is slow, only about 10 to 15 centimetres per second.

Since in the mammalian heart muscular continuity between auricles and ventricles through the band of His is of small extent, the wave of contraction is delayed at this point, and in the dying heart, and in various pathological conditions, the contraction frequently fails altogether to pass this block, and thus the ventricles either stop beating before the auricles, or respond to every second or third auricular contraction.

2*nd*. **Starting Mechanism of Contraction.**—In the early fœtal heart no nerve structures have been found, yet it beats regularly and rhythmically. In the apex of the ventricle of the frog there are no nerve structures, yet, if the apex be cut off and repeatedly stimulated at regular intervals with galvanic making and breaking stimuli, it will, after a time, begin to contract spontaneously, regularly and rhythmically. Not only so, but if the apex be tied on to a tube, and a stream of blood passed through it, it will again start contracting regularly and rhythmically.

These experiments clearly show that regular rhythmic contraction is a function of cardiac muscle.

In the cardiac cycle in the frog each contraction starts in the sinus. What part does the sinus take in initiating contraction?

If a ligature be tightly applied between the sinus and auricles in the frog (*Stannius' Experiment*), the sinus continues to beat, and the auricles and ventricle *usually* stop beating for a longer or shorter period. But ultimately they begin to beat again. Hence it would seem that it is not any special mechanism in the sinus which is essential in starting cardiac contraction. A ligature subsequently applied between auricles and ventricle sometimes starts the ventricle, sometimes the auricles, sometimes neither. Hence we see *that any part of the heart has the power of originating rhythmical contractions*, although usually the sinus initiates it. The sinus more than any other part of the heart has the property of rhythmic contraction. (*Practical Physiology.*)

We have no evidence that the nerve cells in the sinus or elsewhere have anything to do with this; and so far as we at present know, the initiation as well as the propagation of the cardiac contraction is a function of the muscular fibres.

3rd. **Intra-cardiac Nervous Mechanism.** — In the frog's heart nervous structures exist, and are distributed as follows (fig. 119):—

1*st.* In the wall of the sinus venosus there is a plexus of nerve cells and nerve fibres constituting the ganglion of the sinus (Remak's ganglion).

2*nd.* In the inter-auricular septum a similar plexus constitutes the ganglion of the auricular septum.

3*rd.* In the auriculo-ventricular groove a plexus forms the auriculo-ventricular ganglion (Bidder's ganglion). With these intra-cardiac ganglia the terminations of the nerves to the heart form definite synapses.

Nerve cells exist in the mammalian heart, but there is not the same differentiation into distinct groups. Nevertheless they are abundant round the mouths of the great veins, round the edges of the inter-auricular septum, and round the auriculo-ventricular groove.

While there is no evidence that the nervous structures play an important part in starting or keeping up the contractions, there is evidence that they exercise a checking or controlling action.

If the region between the sinus and auricles in the frog's heart is stimulated by the interrupted current from an induction coil, the heart is slowed or stopped. (*Practical Physiology.*)

If atropine be first applied electric stimulation is without result. (*Practical Physiology.*)

These experiments seem to indicate that *there is in the heart a checking mechanism which may be stimulated by electricity, and which is paralysed by atropine.*

4*th*. **Connections of the Heart with the Central Nervous System.**—In the **frog** a branch from the vagus connects the central nervous system with the heart. When the branch is cut no effect is produced, showing that it is not constantly in action; but when the lower end is stimulated, the heart is generally slowed or brought to a standstill. Sometimes the effect is not marked. The reason for this is that the cardiac branch of the vagus in the frog is really a double nerve derived in part from the spinal accessory and in part from fibres which reach the vagus from the superior thoracic sympathetic ganglion. If the spinal accessory is stimulated, the heart is always slowed; and if the sympathetic fibres are stimulated, it is quickened. Generally stimulation of the cardiac branch containing these two sets of fibres simply

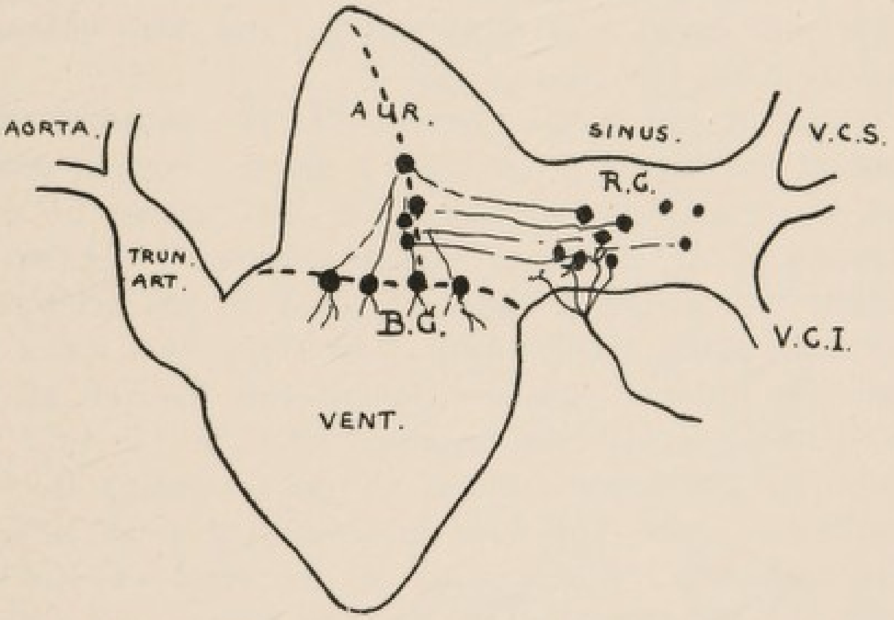


FIG. 119.—Scheme of the various chambers of the Frog's Heart and of the distribution of the intracardiac nervous mechanism.

gives the result of stimulating the former, but sometimes the stimulation of the latter masks this effect. (*Practical Physiology.*)

In the **mammal** three sets of nerve fibres pass to the heart:—

1*st.* The superior cardiac branch of the vagus starts from near the origin of the superior laryngeal nerve, and passes to the heart to end in the endocardium (fig. 120, *S.C.*).

2*nd.* The inferior cardiac branch of the vagus leaves the main nerve near the recurrent laryngeal, and passes to join the superficial cardiac plexus in the heart (fig. 120, *I.C.*).

3*rd.* The sympathetic nerve fibres come from the superior thoracic and inferior cervical ganglia, and also end in the superficial cardiac plexus (fig. 120, *S.*).

Functions of the Cardiac Nerves.—A. The **Superior Cardiac Branch of the Vagus** is an ingoing nerve. Section produces no effect; stimulation of the lower end causes no effect; stimulation of the upper end causes slowing of the heart and a marked fall in the pressure of blood in the arteries, and it may cause pain. The slowing of the heart is a reflex effect through the inferior cardiac branch; and the fall of blood pressure, which is the most manifest effect, is due to a reflex dilatation of the vessels of the abdomen, causing the blood to accumulate there, and thus to lessen the pressure in the arteries generally. On account of its effect on the blood pressure, this nerve is called *the depressor nerve.*

B. Inferior Cardiac Branch of Vagus.—Section of the vagus or of this branch causes acceleration of the action of the heart. The nerve is therefore constantly in action. Stimulation of its central end has no effect; stimulation of its peripheral end causes a slowing or stoppage of the heart. It is therefore the checking or inhibitory nerve of the heart.

1. *Course of the Fibres.*—These fibres leave the central nervous system by the spinal accessory, and pass to the heart to form connections with the cells of the cardiac plexuses.

2. *Centre.*—The fibres arise from a centre in the medulla oblongata, which can be stimulated to increased activity either directly or reflexly. (1) *Direct stimulation* is brought about by (*a*) sudden anæmia of the brain, as when the arteries

to the head are clamped or occluded; (*b*) increased venosity of the blood, as when respiration is interfered with; (*c*) the

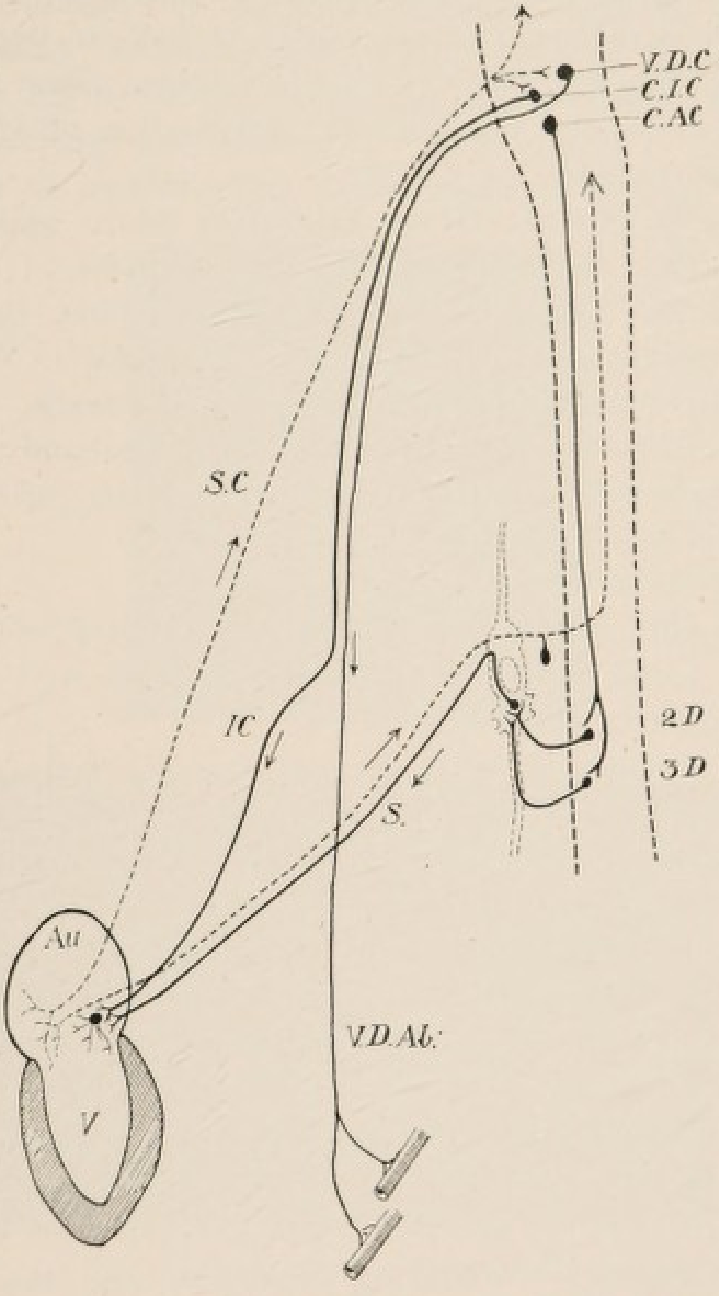


Fig. 120.—Connections of the Heart with the Central Nervous System. *Au.*, auricle; *V.*, ventricle; *V.D.C.*, abdominal vaso-dilator centre; *C.I.C.*, cardiac inhibitory centre; *C.A.C.*, cardio-augmentor centre; *S.C.*, superior cardiac branch of the vagus; *I.C.*, inferior cardiac branch of the vagus with cell station in the heart; *S.*, cardio-sympathetic fibres with cell station in the lenticular ganglion; *V.D.Ab.*, vaso-dilator fibres to abdominal vessels. The continuous lines are outgoing, the broken lines are ingoing nerves.

concurrent action of the respiratory centre (see p. 310). (2) *Reflex stimulation* is produced through many nerves. In the rabbit stimulation of the 5th cranial nerve by the inhalation of ammonia vapours has this action, and in all animals stimulation of the abdominal nerves produces the same effect. This reflex stimulation of the centre is used to determine its position in the medulla. It can be induced after removal of the brain above the medulla, but destruction of the medulla entirely prevents it.

3. *Mode of Action.*—These inhibitory fibres appear to act by stimulating the local inhibitory mechanism in the heart; and when this has been poisoned by atropine, they cannot act. According to the observation of Gaskell, they excite in the heart anabolic changes, since the electric current of injury is increased when they are stimulated, indicating that the difference between the living part of the heart and the injured part is increased.

4. *Result of Action.*

(*a*) The output of blood from the heart is diminished, and thus less blood is forced into the arteries, and the blood pressure falls (fig. 126).

(*b*) The rhythm of both auricles and ventricles is slowed, but the effect on the auricles is more marked than upon the ventricles, and the ventricles may show a contraction rhythm independent of that of the auricles (fig. 121, *A.*).

(*c*) The force of contraction of the auricles is decreased. In the ventricles the systole becomes less complete and the cavities become more and more distended, either as a result of decrease in the force of contraction or as a mechanical result of the accumulation of blood due to the decreased output per unit of time. In the heart of the tortoise excitability and conductivity are decreased, and the auricular contraction may fail to pass to the ventricles.

C. Sympathetic Fibres.—The *outgoing* fibres are the augmentors and accelerators of the heart's action. When they are cut the heart may beat slower. When the peripheral end is stimulated, the rate and force of the heart are increased.

1. *Course of the Fibres.*—These are small medullated fibres. They leave the spinal cord by the anterior roots of the 2nd, 3rd and 4th dorsal nerves, passing to the stellate ganglion where they have their cell stations (fig. 120). From the cells in this ganglion non-medullated fibres run on in the annulus

of Vieussens, and from this and from the inferior cervical ganglion they pass out to the muscular fibres of the heart.

2. *The Centre* is in the medulla, and it may be stimulated by stimulating various ingoing nerves, such as the sciatic; or it may be set in action from the higher nerve centres in various emotional conditions.

3. *Mode of Action.*—The fibres seem to act (*a*) upon the muscular fibres, increasing their excitability and conductivity; (*b*) upon the inhibitory mechanism, throwing it out of action.

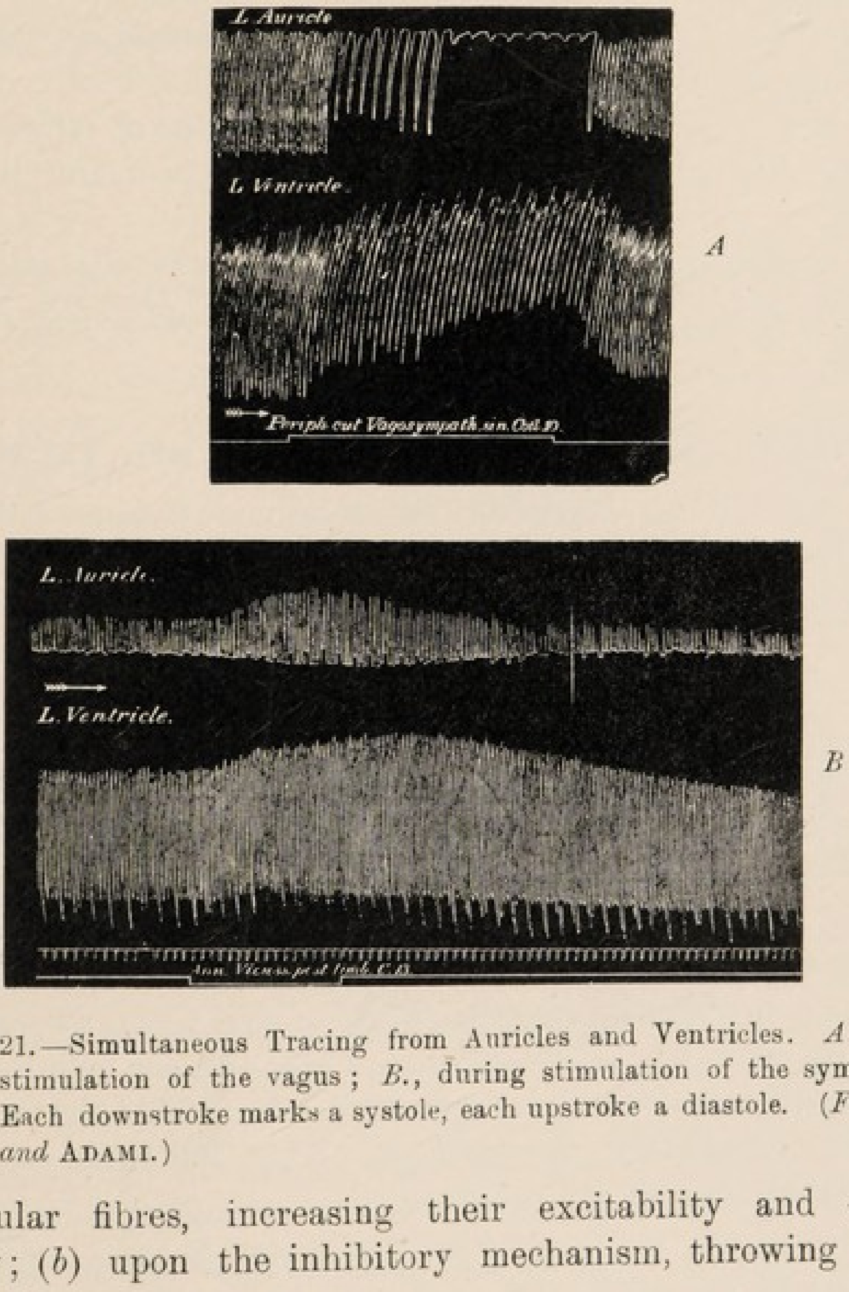


FIG. 121.—Simultaneous Tracing from Auricles and Ventricles. *A.*, during stimulation of the vagus; *B.*, during stimulation of the sympathetic. Each downstroke marks a systole, each upstroke a diastole. (*From* ROY *and* ADAMI.)

4. *Result of Action*—

(*a*) The output of blood from the heart is increased, and the pressure of blood in the arteries is raised.

(*b*) The rate of the rhythmic movements of auricles and ventricles is increased.

(*c*) The force of contraction of auricles and ventricles is increased.

It is probable that the cardiac sympathetic also carries *ingoing fibres* which enter the cord in the lower cervical region. The pain experienced in the arm in heart disease is generally thought to be due to the implication of these fibres leading to the sensation which is referred to the corresponding somatic nerves (p. 151).

The vagus is thus the protecting nerve of the heart, reducing its work and diminishing the pressure in the arteries.

The sympathetic is the whip which forces the heart to increased action in order to keep up the pressure in the arteries.

III. CIRCULATION IN THE BLOOD AND LYMPH VESSELS

The general distribution of the various vessels—arteries, capillaries, veins, and lymphatics—has been already considered (fig. 107, p. 225).

Structure

(*The structure of the walls of each must be studied practically.*)

The capillaries are minute tubes of about 12 micromillimetres in diameter, forming an anastomising network throughout the tissues. Their wall consists of a single layer of endothelium. On passing from the capillaries to arteries on the one side, and to veins and lymphatics on the other, non-striped muscle fibres make their appearance encircling the tube. Between these fibres and the endothelium a fine elastic membrane next appears, while outside the muscles a sheath of fibrous tissue develops. Thus the three essential coats of these vessels are produced:—

Tunica intima, consisting of endothelium set on the internal elastic membrane.

Tunica media, consisting chiefly of the visceral muscular fibres.

Tunica adventitia, consisting of loose fibrous tissue.

The coats of the arteries are thick; those of the veins are thin. In the large arteries the muscular fibres of the media are largely replaced by elastic fibres, so that the vessels may better stand the strain of the charge of blood which is shot from the heart at each contraction. In the veins double flaps of the tunica intima form valves which prevent any regurgitation of blood.

The great characteristic of the walls of the *large arteries* is the toughness and elasticity given by the abundance of elastic fibrous tissue, of the *small arteries* the contractility due to the preponderance of muscular fibres.

Physiology

The circulation of blood in the vessels is that of a fluid in a closed system of elastic-walled tubes, at one end of which (the great arteries) a high pressure, and at the other (the great veins) a low pressure, is kept up. As a result of this distribution of **pressure** there is a constant **flow** of blood from arteries to veins.

Many points in connection with the circulation may be conveniently studied on a model or scheme made of indiarubber tubes and a Higginson's syringe. (*Practical Physiology.*)

A.—BLOOD PRESSURE

The distribution of pressure is the cause of the flow of blood, and must first be considered.

1. General Distribution of Pressure

That the pressure throughout the greater part of the blood vessels is positive—greater than the pressure of the atmosphere—is indicated by the fact that if a vessel is opened, the blood flows out of it. *The force with which blood escapes is a measure of the pressure in that particular vessel.* If an artery be cut, the blood escapes with great force; if a vein be cut, with much less force (fig. 122).

Arteries.—If the pressure in the aorta, in the radial, in the dorsalis pedis, and in one of the smallest arteries is measured, it is found that while it is great in the great arteries—about 160 mm. Hg in the aorta—it is much less in the small arteries. This distribution of arterial pressure might be plotted out as in fig. 122, *Ar.*

Veins.—If the pressure in any of the small veins in a medium vein, and in a large vein near the heart be measured, it will be found—

1*st.* That the venous pressure is less than the lowest arterial pressure.

2*nd.* That it is highest in the small veins, and becomes lower in the larger veins. In the great veins entering the heart it is lower than the atmospheric pressure during the first part of each ventricular diastole (fig. 122, *V.*).

Capillaries.—The pressure in the capillaries must obviously be intermediate between that in the arteries and in the veins.

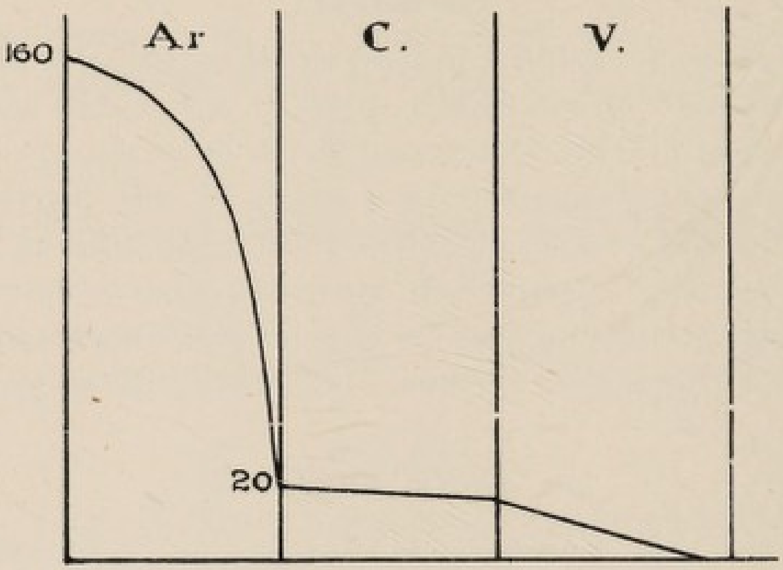


Fig. 122 —Diagram of the Distribution of Mean Blood Pressure throughout the Blood Vessels. *Ar.*, the arteries ; *C.*, the capillaries ; *V.*, the veins.

It is not so easily measured, but it may be approximately arrived at by finding the pressure which is required to empty the capillaries—*e.g.* to blanch a piece of skin.

The pressure in any part of a system of tubes depends upon two factors—

1*st.* The force propelling fluid into that part of the tubes.

2*nd.* The resistance to the outflow of fluid from that part of the tubes.

The pressure in the **Arteries** is high, because with each beat of the heart about 80 grms. of blood are thrown with the whole contractile force of each ventricle into the corresponding artery; and because the resistance offered to the outflow of blood from the arteries into the capillaries and veins is enormous. For, as the blood passes into innumerable small vessels, it is subjected to greater and greater friction—just as a river in flowing from a deep narrow channel on to a broad shallow bed is subjected to greater friction.

Thus in the arteries the powerful propulsive force of the heart and the great resistance to outflow keep the pressure high.

When the **capillaries** are reached much of the force of the heart has been lost in dilating the elastic coats of the arteries, and thus the inflow into the capillaries is much weaker than the inflow into the arteries. At the same time the resistance to outflow is small, for in passing from capillaries to veins the channel of the blood is becoming less broken up and thus opposes less friction to the inflow of the blood.

When the **veins** are reached the propelling force of the heart is still further weakened, and hence the force of inflow is very small. But, instead of there being a *resistance* to outflow from the veins into the heart, this is favoured by the suction action of the heart during diastole, and also by the fact that the great veins, in entering the heart, pass into the thorax, an air-tight box in which during each inspiration a very low pressure is developed.

What has been said of the veins applies equally to the **lymphatics**.

2. Rhythmic Variations in Blood Pressure

Before considering the exact measurements of pressure in these different vessels, certain rhythmic variations in pressure may first be considered.

A. Synchronous with the Heart Beats

Arterial Pulse

With each ventricular systole about 80 grms. of blood are thrown into the already full arteries, and the pressure in these vessels is suddenly raised.

If the finger be placed on an artery, a distinct expansion will be felt following each systole, and due to this rise of pressure. This is the arterial pulse.

This expansion develops suddenly and disappears more slowly. In some cases it may be felt by simply laying the finger on the surface of the artery without exerting marked pressure, in other cases it may be necessary to compress the artery before the pulsation is distinctly felt.

If a vein be investigated in the same way it will be found that no such pulse can be detected. In the capillaries too this pulse does not exist.

It is best marked in the great arteries, and becomes less and less distinct as the small terminal arteries are reached.

Cause of Pulse.—The arterial pulse is due to—

1*st*. The intermittent inflow of blood. The arteries expand from the sudden increase of pressure due to each sudden flow of 80 grms. of blood from the heart into the arterial system.

2*nd*. The resistance to outflow from the arteries into the capillaries.

If blood could flow freely from the arteries into the capillaries, then the inrush of blood from the heart would simply displace the same amount of blood into the capillaries and the arteries would not be expanded. As already indicated, the friction between the walls of the innumerable small arterioles and the blood is so great that the flow out of the arteries is not so free as to allow the blood to pass into the capillaries so rapidly as it is shot into the arteries. Hence, with each beat of the heart, an excess of blood must accumulate in the arteries.

3*rd*. To allow of their expanding to accommodate this excess of blood their walls must be *elastic*.

It is upon these three factors that the arterial pulse depends. Do away with any of them, and the pulse at once disappears.

Why is there no Pulse in the Veins?—Their walls are elastic, but, in the first place, instead of there being an obstruction to the outflow of blood from the veins into the heart, this is favoured by the suction action of the heart and thorax. Hence, even if an intermittent inflow were well marked, the absence of resistance to outflow would in itself prevent the development of a venous pulse. But the inflow is not intermittent. With each beat of the heart the blood does not pass freely from the arteries into the capillaries and veins, but it only slowly escapes, *just as much passing out between the beats as during the beats.* Hence the most important factor in causing a pulse, an intermittent inflow, is absent.

With no sudden intermittent inflow, and with no resistance to outflow, the development of a pulse is impossible.

In certain abnormal conditions, where, from the extreme dilatation of the arterioles, the inflow into the veins is very free, and where the outflow from the part of the body is not so free, a local venous pulse may develop.

Characters of the Pulse Wave.—If a finger be placed on the carotid artery and another upon the radial artery it will be felt that the artery near the heart expands (pulses) before that further from the heart.

The pulse **develops first in the arteries near the heart** and passes outwards towards the periphery. The reason for this is obvious. The arteries are always overfilled with blood. The ventricle drives its contents into this overfilled aorta, and to accommodate this the aortic wall expands. But since the aorta communicates with the other arteries this increased pressure passes outwards along them, expanding their wall as it goes.

The pulse wave may thus be compared to a wave at sea, which is also a wave of increased pressure, the only difference being that, while the waves at sea travel freely over the surface, the pulse wave is confined in the column of blood, and manifests itself by expanding the walls of the arteries.

It greatly simplifies the study of the pulse to regard it in this light, and to study it just as we should study a wave at sea.

1. *Velocity.*—To determine how fast a wave is travelling we might select two points at a known distance from one another, and with a watch note how long the wave takes to pass from one to the other. So with the pulse wave, two points on an artery at a known distance from one another may be taken and the time which the wave takes to pass between them may be measured.

It is thus found that the pulse wave travels at about 9 or

10 metres per second—about thirty times as fast as the blood flows in the arteries.

2. *Length of the Wave.*—To determine this in a wave at sea is easy if we know its velocity and know how long it takes to pass any one point. Suppose it is travelling at 50 feet per second, and that it takes 1 second to pass a particular point, obviously it is 50 feet in length. The same method may be applied to the pulse wave. We know its velocity, and by placing the finger on an artery we may determine that one wave follows another in rapid succession, so that there is no pause between them. Each wave corresponds to a ventricular systole, and therefore each wave must last, at any point, just the time between two ventricular systoles—just the time of a cardiac cycle. There are about 40 cycles per minute—*i.e.* per 60 seconds; hence each must last 1·5 seconds. The pulse wave takes 1·5 seconds to pass any place, and it travels at 10 metres per second; its length then is 15 metres. It is then an enormously long wave, and it has disappeared at the periphery long before it has finished leaving the aorta.

3. *The Height of the Wave.*—The height of the pulse wave, as of a wave at sea, depends primarily on the pressure causing it, but the character of the arterial wall modifies it very largely. Thus the true height of the pulse wave in the great arteries near the heart is masked by the thickness of the arterial wall.

Speaking generally, however, we may say that the pulse wave is highest near the heart, and becomes lower and lower as it passes out to the periphery, where it finally disappears altogether (fig. 128). This disappearance is due to its force becoming expended in expanding the arterial wall.

4. *The Form of the Wave.*—Waves at sea vary greatly in form, and the form of the wave might be graphically recorded on some moving surface such as the side of a ship by some floating body. If the ship were stationary a simple vertical line would be produced, but if she were moving a curve would be recorded, more or less abrupt according to her speed. From this curve the shape of the wave might be deduced, if the speed of the vessel is known.

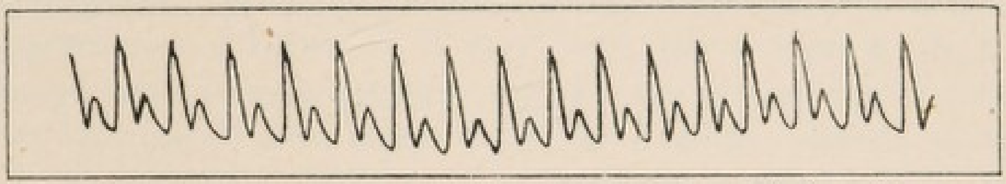
The same method may be applied to the arterial pulse.

By recording the changes produced by the pulse wave as it passes any point in an artery the shape of the wave may be deduced.

This may be done by any of the various forms of **sphygmograph.** (*Practical Physiology.*)

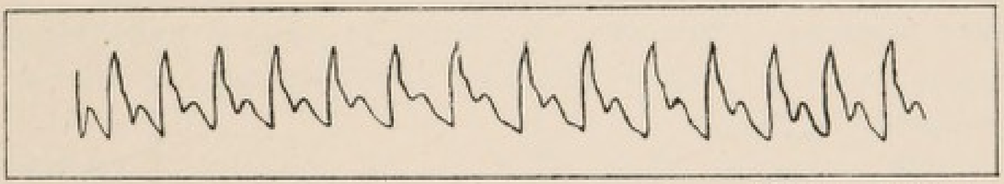
Such a tracing is not a true picture of the wave, but simply of the effect of the wave on one point of the arterial wall. Its apparent length depends upon the rate at which the recording surface is travelling and not on the length of the wave.

1.



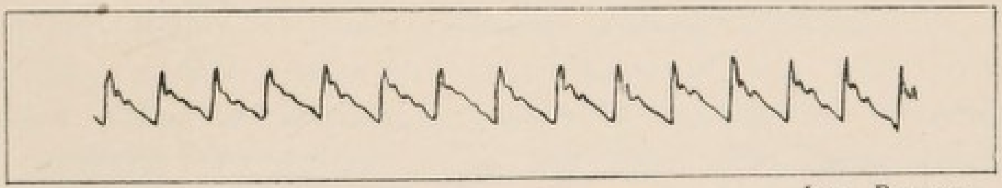
Medium Pressure.

2.



Medium Pressure.

3.



Low Pressure.

Fig. 123.—Three Sphygmographic Tracings made from the radial artery of a healthy man in the course of one hour without removing the Sphygmograph. 1 was made immediately after muscular exercise ; 2 was made after sitting still for half an hour ; and 3, after an hour.

Its height depends in part upon the length of the recording lever, in part upon the resistance offered by the instrument, in part upon the degree of pressure, with which the instrument is applied to the artery, and in part on the thickness of the arterial wall.

Such a trace shows (fig. 123)—

1*st*. That the pulse waves generally follow one another without any interval.

2nd. That the rise of the wave is much more abrupt than the fall.

3rd. That upon the descent of the primary wave there are one or more secondary waves.

One of these is constant and is very often well marked. It forms a second crest, and is hence called *the dicrotic wave.*

Between the chief crest and this secondary crest, a smaller crest is often manifest (fig. 123, 3). From its position, it is called *the predicrotic wave.* Sometimes other crests appear. If the wave has only one crest it is called a one-crested or monocrotic wave. If only the dicrotic crest is well marked it is called dicrotic. If three crests are present, tricrotic; if several crests, polycrotic.

To understand the various parts of the pulse wave it is necessary to compare it with the intra-ventricular pressure changes. This may be done by taking synchronously tracings of the intra-ventricular pressure, and of the aortic pressure (fig. 124).

Such a tracing shows that at the moment of ventricular systole the pressure in the aorta is higher than that in the left ventricle.

As ventricular systole advances the intra-ventricular pressure rises and becomes higher than the aortic. At that moment the aortic valves are thrown open and a rush of blood takes place into the aorta, raising the pressure and expanding the artery, and causing the upstroke, and *crest* of the pulse curve. As the ventricle empties itself the intra-ventricular pressure tends somewhat to fall, and, at the same time, a fall in the intra-aortic pressure also takes place. If all the blood does not leave the ventricle in the first gush, *e.g.* when the intra-aortic pressure is high as compared with the force of the heart (fig. 124, continuous line), there is a residual outflow which arrests the diminution in the aortic pressure, or may actually raise it, causing the *predicrotic wave.* As this residual outflow diminishes, the aortic pressure again falls and continues to fall until the moment of ventricular diastole. At this instant the intra-ventricular pressure suddenly becomes less than the intra-aortic, and the semilunar valves are forced downwards towards the ventricles, and thus the capacity of the aorta is slightly increased and the pressure falls. This fall in pressure is indicated by the *dicrotic notch.* But the elasticity of the semilunar valves at once makes them again spring up, thus increasing the pressure in the aorta and causing the second crest, *the dicrotic wave.* After this the pressure in the arteries steadily diminishes till the mean is reached, to be again increased by the next ventricular systole.

The form of the pulse wave varies according to the relationship between the arterial pressure and the activity of the heart.

If the heart is active and strong in relation to the arterial pressure, the main mass of the blood is expelled in the first sudden outflow, and the residual flow is absent or slight (fig. 124, dotted line). In this case there is a sudden and marked rise of the arterial pressure, followed by a steady fall till the moment of ventricular diastole. The rebound of the semilunar valves is marked in this case and causes a very prominent dicrotic wave, while the predicrotic wave is absent (fig. 123, 1). Such a condition is well seen after violent muscular exertion, and in certain fevers. In these conditions the dicrotic wave is so well marked that it can be readily felt with the finger. It is to this form of pulse that the term dicrotic is applied in medicine.

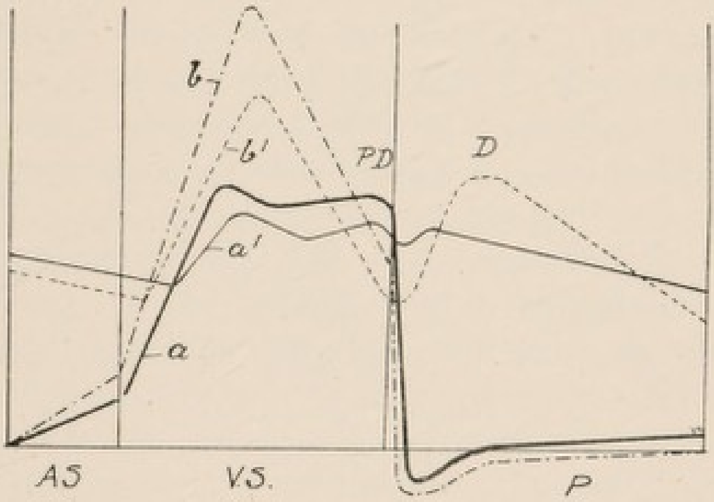


FIG. 124.—Diagram to show the relationship of the pulse wave to the cardiac cycle and the effect of altering the relationship between the activity of the heart and the arterial blood pressure. —·—·— b is the curve of intraventricular pressure, and ----- b^1 is a pulse curve with an active heart and a relatively low arterial pressure. — a and a^1 are the same with a sluggish heart and a relatively high arterial pressure.

On the other hand, if the ventricles are acting slowly and feebly in relationship to the arterial pressure, the initial outflow of blood does not take place so rapidly and completely (fig. 124, continuous line), and the initial rise in the pulse is thus not so rapid. The residual outflow of blood is more marked and causes a well-marked secondary rise in the pulse curve—the predicrotic wave. In certain cases this may be higher than the primary crest, producing the condition known as the anacrotic pulse. The relatively high intra-arterial pressure here prevents the development of a well-marked dicrotic wave.

In extreme cases of this kind, when the arterial walls are very tense, they may recover after their expansion in an irregular jerky manner, and may give rise to a series of katacrotic crests producing a polycrotic pulse (fig. 123, 3).

From what has been said it will be seen that a study of the pulse wave gives most valuable information as regards the state of the circulation, and the physician constantly makes use of the pulse in diagnosis.

Palpation of Pulse.—On placing the finger on the radial artery the points to determine are—

1*st*. The **rate** of the pulse—*i.e.* the rate of the heart's action.

2*nd*. The **rhythm** of the pulse—*i.e.* of the heart's action as regards—(1) *Strength of the various beats.*—Normally the beats differ little from one another in force—since the various heart beats have much the same strength. Respiration has a slight effect which will afterwards be considered (see p. 321). In pathological conditions great differences in the force of succeeding pulse waves occur. (2) *Time relationship of beats.*—Normally the beats follow one another at regular intervals — somewhat shorter during inspiration — somewhat longer during expiration. In pathological conditions great irregularities in this respect may occur.

3*rd*. The **volume** of the pulse wave. Sometimes the wave is high and greatly expands the artery—sometimes less high and expanding the artery less. The former condition is called a full pulse (*pulsus plenus*), the latter a small pulse (*pulsus parvus*). The fulness of the pulse depends upon two factors:—1*st*. The average tension in the arteries between the pulse beats.

If this is high, the walls of the artery are already somewhat stretched, and therefore the pulse wave expands them only slightly further. On the other hand, if the average pressure is low, the arterial wall is lax, and is readily stretched to a greater extent. *2nd.* The force of the heart. To stretch the arterial wall to a large extent requires an actively acting heart throwing a sudden large wave of blood into the arterial system at each systole. The full pulse is well seen after violent exertion, when the heart is active and the peripheral vessels fully dilated, thus allowing a free flow of blood from the arteries and thus keeping the mean arterial pressure low

4th. **Tension** of the pulse. Sometimes the pulse wave is easily obliterated by pressing on the artery—sometimes considerable force is required to prevent it from passing. To test this, two fingers must be placed on the artery. That placed nearer the heart must be pressed more and more firmly on the vessel until the pulse wave is no longer felt by the second finger. In this way the tension or force of the pulse, the maximum systolic pressure in the artery, may be roughly determined. So important, however, is this point, that various instrumental methods for determining it have been devised (see p. 273).

The tension of the pulse varies directly with the force of the heart and with the peripheral resistance. The first statement is so obvious as to require no amplification. It is also clear that if the peripheral resistance is low, so that blood can easily be forced out of the arteries into the capillaries, the arterial wall will not be so forcibly expanded as when the resistance to outflow is great. Hence a high-tension pulse is indicative of a strongly acting heart with constriction of the peripheral vessels. It is well seen during the shivering fit which so frequently precedes a febrile attack, since at that time the peripheral vessels are constricted and the heart's action excited. The tension of the pulse wave must not be confused with the mean arterial pressure (see p. 273).

5th. The **form** of the pulse wave may be investigated by means of the finger alone or by means of the sphygmograph. The points to be observed are—

(1) Does the wave come up suddenly under the finger? In the *pulsus celer* (or active pulse) it does so; in the *pulsus tardus*, on the other hand, it comes up slowly. The

former condition is indicative of an actively acting heart with no great peripheral resistance—the latter indicates that the heart's action is weak in relationship to the arterial blood pressure.

(2) Does the wave fall slowly or rapidly? Normally the fall should not be so sudden as the ascent. When the aortic valves are not properly closed the descent becomes very rapid.

(3) Are there any secondary waves to be observed? The only one of these which can be detected by the finger is the dicrotic wave, and this only when it is well marked. When it can be felt, the pulse is said to be dicrotic, and, as before stated, this indicates an actively acting heart with an arterial pressure low relatively to the strength of the ventricles.

B. Capillary Pulse

Normally there is no pulse in the capillaries. Their thin endothelial wall is not well adapted to bear such an intermittent strain. If, however, the arterioles to a district are freely dilated so that little resistance is offered to the escape of blood from the arteries, and if at the same time the outflow from the capillaries is not proportionately increased, intermittent inflow and resistance to outflow are developed, and a pulse is produced. Such a condition is seen in certain glands during activity.

C. Venous Pulse

1. The absence of a general venous pulse has been already explained. But just as in the capillaries so in the veins, a local pulse may develop.

2. In the veins entering the auricles a pulse occurs, but a pulse having no resemblance to the arterial pulse, although depending on the same three factors.

Its form is indicated in fig. 125.

Its features are to be explained as follows:—

Blood is constantly flowing into the great veins, pressed, on from behind. When the auricles contract, the outflow from these veins into the heart is suddenly checked, and consequently the veins distend. At the moment of auricular diastole the outflow is again free, a rush of blood takes place into the distending auricles, and thus the pressure in the veins falls. But as this is occurring, blood is shot from the ventricles into the arteries, and the carotid, lying behind the jugular vein, transmits its pulse to the vein as a crest. While the ventricle is contracted blood cannot pass on from the auricles, and hence it accumulates in the great vein and makes a third crest at the end of the ventricular systole. At the moment when the ventricles dilate a sudden rush of blood takes place from the veins and auricles into the ventricles, and thus a sudden fall in the pressure is produced. Gradually, as the ventricles fill, the pressure in the auricles and veins increases and they are again expanded.

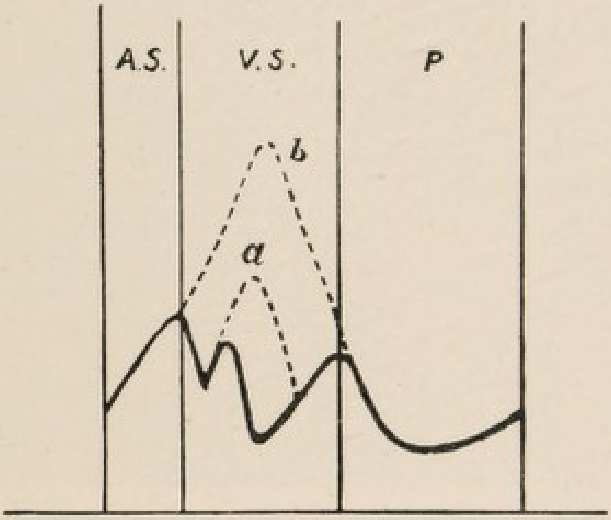


FIG. 125.—Tracings of the Pulse in the great Veins in relationship to the Cardiac Cycle. —— normal venous pulse. - - - *a* and *b* venous pulse in tricuspid incompetence.

This is the normal venous pulse. But, if the auriculo-ventricular valves are incompetent, blood is forced back into the auricles and veins when the ventricles contract, and a crest develops after the carotid crest which it may replace. The height of this crest is a good index of the amount of regurgitation.

Respiratory Variations in Blood Pressure

Not only do rhythmic changes in the *arterial* pressure occur with each beat of the heart, but larger changes are caused by the respirations—the rise in pressure in great measure corresponding to the phase of inspiration, the fall in pressure to the phase of expiration. This statement is not quite accurate, as will be seen when considering the influence of respiration on circulation (see page 311). These variations are easily seen in a tracing of the arterial pressure taken with the mercurial manometer (fig. 127, *A*).

A pulse synchronous with the respirations may also be observed in the *great veins at the root of the neck* and in the venous sinuses of the cranium when it is opened. With each inspiration they tend to collapse, with each expiration they again expand. The reason for this is that during inspiration the pressure inside the thorax becomes low and hence blood is sucked from the veins into the heart, while during expiration the intra-thoracic pressure becomes higher and thus the entrance of blood into the heart is opposed.

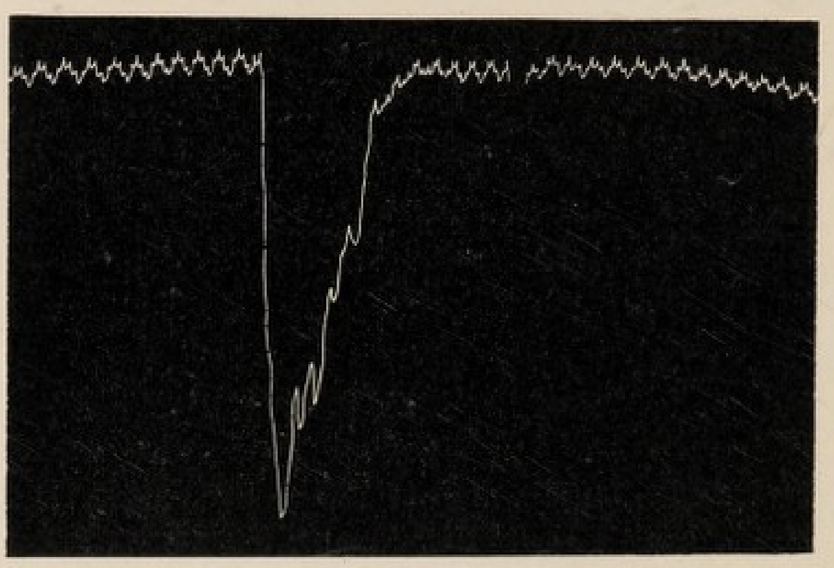


FIG. 126.—Tracing of the arterial blood pressure to show large respiratory variations, and small variations due to heart beats upon these, and the sudden fall in the pressure produced by stimulating the inferior cardiac branch of the vagus nerve.

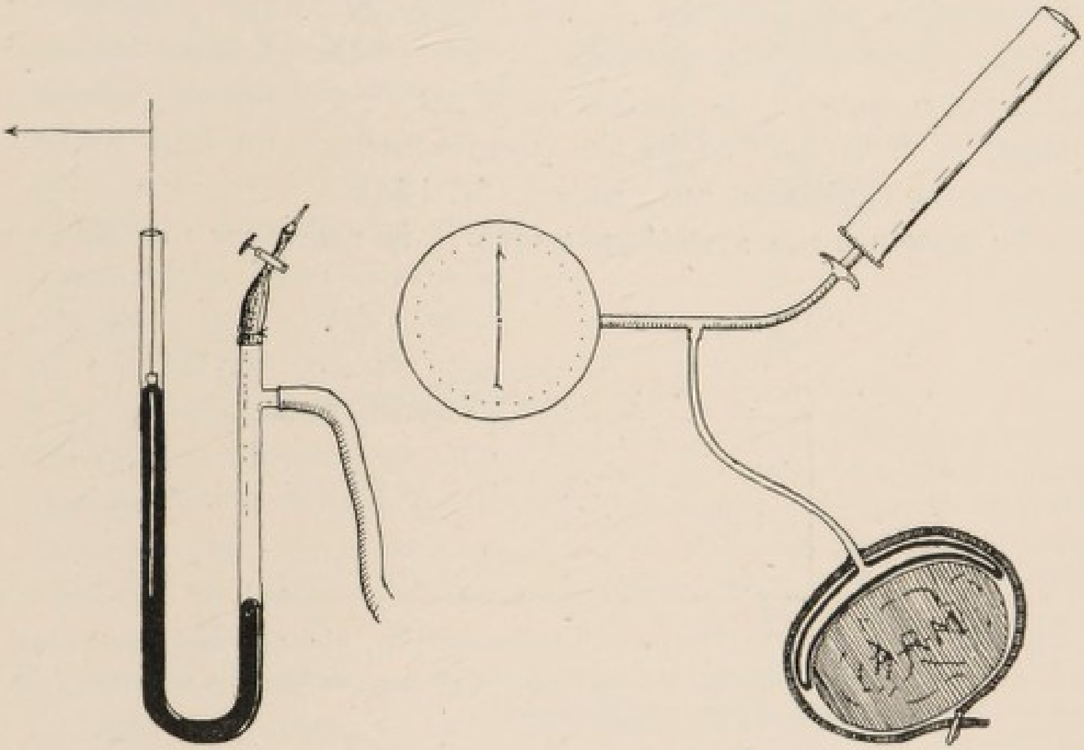
3. Mean Blood Pressure

I. PRESSURE IN THE ARTERIES

A. Methods

The first investigation of the pressure in the blood vessels was made by the Rev. Stephen Hales in 1733. He fixed a long glass tube in the femoral artery of a horse laid on its back, and found that the pressure supported a column of blood of 8 feet 3 inches, while, when the tube was placed in a vein, only 1 foot was supported. The capillary pressure is, of course, intermediate between these two.

At the present time, instead of letting the blood pressure act directly against the force of gravity, it is found more convenient, in studying the pressure in an artery, to let it act through a column of mercury placed in a U tube (fig. 127, *A.*). To record the changes in pressure a float is placed upon the mercury in the distal limb of the tube, and this carries a writing style which records the changes upon a moving surface. With such an apparatus a record such as is shown in fig. 126 is given. The actual pressure is measured by taking the difference between the level of the mercury in the two limbs of the tube. To make the measurement it is customary to describe an abscissa when the mercury is at the same level in the two sides of the tube. The difference between this and the level of the style at any moment multiplied by two, on



A *B*

Fig. 127.—*A*, The Mercurial Manometer with recording float, used in taking records of the arterial blood pressure of lower animals. *B*, The Hill-Barnard Sphygmometer, for measuring the arterial pressure without opening a vessel.

account of the depression in the proximal limb which accompanies the elevation in the distal limb, gives the blood pressure in mm. of mercury.

On the record made with such an instrument the rhythmic variations in the arterial blood pressure already considered on p. 262 and p. 271 are clearly visible. (*Practical Physiology.*)

The arterial pressure may be measured by various methods without operative interference. Some of these give the systolic pressure, *i.e.* the pressure at the maximum of the pulse wave; while others give the diastolic pressure—the pressure between the pulse waves. As shown in p. 262, the difference between these is most marked in the great arteries, and falls to zero before the capillaries are reached (fig. 128).

To measure the **systolic pressure** it is necessary to find the pressure which must be applied to an artery in order to prevent the pulse from passing.

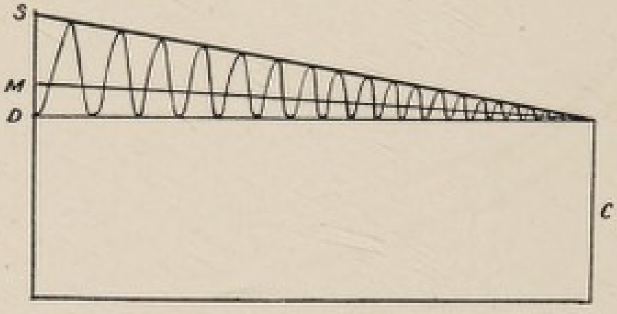


FIG. 128.—To show the difference between systolic, diastolic and mean blood pressure throughout the arterial system. *S*, systolic pressure; *D*, diastolic pressure; *M*, mean pressure.

This may be done with Riva Rocci's apparatus, by applying a bag round a limb so that it rests upon an artery. The bag is firmly strapped on by means of a broad supporting belt, and it is connected with a pump by which the pressure within it may be raised, and with a mercurial manometer by which the pressure applied may be measured in mm. of mercury. The pressure is then raised till the pulse beyond is no longer felt, and the column of mercury indicates the systolic pressure in the artery. (*Practical Physiology.*)

Instead of using the arterial pulse as the index, the passage of blood into a region rendered bloodless may be used. In Gaërtner's tonometer the bag and band are applied round the finger rendered bloodless at a pressure sufficient to prevent the blood from passing, and then the pressure is slowly lowered till the blood passes and the finger again flushes. The height of the column of mercury at that moment gives the systolic pressure in the small arteries of the finger.

The **diastolic pressure** may be measured by taking advantage of the fact that when the pressures inside and outside an artery are equal the pulse wave is best marked. A bag and band are applied to a limb upon an artery, and the movements of the pulse are observed in the column of mercury or on an aneroid barometer in the Hill Barnard instrument, or by a record taken with a small tambour on a revolving cylinder in Erlanger's instrument (fig. 129). Erlanger's instrument may also be used as the Riva Rocci for systolic pressures, and it is therefore the most valuable instrument for the study of the arterial pressure in the man. (*Practical Physiology.*)

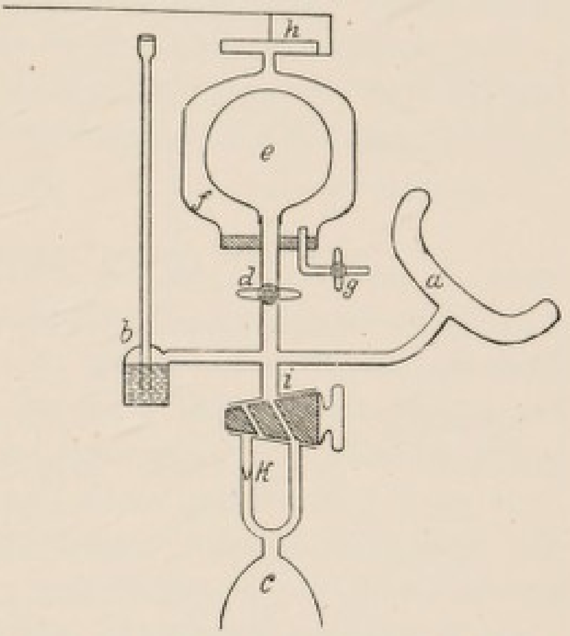


Fig. 129.—Scheme of Erlanger's apparatus for determining the arterial blood pressure without opening a blood vessel. *a*, elastic bag for arm; *b*, mercurial manometer; *c*, pump; *f*, glass bulb; *l*, rubber ball; *h*, tambour with lever.

B. Results

By these methods it has been found that the systolic pressure in the brachial artery of man is about 110 mm. of mercury, while the diastolic pressure is only about 65 mm. The difference between these, of course, gives the pulse pressure or tension.

The force of the heart and the degree of peripheral resistance both modify the arterial pressure, and normally these so act together that disturbance of one is compensated for by changes in the other. Thus, if the heart's action becomes increased and tends to raise the arterial pressure, the peripheral resistance falls and prevents any marked rise. Similarly, if the peripheral resistance is increased, the heart's action is diminished, and no rise in the pressure occurs. Under certain conditions, however, this compensatory action is not complete, and changes in the arterial pressure are thus brought about.

The *volume of blood* has a comparatively small influence on the arterial pressure, because the veins are so large that they accommodate very varying amounts of fluid.

Factors controlling Arterial Pressure

(*a*) **Heart's Action.**—The influence of this may be readily demonstrated by stimulating the vagus nerve while taking a tracing of the arterial pressure. The heart is inhibited, less blood is forced into the arteries, and the pressure falls (fig. 127).

If, on the other hand, the accelerator nerve is stimulated, the increased heart's action drives more blood into the arteries, and the pressure rises.

(*b*) **Peripheral Resistance.**—The resistance to outflow from the arteries depends upon the resistance offered in the small arteries, the walls of which are chiefly composed of visceral muscle fibres. When these fibres are contracted, the lumen of the vessels is small and the resistance is great. When they are relaxed, the lumen of the vessels dilates, and the resistance to outflow is diminished. **This muscular tissue of the arterioles acts as a stop-cock to the flow of blood from the arteries to the capillaries.** It is of great importance—

1*st*. In maintaining the uniform pressure in the arteries.

2*nd*. In regulating the flow of blood into the capillaries.

During the functional activity of a part, a free supply of blood in its capillaries is required. This is brought about by a relaxation of the muscular coats of the arterioles leading to the part. When the part returns to rest, the free flow of blood is checked by the contraction of the muscular walls of the arterioles.

The action of the arterioles is well seen under the influence of certain drugs (vaso-dilators and vaso-constrictors). If, while a tracing of the arterial pressure is being taken, nitrite of amyl is administered to the animal, it will be seen that the skin and mucous membranes become red and engorged with blood, while at the same time the arterial pressure falls.

Nitrites cause the muscular coat of the arterioles to relax, and thus, by diminishing peripheral resistance, permit blood to flow freely from the arteries into the capillaries.

Salts of barium have precisely the opposite effect, causing the skin to become pale from imperfect filling of the capillaries, and producing a marked rise in the arterial pressure. Contraction of the muscles of the arterioles is produced, and the flow of blood from arteries to capillaries is retarded.

Not only is the state of the arterioles influenced thus by drugs, but it is also affected by the internal secretions (see p. 416) from certain organs. A powerful vaso-constrictor *adrenalin* is produced in the medulla of the suprarenals.

The condition of the arterioles may be studied in many different ways—

1*st*. *By direct observation.*—1. With the naked eye. A red engorged appearance of any part of the body may be due to dilatation of the arteriole leading to it. It may, however, be due to some obstruction to the *outflow* of blood from the part. 2. With the microscope. In certain transparent structures, such as the web of the frog's foot, or the wing of the bat, or the mesentery, it is possible to measure the diameter of the arterioles by means of an eye-piece micrometer, and to study their dilatation and contraction.

2*nd*. The engorgement of the capillaries brought about by dilatation of the arterioles manifests itself also in an increased *size of the part*. Everyone knows how on a hot day, when the arterioles of the skin are dilated, it is difficult to pull on a glove which, on a cold day, when the cutaneous arterioles are contracted, feels loose. By enclosing a part of the body in a case with rigid walls filled with fluid or with air which is connected with some form of recording tambour, an increase or decrease in the size of the part due to the state of its vessels may be registered. Such an instrument is called a **plethysmograph.**

3*rd*. When the arterioles to a part are dilated and the blood is flowing freely into the capillaries, the part becomes warmer, and by fixing a **thermometer** to the surface, conclusions as to the condition of the arterioles may be drawn.

4*th*. By streaming blood through the vessels and observing the rate at which it escapes the changes in the state of the arterioles may be made out. This **perfusion method** is much used in studying the action of drugs. (*Practical Physiology.*)

5*th*. Since the state of the arterioles influences the arterial pressure, *if the heart's action is kept uniform*, changes in the **arterial blood pressure** indicate changes in the arterioles, a fall of pressure indicating dilatation, a rise of pressure, constriction.

Normal State of Arterioles. — If an arteriole in some transparent tissue be examined, it will be found to maintain a fairly uniform size, but to undergo periodic slow changes in calibre. If the ear of a white rabbit be studied, it will be seen to undergo slow changes, at one time appearing pale and bloodless, at another time red and engorged. During this latter phase numerous vessels appear which in the former condition were invisible. These slow changes are independent of the heart's action and of the rate of respirations. They appear to be due to the periodic rhythmic contraction which is a characteristic property of visceral muscle fibres. This rhythmic action is better marked in some vessels than in others.

Vaso-motor Mechanism.—If the sciatic nerve of a frog be cut, the arterioles in the foot at once dilate. If the sciatic be stimulated, the arterioles become smaller. The same results follow if the anterior roots of the lower spinal nerves, from which the sciatic takes origin, be cut or stimulated.

We must, therefore, conclude (1) that the central nervous system exerts a constant *tonic* influence upon the arterioles, keeping them in a state of semi-contraction; and (2) that this influence may be increased, and thus a constriction of the arterioles caused, and in this way the flow of blood from arteries to capillaries obstructed and the arterial pressure raised; and (3) that this influence may be diminished, so that the arterioles dilate and allow an increased flow into the capillaries from the arteries, and thus lower the arterial pressure.

These mobile arterioles, under the control of the central nervous system, constitute a *vaso-motor mechanism*, which plays a most important part in connection with nearly every vital process in the body. By it the pressure in the arteries is governed, by it the supply of blood to the capillaries and tissues is controlled, and by it the loss of heat from the body is largely regulated (p. 385).

This vaso-motor mechanism consists of the three parts :—

1*st*. The contractile muscular walls of the arterioles with the nerve terminations in them.

2*nd*. The nerves which pass to them.

3*rd*. The portions of the central nervous system presiding over these.

1. **Muscular Walls of the Arterioles.**—The muscular fibres are maintained in a state of tonic semi-contraction by nerves passing to them, and when these nerves are divided, the muscular fibres relax. But if, after these nerves have been cut, the animal be allowed to live, in a few days the *arterioles again pass into a state of tonic semi-contraction*, although no union of the divided nerve has taken place.

Certain drugs, *e.g.* digitalis and the salts of barium, act as direct stimulants to these muscle fibres.

It appears that the *muscular fibres* in the arterioles, as elsewhere, tend to maintain themselves in a state of partial contraction, which increases and diminishes in a regular rhythmic manner.

The precise part played by the nerve terminations has not been definitely established, but certain drugs appear to act specially upon them. Thus apocodeine, while it does not prevent barium salts from constricting the vessels, prevents the constricting action of extracts of the medulla of the suprarenals, even when the nerves are cut. Hence it must be concluded that it paralyses a nervous mechanism in the arteriole wall which is stimulated by the suprarenal extract.

Normally this muscular mechanism is controlled by the nervous system.

2. **Vaso-motor Nerves.**—When a nerve going to any part of the body is cut the arterioles of the part generally dilate, when it is stimulated the arterioles are *usually* contracted; sometimes, however, they are dilated. In no case does section of a nerve cause constriction of the arterioles.

These facts prove that the vaso-motor nerves may be divided into two classes:—

1*st*. Vaso-constrictor.

2*nd*. Vaso-dilator.

A. **Vaso-constrictor Nerves.**—The fact that section of these at once causes a dilatation of the arterioles proves that they are constantly transmitting impulses from the central nervous system.

Course.—The course of these fibres has been investigated by section and by stimulation (fig. 130).

They leave the spinal cord chiefly in the dorsal region by the anterior roots of the spinal nerves, pass into the sympathetic ganglia, where they have their cell stations, and then as non-medullated fibres pass, either along the various sympathetic nerves to the viscera, or back through the grey ramus (see fig. 75, p. 151), into the spinal nerve, and run in it to their terminations.

B. **Vaso-dilator Nerves.**—A good example of such a nerve is to be found in the chorda tympani branch of the facial nerve, which sends fibres to the submaxillary and sublingual salivary glands. If this nerve be cut, no change takes place in the vessels of the gland, but, when it is stimulated, the arterioles dilate and allow an increased flow of blood through the capillaries. These fibres, therefore, instead of increasing the activity of muscular contraction, diminish or inhibit it. They

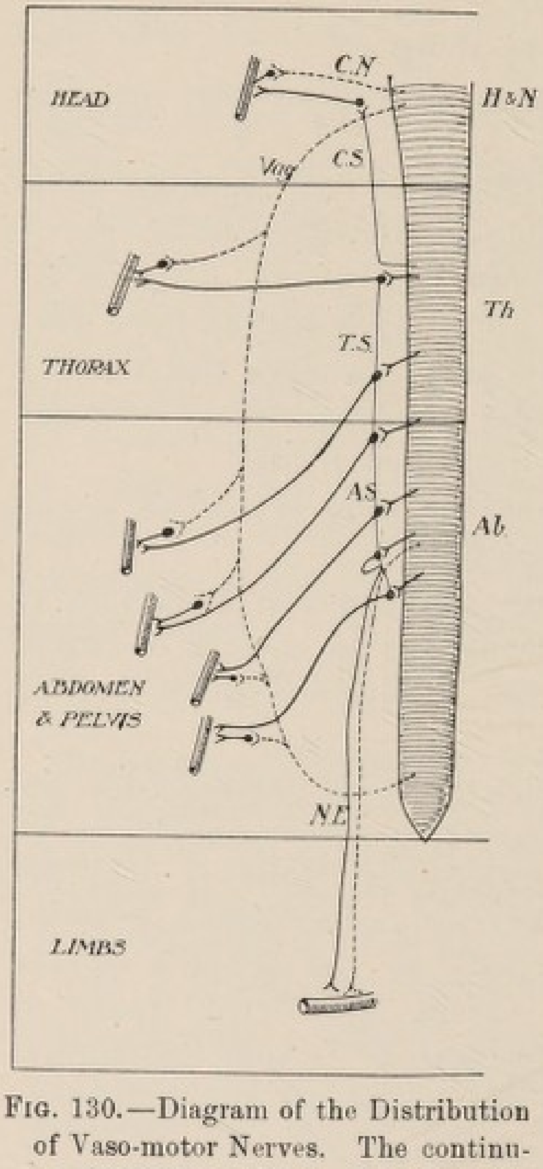


FIG. 130.—Diagram of the Distribution of Vaso-motor Nerves. The continuous line shows the vaso-constrictors, the dotted line the vaso-dilators. *C.N.*, cranial nerves; *Vag.*, vagus; *T.S.*, thoracic sympathetic; *A.S.*, abdominal sympathetic; *N.L.*, nerves to the leg.

play the same part in regard to the muscular fibres of the arterioles as the inferior cardiac branch of the vagus does in regard to the cardiac muscular fibres. As examples of vaso-dilator nerves the gastric branches of the vagus carrying vaso-dilator fibres to the mucous membrane of the stomach, and the nervi erigentes carrying vaso-dilator fibres to the external genitals, may be taken.

The vaso-dilator nerves of most parts of the body run side by side with the vaso-constrictor nerves; and, hence, curious results are often obtained. If the sciatic nerve of a dog be cut, the arterioles of the foot dilate. If the peripheral end of the cut nerve is stimulated, the vessels contract. But, after a few days, if the nerve be prevented from uniting, the arterioles of the foot recover their tonic contraction, and, if the sciatic nerve is then stimulated, a dilatation, and not a constriction, is brought about. The vaso-constrictor fibres seem to die more rapidly than the vaso-dilator fibres which run alongside of them. Under certain conditions the activity of the vaso-dilator fibres seems to be increased. Thus, if, when the limb is warm, the sciatic nerve is stimulated, dilatation rather than constriction may occur. Again, while rapidly repeated and strong induction shocks are apt to cause constriction, slower and weaker stimuli tend to produce dilatation.

Course.—The vaso-dilator nerves pass out chiefly by the anterior roots of the various spinal nerves, and do not pass through the sympathetic ganglia, but run as medullated fibres to their terminal ganglia (fig. 130). Bayliss has recently shown that the vaso-dilator fibres for the hind limb leave the cord by the posterior roots, and that they are connected with the cells in the ganglia.

3. **Portions of Nervous System Presiding over the Vasomotor Mechanism.**—Since a set of nerves causing constriction of the arterioles, and another set causing dilatation exist, we must conclude that there are two mechanisms in the central nervous system—one a vaso-constrictor, the other a vaso-dilator.

A. Vaso-constrictor Centre.—(*a*) *Mode of Action.*—This mechanism is constantly in action, maintaining the tonic contraction of the arterioles.

If any afferent nerve be stimulated, the effect is to increase the activity of the mechanism, to cause a general constriction of arterioles, and thus to raise the general arterial pressure. The centre is, therefore, capable of **reflex** excitation. In ordinary conditions so many afferent nerves are constantly being stimulated, that it is not easy to say how far the tonic action of this centre is reflex and dependent on the stream of afferent impulses.

But this centre may also be **directly acted upon** by the condition of the blood and lymph circulating through it. When the blood is not properly oxygenated and freed from carbon dioxide, as in asphyxia or suffocation, this centre is stimulated and a general constriction of arterioles with high blood pressure results.

(*b*) *Position.*—In investigating the position of the centre we may take advantage of—

1*st*. Its constant tonic influence. Removal of the centre at once causes dilatation of arterioles.

2*nd*. The fact that it may be reflexly stimulated. If the vaso-constrictor centre be removed, stimulation of an afferent nerve no longer causes constriction of the arterioles.

Removal of the whole brain above the pons Varolii leaves the centre intact.

Separation of the pons Varolii and medulla oblongata from the spinal cord at once causes a dilatation of the arterioles of the body, and prevents the production of reflex constriction by stimulation of an afferent nerve.

The main part, at least, of the vaso-constrictor mechanism is therefore situated in the pons Varolii and medulla oblongata.

The extent of this centre has been determined by slicing away this part of the brain from above downwards, and studying the influence of reflex stimulation after the removal of each slice.

It is found that at a short distance below the corpora quadrigemina, the removal of each succeeding part is followed by a diminution in the reflex constriction, until, at a point close to and just above the calamus scriptorius, all reflex response to stimulation stops.

The centre is therefore one of very considerable longitudinal extent.

But it has been found that, if, after section of the spinal cord high up, the animal be kept alive for some days, the dilated arterioles again contract, and stimulation of afferent nerves entering the cord below the point of section causes a further constriction. If now another section be made further down the cord, the arterioles supplied by nerves coming from below the point of section will again dilate. This shows that **secondary vaso-constrictor centres,** tonic in action and capable of having their activity reflexly increased, exist all down the grey matter of the spinal cord. Normally these are under the domain of the dominant centre, but when this is out of action they then come into play.

B. Vaso-dilator Centre. — (*a*) *Mode of Action.* — This mechanism is not constantly in action. Section of a vaso-dilator nerve does not cause vascular dilatation. It may be excited reflexly, but in a different manner from the vaso-constrictor mechanism.

Stimulation of an afferent nerve causes a dilatation of the arterioles in the part from which it comes, and a constriction of the arterioles throughout the rest of the body. If a sapid substance, such as pepper, be put in the mouth, the buccal mucous membrane and the salivary glands become engorged, while there is a constriction of the arterioles throughout the body. The vaso-dilator central mechanism is not general in its action like the vaso-constrictor, but is specially related to the different parts of the body.

This is a matter of the greatest importance in physiology and pathology. It explains the increased vascularity of a part when active growth is going on. The changes in the part, or the products of these, stimulate the afferent nerve. This reflexly stimulates the vaso-dilator mechanism of the part, and thus causes a free flow of blood into the capillaries, and at the same time maintains or actually raises the arterial pressure by causing a general constriction of the arterioles, and thus forces more blood to the situation in which it is required.

The same process occurs in the case of the stomach during digestion, in the case of the kidney during secretion, and in the process of inflammation.

Not only does peripheral stimulation act in this way, but various states of the brain, accompanied by emotions, may stimulate part of the vaso-dilator mechanism, as in the act of blushing.

Again, it has been shown that stimulation of the central end of the depressor nerve (superior cardiac branch of the vagus) causes a dilatation of the arterioles chiefly in the abdominal cavity, but also throughout the body generally. This is the most generalised vaso-dilator reflex known (see p. 254).

(*b*) *Position.*—While the dominant vaso-constrictor centre is in the medulla, the vaso-dilator centres seem to be distributed throughout the medulla and spinal cord.

II. PRESSURE IN THE CAPILLARIES

This may be determined by finding the pressure required to blanch the skin or to occlude the capillaries of some transparent membrane.

It has already been shown that the pressure is less than in the arteries and greater than in the veins.

Like the pressure in the arteries, it depends upon the two factors—

1*st.* Force of inflow.

2*nd.* Resistance to outflow.

1*st.* **Variations in the Force of Inflow.**—The capillary pressure may undergo marked local changes through the *vaso-motor mechanism.* Wherever the function of a part is active, dilatation of the arterioles and an increased capillary pressure exists, and, when the influence of vaso-dilator nerves is withdrawn, the capillary pressure falls.

But the capillary pressure may also be modified by the *heart's action*, inasmuch as the arterial pressure, by which blood is driven into the capillaries, depends upon this. In cardiac inhibition not only is arterial pressure lowered, but capillary pressure may also fall. In augmented heart action both arterial and capillary pressure are raised.

2*nd.* **Variations in Resistance to Outflow.**—Normally the flow from capillaries to veins is free and unobstructed; but, if the veins get blocked, or if the flow in them is retarded by gravity, the capillaries get engorged with the blood which cannot escape from them. This increased pressure in the capillaries is very different from that caused by increased inflow. The flow through the vessels is slowed or may be stopped instead of being accelerated, and the blood gets deprived of its nourishing constituents, loaded with waste products, and tends to exude into the lymph spaces, causing *dropsy*.

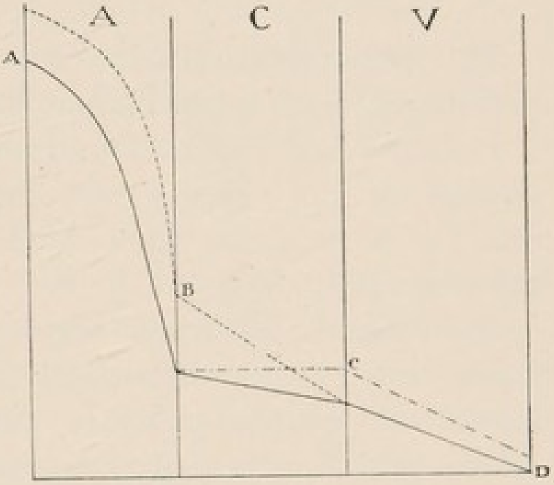


FIG. 131.—The Changes in Blood Pressure in the Capillaries produced by increasing the arterial pressure - - - - - - , and by obstructing the venous flow — - — - —. *A*, arteries; *C*, capillaries; *V*, veins.

It is, therefore, most important to distinguish between high capillary pressure from dilated arterioles or an active heart, and high pressure due to venous obstruction.

A condition very similar to that described, but producing a *capillary pressure high relatively to the pressure in the arteries—though not absolutely high*—is seen in cases of failure of the heart, when that organ is not acting sufficiently strongly to pass the blood on from the venous into the arterial system. Here the arterial pressure becomes lower and lower, the venous pressure higher and higher, and along with this the capillary pressure becomes high in relationship to the arterial pressure. The blood is not forced through these channels, and congestion of the capillaries and dropsy may result.

The *influence of gravity* plays a very important part on the capillary pressure, since it has so marked an influence on the flow of blood in the veins. When, through heart failure, the blood is not properly sucked up from the inferior extremities, this increased pressure becomes very marked indeed.

3rd. But the pressure in the capillaries may also to a certain extent be varied by the *withdrawal of water from the body*, as in purgation or diuresis, or by the addition of large quantities of fluid to the blood. The venous system is, however, so capacious that very great changes in the amount of blood in the vessels may take place without materially modifying the arterial or capillary pressure while affecting temporarily the venous pressure.

III. PRESSURE IN THE VEINS

The pressure in the veins is so low that it may best be determined by a water manometer.

In the veins the force of inflow is small; the resistance to outflow is nil. Hence the pressure is small, and steadily diminishes from the small veins to the large veins entering the heart (fig. 131).

The **venous pressure may be modified by** variations in these two factors. Constriction of the arterioles tends to lower the venous pressure, dilatation to raise it. On the other hand, **increased heart's action**, which so markedly tends to raise arterial pressure, diminishes the pressure in the larger veins, because the blood is thus more rapidly driven from veins into arteries, and because the heart, which in its powerful systole drives out more blood, in its diastole sucks in more.

Compression of the thorax has a very marked effect in retarding the flow of blood from the great veins into the heart, and thus tends to raise the venous pressure and to lower the arterial pressure. Venous pressure may be temporarily modified by the *loss or gain of water*.

IV. PRESSURE IN THE LYMPHATICS

No exact determination of the lymph pressure in the tissue spaces has been made, but since there is a constant flow from these spaces through the lymphatic vessels and through the thoracic duct into the veins at the root of the neck, the pressure in the tissue spaces must be higher than the pressure in the great veins.

This pressure is kept up by the formation of lymph from the blood, and from the cells of the tissues (see p. 223).

B.—FLOW OF BLOOD

The flow of blood, as already indicated, depends upon the distribution of pressure, a fluid always tending to flow from the point of higher pressure to the point of lower pressure. Since a high pressure is maintained in the aorta and a low pressure in the veins entering the heart and in the cavities of the heart during its diastole, the blood must flow through the circulation from arteries to veins. (*Practical Physiology.*)

Velocity

The velocity of the flow of a fluid depends upon the **width of the channel.** Since in unit of time unit of volume must pass each point in a stream if the fluid is not to accumulate at one point, the velocity must vary with the sectional area of the channel. In the case of a river, in each second the same amount of water must pass through the narrowest and through the widest part of its channel. Now for a ton of water to get through any point in a channel one square yard in sectional area in the same time as it takes to pass a point in a channel ten square yards in area, it must obviously flow with greater velocity. This may be stated in the proposition that the velocity (V) of the stream is equal to the amount of blood passing any point per second (v) divided by the sectional area of the stream (S)—

$$V = \frac{v}{S}$$

where S is the radius squared multiplied by the constant 3·14.

In the vascular system the sectional area of the aorta is small when compared with the sectional area of the smaller arteries; while the sectional area of the capillary system is no less than 700 times greater than that of the aorta. In the venous system the sectional area steadily diminishes, although it never becomes so small as in the corresponding arteries, and where the great veins enter the heart it is about twice the sectional area of the aorta (fig. 132).

This arrangement of the sectional area of the stream gives rise to a rapid flow in the arteries, a somewhat slower flow in the veins, and to a very slow flow in the capillaries.

The suddenness of the change of pressure has a certain influence on the rapidity of flow, as is well seen in a river. If the water descends over a sudden declivity to a lower level it attains a much greater velocity than if the declivity is gentle. In the first case the change of pressure is sudden, in the second case it is slow.

Hence, if, from any cause, the pressure is raised at any point, the flow will tend to be more rapid from that point onwards till the normal distribution of pressure is re-established.

Friction has also a certain effect. A river runs much faster in mid-stream than along the margins, because near the banks the flow is delayed by friction, and the more broken up and subdivided is the channel, the greater is the friction and the more is the stream slowed.

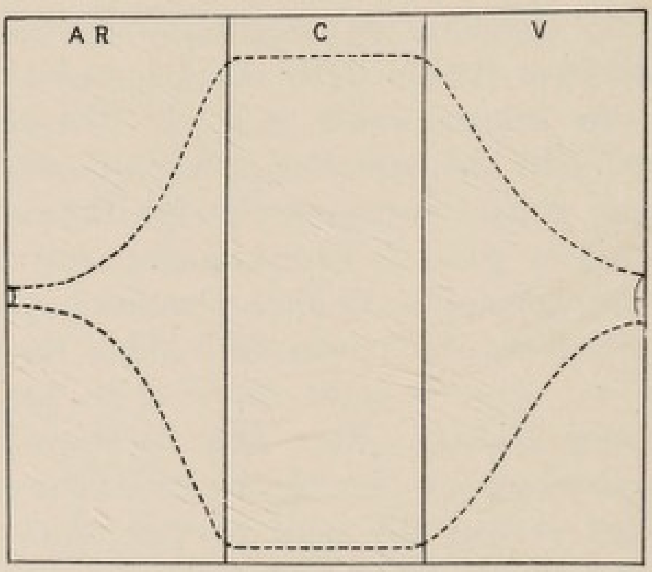


FIG. 132.—Diagram of the Sectional Area of the Vascular System, upon which the Velocity of the Flow depends. *AR*, arteries; *C*, capillaries; *V*, veins.

When, therefore, in the capillary system the blood stream is distributed through innumerable small channels, the friction is very great, and this tends to dam back the blood.

The velocity of flow in the arteries and veins may be measured by various methods, of which one of the best is that by means of the *stromuhr*, an instrument by which the volume of blood passing a given point in an artery or vein in a given time may be determined.

The velocity of the flow in the capillaries may be measured in transparent structures by means of a microscope with an eye-piece micrometer. The velocity of the blood is—

Carotid of the dog about . .	300 mm. per sec.
Capillaries about . . .	0·5 to 1 m. ,,
Vein (jugular) about . .	150 mm. ,,

It is not so easy to give definite figures for the velocity of the lymph stream.

Disturbance of any of the factors which govern the rate of flow will bring about alterations in the velocity of the blood in arteries, capillaries, and veins. Thus, an increased venous pressure, by leading to a diminution in the difference of pressure between arteries and veins, will materially slow the blood stream. Great dilatation of the arterioles will slow the blood stream in them; and increased viscosity of the blood by increasing friction with the vessel wall will also slow the stream.

Special Characters of Blood Flow

(*a*) *Arteries.*—The flow of blood in an artery is rhythmically accelerated with each ventricular systole. This is due to the pulse wave. As the wave of high pressure passes along the vessels, the blood tends to flow forwards and backwards from it—so that in front of the wave there is an acceleration of the stream and behind it a retardation. In a wave at sea the same thing happens, and a cork floating on the surface is moved forward in front of the wave and again backwards after the wave has passed.

(*b*) *Capillaries.*—In the capillaries the flow is uniform.

(*c*) *Veins.*—In most veins, too, it is uniform, but in the great veins near the heart it undergoes accelerations—

1*st*. With each diastole of auricle and ventricle.

2*nd*. With each inspiration.

3*rd*. By muscular action squeezing the blood out of the small veins.

In all vessels the blood in the centre of the stream moves more rapidly than that at the periphery on account of the friction between the blood and the vessels. An "*axial*" rapid and "*peripheral*" slow stream are, therefore, described.

This is well seen in any small vessel placed under the microscope, and in such situations it will be found that, while the erythrocytes are chiefly carried in the axial stream, the leucocytes are more confined to the peripheral stream, where they may be observed to roll along the vessel wall with a tendency to adhere to it.

When from any cause the flow through the capillaries is brought to a standstill, the leucocytes creep out through the vessel wall and invade the tissue spaces. This is the process of *diapedesis*, which plays an important part in inflammation.

SPECIAL CHARACTERS OF THE CIRCULATION IN CERTAIN SITUATIONS

1. **Circulation Inside the Cranium** (fig. 133).—Here the blood circulates in a closed cavity with rigid walls, and therefore its amount can vary only at the expense of the cerebro-spinal fluid. This is small in amount, and permits of very small variations in the volume of blood. Increased arterial pressure in the body does not therefore increase the amount of blood in the brain, but simply drives the blood more rapidly through the organ. There seems to be no regulating nervous mechanism connected with the arterioles of the brain, and the cerebral pressure simply follows the changes in the general arterial pressure. The splanchnic area is the great regulator of the supply of blood to the brain. Since the cerebral arteries are supported and prevented from distending by the solid wall of the skull, the arterial pulse tends to be propagated into the veins. In these veins the respiratory pulse also is very well marked.

2. **Circulation in the Lungs.**—Vaso-motor nerves seem to be absent, and hence drugs like adrenalin fail to cause a constriction of the arterioles. The amount of blood in the lungs is regulated by the blood pressure in the systemic vessels.

3. **Circulation in the Heart Wall.**—A peripheral vaso-motor mechanism is not present in the arterioles of the coronary vessels (see also p. 245).

4. **Circulation in the Spleen.**—Here the blood has to flow through a labyrinth of spaces in the spleen pulp, and it is driven on by the alternate contraction and relaxation of the non-striped muscles in the capsule and trabeculæ (see p. 221).

EXTRA-CARDIAC FACTORS MAINTAINING CIRCULATION

In considering the flow of blood through the vessels due to the distribution of pressure in arteries and veins, it must be remembered that the central pump or heart is not the only factor maintaining it (fig. 133).

The thorax in the movements of respiration is a suction pump of considerable power, which draws blood into the heart during inspiration. While the auricles may be regarded as the *cisterns* of the heart, the abdominal blood vessels are the great blood *reservoir*, and the diaphragm contracting in inspiration presses the blood from this reservoir up into the thorax and heart. When, in intermittent **muscular exercise,** the abdominal muscles are tightened and the respiratory move-

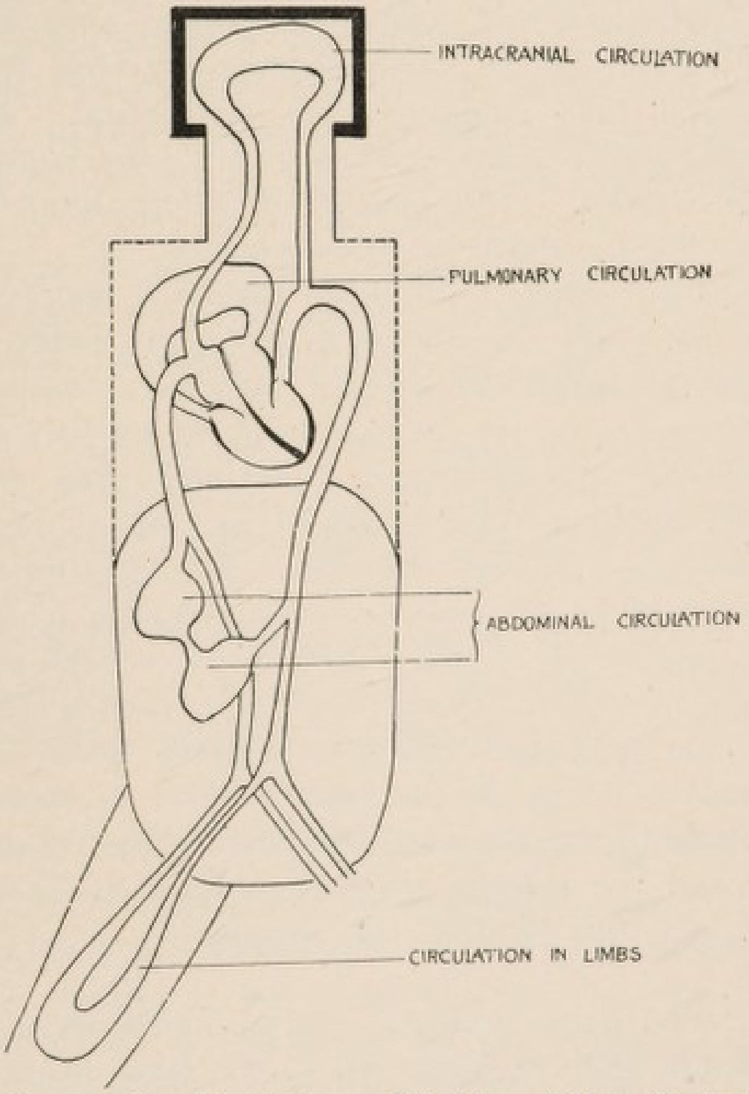


FIG. 133.—Scheme of the Circulation, modified from Hill, to illustrate the influence of the various extra-Cardiac Factors which maintain the Flow of Blood.

ments of the thorax are increased in the panting which accompanies it, the blood is partly pressed, and partly sucked from the abdomen into the heart, and so forced on into the arteries. Even expiration helps in this, for the blood which has filled the vessels of the lungs in inspiration is driven on into the left side of the heart in expiration. The blood is thus forced on into the arteries and so to the muscles, and they, by their alternate contraction and relaxation, further help to drive it on to the veins where the valves prevent any back flow during relaxation and thus accelerate the circulation. The high arterial tension thus produced tends to drive the blood through the cranial vessels. The benefit of intermittent muscular exercise on the circulation is thus manifest.

When, on the other hand, some **sustained muscular strain** has to be undergone, the thorax is fixed, and hence (1*st*) the pressure on the heart and thoracic organs is raised, and the increased pressure in the thorax helps to support the heart and to prevent over-distension. The abdominal vessels are also pressed upon, and the sustained contraction of the limb muscles tends to prevent the blood flowing through them. It is thus forced to the central nervous system in which the pressure rises, and if a weak spot in the vessels is present, rupture is apt to occur. (2*nd*) But, if the effort is still further sustained, the high intra-thoracic pressure tends to prevent proper diastolic filling of the heart; blood is therefore not sent on from the veins into the arteries, the veins become congested and the arterial pressure falls, less blood goes to the brain, and thus fainting may result.

In the "head down position," the accumulation of blood in the dependent parts is prevented in the head by the vessels being packed inside the skull, and in the right side of the heart by the supporting pericardium.

In man the position of the abdominal reservoir of blood at a lower level than the heart increases the work of that organ. In the horizontal position, when the reservoir is on the same level as the pump, the work is much easier.

Fainting is a sudden loss of consciousness produced by failure in the supply of blood to the brain. It is accompanied by loss of control over the muscles, so that the individual falls to the ground. It may be induced by any sudden lowering of the arterial blood pressure, whether due to decreased inflow of blood or to decreased peripheral resistance.

Decreased inflow may be caused by;—(*a*) Cardiac inhibition brought about reflexly (1) by strong stimulation of ingoing nerves, and more especially of the nerves of the abdomen; (2) by strong stimulation of the upper brain neurons accompanied by changes in the consciousness of the nature of emotions;—(*b*) Failure of the heart to pump blood from veins to arteries against the force of gravity, as when the erect position is suddenly assumed by people with weak hearts.

Decreased resistance to outflow through sudden dilatation of arterioles may result from changes in the upper brain neurons, accompanied by emotional states and also in digestive disturbances.

However induced, the anæmic state of the brain leads to a stimulation of the cardiac inhibitory centre and the condition is thus accentuated. The cerebral anæmia is accompanied by pallor of the face.

The treatment consists in depressing the head to allow the force of gravity to act in filling the central vessels and in giving diffusible stimuli to increase the action of the heart.

THE TIME TAKEN BY THE CIRCULATION

This was first determined by injecting ferrocyanide of potassium into the proximal end of a cut vein, and finding how long it took to appear in the blood flowing from the distal end. From observation in the horse, dog, and rabbit, it appears that the time corresponds to about twenty-seven beats of the heart.

Stewart has investigated the rate of flow through different organs by injecting salt solution into the artery, and by detecting its appearance in the vein by the change in the electric conductivity of the contents of the vessel.

SECTION VI

SUPPLY OF NOURISHING MATERIAL TO THE BLOOD AND LYMPH, AND ELIMINATION OF WASTE MATTER FROM THEM

I. RESPIRATION

IF an animal be placed in a closed chamber filled with ordinary atmospheric air which contains by volume 79 parts of nitrogen and 21 parts of oxygen, and if the air be examined after a time, it will be found that the oxygen has diminished in amount, and that a nearly corresponding amount of carbon dioxide has been added. (*Practical Physiology.*)

The same thing occurs in aquatic animals—the water round them loses oxygen and gains carbon dioxide. **An animal takes up oxygen and gives off carbon dioxide.** This is the process of **external respiration.**

A. EXTERNAL RESPIRATION

I. Respiratory Mechanism

In aquatic animals the mechanism by which this process is carried on is a **gill** or gills. Each consists of a process from the surface covered by a very thin layer of integument, just below which is a tuft of capillary blood vessels. The oxygen passes from the water to the blood; the carbon dioxide from the blood to the water.

A **lung** is simply a gill or mass of gills, turned outside in, with air instead of water outside the integument. While in aquatic gill-bearing animals there is constantly a fresh supply of water passing over the gills, in lung-bearing animals the air in the lung sacs must be exchanged by some mechanical contrivance.

The lungs consist of myriads of small thin-walled sacs attached round the funnel-like expansions in which the air passages (infundibular passages) terminate. (*The structure* *of the various parts of the respiratory tract must be studied practically.*)

Each sac is lined by a layer of simple squamous epithelium, supported by a framework of elastic fibrous tissue richly supplied with blood vessels. It has been calculated that, if all the air vesicles in the lungs of a man were spread out in one continuous sheet, a surface of about 100 square metres would be produced and that the blood capillaries would occupy about 75 square metres of this. Through these vessels about 5000 litres of blood would pass in twenty-four hours.

The larger air passages are supported by pieces of hyaline cartilage in their walls, but the smaller terminal passages, the bronchioles, are without this support, and are surrounded by a specially well-developed circular band of non-striped muscle—the bronchial muscle—which governs the admission of air to the infundibula and air sacs.

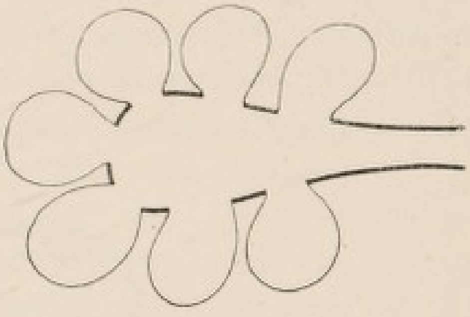


FIG. 134.—Scheme of the Distribution of a Bronchiole, Infundibular Passage, and Air Sacs of the Lung.

The lungs are packed in the thorax round the heart, completely filling the cavity.

They may be regarded as two compound *elastic-walled* sacs, which completely fill an air-tight box with movable walls—the thorax—and communicate with the exterior by the windpipe or trachea.

No air exists between the lungs and the sides and base of the thorax, so that the so-called **pleural cavity** is simply a potential space. If the thoracic wall be punctured so that this potential pleural cavity is brought into connection with the air, the lungs immediately collapse and occupy a small space posteriorly round the large bronchi. This is due to their elasticity (fig. 135).

The lungs are kept in the distended condition in the thoracic cavity by the atmospheric pressure within them.

Their elasticity varies according to whether the organs are stretched or not. As they collapse, their elastic force naturally becomes less and less; as they are expanded, greater and greater. Taken in the average condition of expansion in which they exist in the chest, the elasticity of the excised lungs of a man is capable of supporting a column of mercury of about 30 mm. in height, so that they are constantly tending to collapse with this force.

But the *inside* of the lungs freely communicates with the atmosphere, and this, at the sea level, has a pressure of about 760 mm. Hg. During one part of respiration this pressure becomes a few mm. less, during another part a few mm. more; but the mean pressure of 760 mm. of mercury is constantly expanding the lung, and acting against a pressure of only 30 mm. of mercury, tending to collapse the lung.

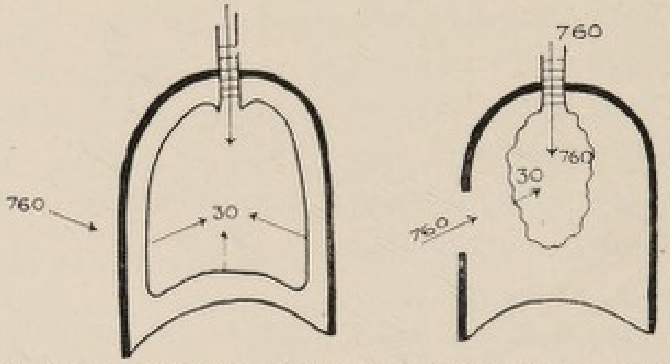


FIG. 135.—Shows the Distribution of Pressure in the Thorax with the chest wall intact, and with an opening into the Pleural Cavity. (↓) indicates the atmospheric pressure of 760 mm. of mercury ; 30 is the elasticity of the lungs also in mm. of mercury.

Obviously, therefore, the lungs must be kept expanded and in contact with the chest wall.

When a pleural cavity is opened, the distribution of forces is altered, for now the atmospheric pressure tells also on the outside as well as on the inside of the lungs and acts along with the elasticity of the organ. So that now a force of 760 mm. + 30 mm. = 790 mm. acts against 760 mm., causing a collapse of the lungs.

In the surgery of the thorax, as well as in the physiology of respiration, these points are of great importance.

II. Physiology

The process of external respiration consists of two parts—

1*st.* The passage of air into and out of the air sacs.

2*nd.* The interchange of gases between the air in the air vesicles and the blood in the capillaries.

A. Passage of Air into and out of the Lungs

This is brought about—

1*st.* By the movements of respiration—breathing.

2*nd.* By diffusion of gases.

The air is made to pass into and out of the lungs by alternate *inspiration* and *expiration.*

I. Movements of Respiration—*A.* **Inspiration.**—During this act the thoracic cavity is increased in all directions—lateral, antero-posterior, and vertical. As the thorax expands, the air pressure inside the lungs keeps them pressed against the chest wall, and **the lungs** expand with the chest. As a result of this expansion of the lungs the pressure inside becomes less than the atmospheric pressure, and air rushes in until the pressure inside and outside again becomes equal. This can be shown by placing a tube in the mouth or in a nostril and connecting it with a water manometer. (*Practical Physiology.*)

This expansion of the lungs can readily be determined in the antero-posterior direction by percussion, and in the vertical planes by measurement. By tapping the chest with the finger over the lung in the right intercostal spaces, a resonant note is produced, while if the percussion is performed behind the level of the lung, a dull note is heard. If the posterior edge of this resonance be determined before an inspiration, and again during it, it will be found to have passed backwards. (*Practical Physiology.*)

As a result of inspiration, the form of the chest is markedly modified, the change being best seen in transverse sections. In expiration the chest in transverse section is an ellipse from above downward, in inspiration it becomes more circular (fig. 136). The change from side to side and from above downward is best marked towards the hinder part of the chest, less marked in the anterior part. These changes may be recorded by means of a Cyrtometer, a piece of flexible gas tubing hinged behind, so that it can be modelled to the chest. (*Practical Physiology.*)

The change from before backwards cannot be directly seen, but it is indicated by an expansion of the wall of the abdomen. It will be described when considering the mechanism by which it is brought about.

The expansion of the chest **in inspiration is a muscular act** and is carried out against the following forces—

1*st. The Elasticity of the Lungs.*—To expand the lungs their elastic force has to be overcome, and the more they are expanded the greater is their elasticity. This factor therefore plays a smaller part at the beginning than towards the end of inspiration.

2*nd. The Elasticity of the Chest Wall.*—The resting position of the chest is that of expiration. To expand the chest the costal cartilages have to be twisted.

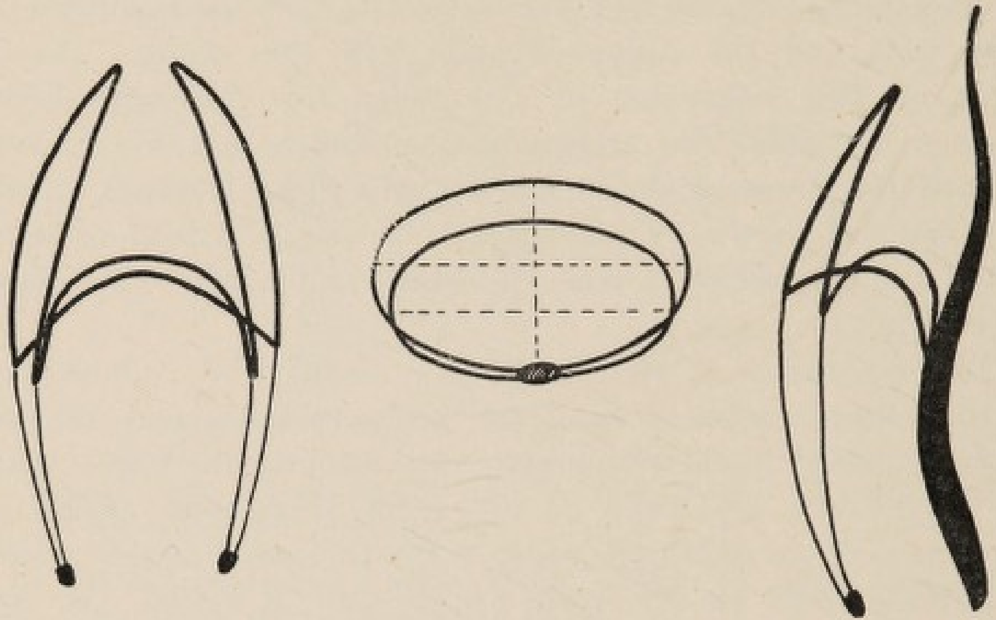


FIG. 136.—Vertical-tangential, Transverse, and Vertical Mesial Sections of the Thorax in Inspiration and Expiration.

3*rd. The Elasticity of the Abdominal Wall.*—As the cavity of the thorax increases backwards, the abdominal viscera are pushed against the muscular abdominal wall, which, in virtue of its elasticity, resists the stretching force.

In studying how these changes are brought about we may consider—

1*st. The Increase in the Thorax from before backwards.*

This is due to the contraction of the **diaphragm** (fig. 136).

In expiration this dome-like muscle, rising from the vertebral column and from the posterior costal margin, arches forwards, lying for some distance along the inner surface of the ribs and then curving inwards to be inserted into the flattened central tendon, to which is attached the pericardium and on which rests the heart.

In inspiration the muscular fibres contract. But the central tendon being fixed by the pericardium does not undergo extensive movement. The result of the muscular contraction is thus to flatten out the more marginal part of the muscle and to withdraw it more or less from the chest wall—thus opening up a space, the **complemental pleura**, into which the lungs expand (fig. 136).

It might be expected that this contraction of the diaphragm would pull inwards the chest wall—but this is prevented by the expansion of the thorax in the lateral and vertical diameters as a result of the mechanism which has next to be considered.

2nd. The Increase in the Chest in the vertical and lateral diameters.

This is brought about by the pulling forward of the ribs which rotate round the axis of their attachments to the vertebral column.

To understand this, the mode of the connection of the ribs to the vertebral column must be borne in mind. The head of the rib is attached to the bodies of two adjacent vertebræ. The tubercle of the rib is attached to the transverse process of the hinder of these vertebræ. From this the shaft of the rib projects outwards, downwards and backwards, to be attached below to the sternum by the costal cartilage. If the rib is made to rotate round its two points of attachment, its lateral margin is tilted forwards and outwards, while its lower end is carried forwards and downwards (see fig. 137).

Further, as we pass from before backwards, each pair of ribs forms the arc of a larger and larger circle, and as each pair rises it takes the place of a smaller pair above. In these ways, the chest is increased from above downwards and from side to side.

The first pair of ribs does not undergo this movement; the motion of the second pair of ribs is slight, but the range of movement becomes greater and greater as we pass downwards until the floating ribs are reached, and these are fixed by the abdominal muscles. This greater movement is simply due to the greater length of the muscles moving the ribs. The muscles are chiefly the **external intercostal muscles,** and these may be considered as acting from the fixed first rib. Now, if the fibres of the first intercostal muscle are one inch in length, the second rib can be pulled forward, say, half an inch. The first and second intercostals acting on the third rib will together be two inches in length, and in contracting they can pull the third rib through, say, half of two inches—*i.e.* one inch. The first, second, and third intercostals, acting on the fourth rib, are three inches in length, and can therefore pull this rib half of three, or one and a half, inches, and so through the other ribs, until the floating ribs fixed by the abdominal muscles are reached.

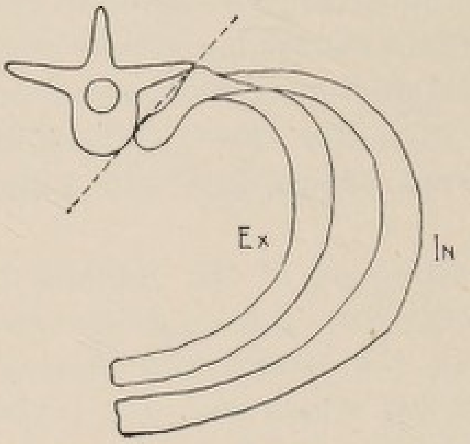


FIG. 137.—Shows the Movements of the Ribs from their Position in Expiration to their Position in Inspiration.

When the diaphragm takes the chief part in inspiration the breathing is said to be **abdominal in type**—when the intercostals chiefly act in raising the ribs it is said to be **thoracic.**

Along with the intercostal muscles, the levatores costarum also act in raising the ribs and in increasing the thorax in the transverse and vertical diameters.

These are the essential muscles of inspiration, but other muscles also participate in the act. In many animals, even when breathing quietly, it will be seen that the nostrils dilate with each inspiration. This is due to the action of the dilatores narium which contract synchronously with the other muscles of inspiration. Again, if the larynx be examined, it will be found that the vocal cords slightly diverge from one another during inspiration. This is brought about by the action of the posterior crico-arytenoid muscles (p. 335).

Forced Inspiration.—This comparatively small group of muscles is sufficient to carry out the ordinary act of inspiration. But, in certain conditions, **inspiration** becomes **forced.**

A forced inspiration may be made voluntarily, often it is produced involuntarily. In it every muscle which can act from the fixed spine, head and shoulder girdle upon the thorax, is brought into play. Normally, these act from the thorax upon the parts into which they are inserted; now they act *from* their insertion *upon* their point of origin. The sterno-mastoids, sterno-thyroids, and sterno-hyoids assist in elevating the thorax. The serratus magnus, pectoralis minor, and anterior fibres of the pectoralis major, and the part of the latissimus dorsi which passes from the humerus to the three last ribs, also pull these structures upwards. The facial and laryngeal movements also become exaggerated.

B. In **Expiration** the various muscles of inspiration cease to act, and the forces against which they contended again contract the thorax in its three diameters—

The *elasticity of the lungs* is no longer overcome by the muscles of inspiration, and the external atmospheric pressure acting along with it drives the chest wall inwards (see p. 296).

The *elasticity of the costal cartilages* causes the ribs again to fall back, and finally the *elasticity of the abdominal wall* drives the abdominal viscera against the relaxed diaphragm and again arches it towards the thorax, squeezing its marginal portion against the ribs and occluding the complemental pleura.

Experimental evidence shows that the internal intercostals contract with each expiration, and help to draw the ribs downwards.

Ordinary expiration is thus normally mainly a passive act, being simply a return of the thorax to the position of rest. But voluntarily, and, in certain conditions, involuntarily, expiration may be forced. **Forced expiration** is then partly due to the above factors, and partly due to the action of muscles. Every muscle which can in any way diminish the size of the thorax comes into play.

Chief of these are the abdominal muscles, which by compressing the viscera push them upwards and press the diaphragm further up into the thorax. At the same time, by acting from the pelvis to pull down the ribs, they decrease the thorax from side to side and from before backwards.

The serratus posticus inferior and part of the sacro-lumbalis pull downwards the lower ribs, and the triangularis sterni also assists in this.

By this constriction of the thorax, brought about by ordinary or by forced expiration, the air inside is compressed and the pressure raised. During ordinary expiration the highest pressure reached is about 2 to 3 mm. Hg, in forced expiration about 80 mm. in man.

The pressure of the air outside is less than this, and the air inside the chest is driven out.

Special Respiratory Movements.—There are several peculiar and special reflex actions of the respiratory muscles, each caused by the stimulation of a special district, and each having a special purpose.

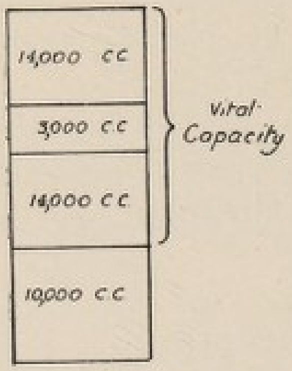


FIG. 138.—The amount of Air respired in ordinary Respiration, and in forced Inspiration and Expiration.

Coughing.—This consists of an inspiration followed by a strong expiratory effort during which the glottis is constricted but is forced open repeatedly by the current of expired air. It is generally due to irritation of the respiratory tract, and its object is to expel foreign matters.

Sneezing.—This is generally produced by irritation of the nasal mucous membrane, and its object is to expel irritating matter. It consists in an inspiratory act followed by a forced expiration during which, by contraction of the pillars of the fauces and descent of the soft palate, the air is forced through the nose.

Hiccough consists in a sudden reflex contraction of the diaphragm causing a sudden inspiration which is interrupted by a spasmodic contraction of the glottis. Abdominal irritation is its chief cause. It is allied to vomiting.

Sighing and *Yawning* are deep involuntary inspirations which serve to accelerate the circulation of the blood when, from any cause, it becomes less active (see p. 291). They are probably due to cerebral anæmia, which they help to correct by increasing the general arterial pressure.

II. Amount of Air respired.—The amount of air respired is different in ordinary and in forced respiration.

In an ordinary respiration in the horse about 3000 c.cms. of air enter and leave the chest. That is called the **tidal air.** Its amount varies with the size and muscular development of the chest.

By a forced inspiration a much larger quantity of air may be made to pass into the lungs—a quantity varying with the size and strength of the individual—but on an average about 14,000 c.cms.

This is called the **complemental air.**

By forced expiration an amount of air much larger than the tidal can be expelled, an amount usually about the same as the complemental air, and called the **reserve air.**

The total amount of air which an individual can draw into and drive out of his lungs is a fair measure of the size and muscular development of the thorax, and it has been called the **vital capacity** of the thorax, and in the horse it amounts to something like 25,000 to 30,000 c.cms.

Even after the whole of the reserve air has been driven out of the chest, a considerable quantity still remains in the air vesicles, its amount depending upon the size of the chest, but averaging about 2000 c.cms. This is called the **residual air.**

This very important point must always be remembered, that *the air taken into the chest never fills the air vesicles, and that air is never driven completely out of them. The air in them is thus not changed by the movements of respiration but by the process of diffusion.*

III. Interchange of Air in the Lungs by Diffusion of Gases.—It has been shown that only the air in the trachea and bronchi undergoes exchange in mass, but that the air of the vesicles is not driven out of the chest. The renewal of this air depends upon the diffusion of gases.

If two gases are brought into relationship with one another they diffuse and tend to form a mixture uniform throughout. But if, at one point of a system, one gas is constantly being taken away and another constantly added, there will be a constant diffusion of the former *towards* the part where it is being taken up, and a constant diffusion of the latter *away from* the point to which it is being added. Suppose a tube (fig. 139) containing oxygen and carbon dioxide, and suppose that at one end of the tube oxygen is constantly being taken up and carbon dioxide constantly given off, a diffusion of the gases in the direction indicated by the arrows will continually go on, and thus a constant supply of oxygen will be conveyed to the bottom of the tube, while carbonic acid will constantly be cleared out. This is exactly the condition in the lungs.

The lower part of the tube corresponds to the air vesicles—the upper part to the air passage in which the air is constantly being exchanged by the movement of respiration.

The mechanism by which the gaseous exchange in the alveoli is carried out is thus a double one.

IV. Breath Sounds.—The air as it passes into and out of the lungs produces sounds, which may be heard on listening over the thorax. The character of the breath sounds are of the utmost importance in the diagnosis of diseases of the lungs, and must be studied practically. (*Practical Physiology.*)

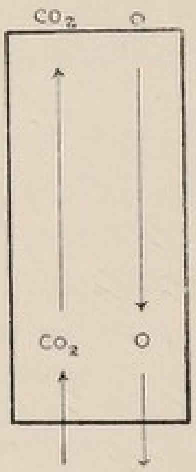


FIG. 139.—Shows the course of diffusion of Oxygen into, and of Carbon Dioxide out of, the Air Vesicles.

On listening over the trachea or over the bifurcation of the bronchi behind, a harsh sound, something like the guttural *ch* (German *ich*), may be heard with inspiration and expiration. This is called the **bronchial sound.**

If the ear be applied over a spot under which a mass of air vesicles lies, a soft sound, somewhat resembling the sound of gentle wind among leaves, may be heard throughout inspiration, and for a third or less of expiration. This is called the **vesicular sound.**

When the air vesicles become consolidated by disease, the vesicular sound is lost and the bronchial sound takes its place. The cause of the vesicular character is therefore to be sought in the vesicles, infundibula, or small bronchi.

The cause of the bronchial sound has been determined by experiments on horses. In the study of the cardiac circulation it was shown that a column of fluid—and the same is true of a column of air—moving along a tube of uniform calibre, or with the calibre only slowly changing, produces no sound. Any sudden alteration in calibre produces vibration and a musical sound, as explained on p. 248. The first sharp constriction of the respiratory tract is at the glottis, and it is here that the bronchial sound is produced. If the trachea is cut below the larynx and drawn freely outwards, the bronchial sound at once stops and the vesicular sound becomes lower and less distinct.

The cause of the vesicular sound is not so satisfactorily explained. It is in part due to propagation of the bronchial sound, altered by passing through vesicular tissue; but it is also probably due to the expansion and contraction of the air vesicles drawing in and expelling air, either through their somewhat narrow openings into the infundibula, or through the narrow opening of the infundibula into the bronchioles. The reason why the sound is best heard during inspiration may be that the sound is best conducted in the direction of the air stream (fig. 134).

V. Rhythm of Respiration.—These movements of respiration are carried on in a regular rhythmic manner. Their rate varies with many factors; but the average number of respirations per minute in the adult **horse** is about ten to twelve or about one to every four or five beats of the heart.

The most important factor modifying the rate of respiration is muscular exercise. After galloping the respirations may rise to over sixty per minute.

The other modifications in the rate of breathing will be better understood after studying the nervous mechanism of respiration.

In these respiratory movements the phase of inspiration bears a certain proportion to that of expiration. Inspiration is much more rapid than expiration (see fig. 142). As soon as inspiration is completed, a reverse movement occurs, which is at first rapid, but gradually becomes slower, and may be followed by a pause, during which the chest remains in the collapsed condition. The existence and duration of this pause varies much, and it may really be considered as the terminal period of expiration. Considering it in this light, we may say that inspiration is to expiration as 6 is to 7.

VI. Controlling Mechanism of Respiration.—The rhythmic movements of respiration require the harmonious action of a number of muscles, and this is directed by the nervous system.

The diaphragm is supplied by the phrenic nerves rising from the third and fourth, and partly from the fifth cervical nerves. The intercostals are supplied by branches from their corresponding dorsal nerves.

If the spinal cord be cut below the fifth cervical nerve the intercostal muscles cease to act. If the section is made above the third cervical nerve, the diaphragm, too, is paralysed, and the animal dies of suffocation.

Respiratory Centre.—Obviously, then, there is some nervous mechanism above the spinal cord presiding over these muscles.

Removal of the brain above the medulla oblongata does not stop the respiratory rhythm.

The mechanism must, therefore, be situated in the medulla oblongata.

If the medulla is split into two by an incision down the middle line, respiration continues, but the two sides do not always act at the same rate. The mechanism, then, is bilateral, but normally the two parts are connected, and thus act together.

Destruction of the part of the medulla lying near the root of the vagus arrests respiration, and it may therefore be concluded that the nervous mechanism presiding over this act is situated there.

It must not be imagined that this centre sends fibres directly to the muscles concerned in respiration. The nerves passing to these come from the cells in the grey matter of the spinal cord, and it is by influencing the activity of these cells that the respiratory centre controls the act of respiration.

Since expiration, when forced, is a complex muscular act, it is reasonable to suppose that the respiratory centre contains two parts—one presiding over inspiration, one presiding over expiration. While the inspiratory centre is constantly in rhythmic action, the expiratory centre is only occasionally at work.

Mode of Action of the Respiratory Centre.—Both parts of the respiratory centre are under the control of higher nerve centres, and through these they may be thrown into action at any time, or even prevented from acting for the space of a minute or so. But, after the lapse of this period, the respiratory mechanism proceeds to act in spite of the most powerful attempts to prevent it.

The activity of the centre is chiefly regulated by the amount of CO_2 in the blood going to it, and everything which leads to an increase in the CO_2 increases the activity of respiration. So perfect is this mechanism that the percentage of CO_2 in the air in the lungs is kept very constant in different conditions.

This is probably the explanation of a peculiar type of breathing, known as Cheyne Stokes breathing, which sometimes occurs in heart disease and in other conditions, when the patient stops breathing for a time, then begins to breathe first quietly, then more forcibly, and after several respirations again with decreasing depth till the respirations stop. In these cases the respiratory centre is less excitable than usual, and is called into action only when CO_2 has accumulated in the blood. After this accumulation has been got rid of by the forcible respirations the activity of the centre again wanes.

Decrease in the amount of oxygen in the blood acts in the same way, but since the amount of oxygen in the arterial blood varies much less than the amount of CO_2, this factor plays a less important part in regulating breathing. At high altitudes the decrease in the pressure of oxygen in the air breathed, leading to its decreased amount in the blood, produces a marked increase of respiratory movements.

But the respiratory centre is also acted upon by **various ingoing nerves.**

Vagus.—Since the vagus is the ingoing nerve of the respiratory tract, we should expect it to have an important influence on the centre (fig. 140).

Section of one vagus causes the respiration to become slower and deeper; but after a time the effect wears off and the previous rate and depth of respiration is regained (fig. 141).

Section of both vagi causes a very marked slowing and deepening of the respiration, which persists for some time, and passes off slowly and incompletely. But if after the vagi have been cut, the connection of the centre with the *upper brain tracts* is severed, the mode of action of the centre changes. Instead of discharging rhythmically it may discharge irregularly.

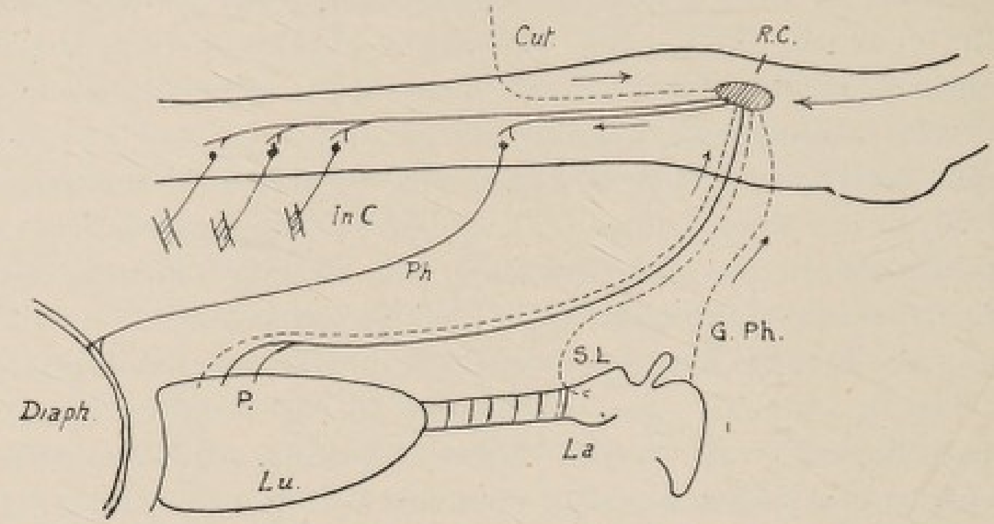


FIG. 140.—Nervous Mechanism of Respiration. *R.C.*, respiratory centre; *Cut.*, cutaneous nerves; *Ph.*, phrenics; *In.C.*, intercostal nerves; *P.*, pulmonary branches of vagus; *S.L.*, superior laryngeal branch of vagus; *La.*, the larynx; *G.Ph.*, glossopharyngeal nerve; *Diaph.*, diaphragm.

To investigate further this influence of the vagus it is necessary to study the effect of stimulating the nerve.

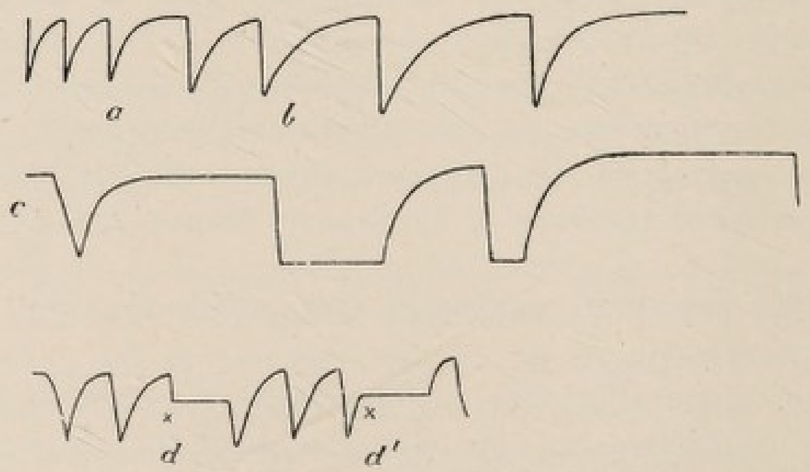


FIG. 141.—Tracings of the Respirations—Downstroke is Inspiration; Upstroke is Expiration. At *a* one vagus nerve was cut; at *b* the second was divided; at *c* the upper brain tracts also were cut off; *d* and *d′* show the effect of stimulating the glossopharyngeal nerve.

Strong stimulation of the pulmonary branches of one vagus (vagus below the origin of the superior laryngeal) causes the respiration to become more and more rapid, the inspiratory phase being chiefly accentuated. If the stimulus is very strong respirations are stopped in the phase of inspiration. Weak stimuli, on the other hand, may cause inhibition of inspiration.

Such experiments prove that impulses are constantly travelling from the lungs to the centre regulating the rhythmic activity of the centre.

How do these impulses originate in the lungs? Apparently from their alternate expansion and contraction.

If the lungs be forcibly inflated—*e.g.* with a bellows—the inspiration becomes feebler and feebler, and finally stops. The nature of the gas, if non-irritant, with which this inflation is carried out is of no consequence. If, on the other hand, the lungs be collapsed by sucking air out of them, the inspiration becomes more and more powerful, and may end in a spasm of the inspiratory muscles.

This shows that with each expiration a stimulus passes up the vagus which acts upon the inspiratory centre to make it discharge. The vagus is thus an excito-motor nerve, making the centre act in a reflex manner. With each collapse of the lung the vagus is thrown into action; as the lungs expand it ceases to act, and, as a result, the inspiratory centre stops acting, the muscles of inspiration cease to contract and expiration occurs.

Action of other Ingoing Nerves on the Respiratory Centre.—The upper part of the respiratory tract, the larynx, receives its sensory fibres from the vagus. Section of the **superior laryngeal branch of the vagus** does not alter the rhythm of respiration. Stimulation of the upper end of the cut nerve causes first an inhibition of inspiration, and, if stronger, produces forced expiratory acts. This is well illustrated by the very common experience of the effect of a foreign body, such as a crumb, in the larynx. The fit of coughing is a series of expiratory acts produced through this nerve.

Another set of visceral nerves having an important influence on the respiratory rhythm are the **splanchnics.** When these are stimulated inspiration is inhibited. Everyone has experienced the "loss of wind" as the result of a blow on the abdomen.

The **glossopharyngeal,** which supplies the back of the tongue, when stimulated, as by the passage of food in the act of swallowing, causes an instant arrest of the respiratory movements either in inspiration or expiration. The advantage of this in preventing the food as it is swallowed from passing into the trachea is obvious (fig. 141, *d* and *d'*).

Stimulation of the **Cutaneous Nerves** stimulates the inspiratory centre and causes a deep inspiration. This is seen when cold water is dashed upon the skin, and is more clearly demonstrated in animals with the vagi and upper nerve tracts cut across. In such animals if the skin be touched an inspiratory movement is made.

The **temperature** of an animal also acts on the respiratory centre. Increase in temperature accelerates the rate of the heart—so, too, it accelerates the rate of the respirations, and in about the same proportion, as is seen in feverish attacks, where pulse and respiration are proportionately quickened so that their ratio remains unaltered. When the respiratory rate rises out of proportion to the rate of the pulse, it is usually an indication that some pulmonary irritation is present.

VII. Interaction of Circulation and Respiration.—The lungs and heart being packed tightly together in the air-tight thorax, and both undergoing periodic changes, necessarily influence one another. At the same time, the close proximity of the respiratory and cardio-motor centres in the medulla seems to lead to the activity of one influencing the other.

Influence of Respiration on Circulation.—The circulation is modified in two ways by respiration. First, the rate of the heart, and second, the arterial blood pressure undergo alterations.

1*st. Rate of Heart.*—If a sphygmographic trace giving the pulse waves during the course of two or three respirations be examined, it will be found that during inspiration the heart is acting more rapidly, while during expiration its action is slower.

If the vagus be cut these changes are not seen, showing that the inspiratory acceleration is not the result simply of the larger amount of blood which enters the heart during inspiration, but is really due to changes in the cardio-motor centre—the accelerating part of which has its activity increased during inspiration, while the inhibitory part is more active during expiration. This is therefore a reflex effect from the lung through the vagus, and it may be in part due to the proximity of the centres in the medulla.

But not only is the pulse more rapid during inspiration and slower during expiration, but the waves are smaller during inspiration and larger during expiration. The size of the wave depends much upon the pressure of blood in the arteries, and this change in the pulse thus leads to the fuller consideration of the changes in the arterial pressure due to respiration.

2nd. *Changes in Blood Pressure.*—If a tracing of the arterial pressure and of the respiratory movements are taken at the same time, it is found that there is a general rise of pressure during inspiration and a general fall during expiration, but that at the beginning of inspiration the pressure is still falling, and at the beginning of expiration it is still rising. This influence of respiration on arterial pressure is chiefly a mechanical one, depending on the variations in the pressure in the thorax during inspiration and expiration.

During inspiration the pressure in the thorax falls to below the atmospheric pressure, and thus during this period the heart and great vessels are under a diminished pressure. This diminution in pressure has little influence on the thick-walled ventricles and arteries, but tells markedly on the thin-walled auricles and veins. In these there occurs a diminution in pressure, which, in the case of the vena cava, may fall below an atmospheric pressure, and as a result an increased flow of blood into these vessels from the veins outside the thorax takes place (fig. 133, p. 291).

But when more blood enters the heart the activity of the organ is increased, and more blood is pumped through it into the arteries, and the pressure in these rises. This explains the great rise in arterial blood pressure during inspiration.

During expiration the pressure in the thorax rises to above the atmospheric pressure, and thus the pressure on the vessels in the thorax is increased. This tells on the thin-walled veins and auricles; and thus the flow of blood into them is retarded, and less blood passing into the heart, less is pumped into the arteries, and the arterial pressure falls.

This, however, does not explain the slight fall of pressure at the beginning of inspiration, or the slight rise at the beginning of expiration. To understand these, the action of the pulmonary circulation has to be taken into account.

As inspiration develops the lungs are dilated, and the capillaries in them are also expanded. These expanding capillaries require more blood to fill them. They are situated on the course of the blood from the right side to the left side of the heart, and thus blood is retained from this stream to fill them, and less blood passes on into the left side of the heart, and out into the arteries, and a small fall in the arterial pressure occurs at the beginning of inspiration.

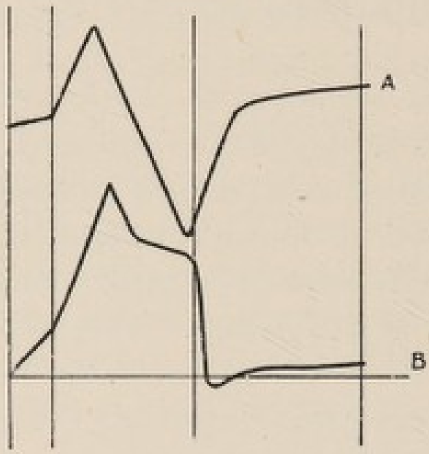


Fig. 142.—To show relations of Cardio-pneumatic Movements, A, to the Cardiac Cycle, B. In A the upstrokes are expiratory, the downstrokes inspiratory.

Similarly, at the beginning of expiration the lungs are compressed and their blood vessels squeezed, and thus the blood is driven out from them. Now, this blood cannot pass back into the right side of the heart, so it must pass on into the left side. More blood is thus driven into the arteries, and the pressure rises. As soon, however, as the excess of blood has been squeezed out of the lungs, the contracted state of the vessels further retards the passage of blood to the left side of the heart and assists in diminishing the arterial pressure.

Influence of the Action of the Heart on Respiration.—The heart lies in the thorax surrounded by the elastic lungs. As it contracts and dilates it must alternately pull upon and compress the lungs, and thus tend to cause an inrush and an outrush of air—the **cardio pneumatic movements.**

If a simultaneous tracing of the heart-beat and of the movements of the air column be taken, it will be seen that (1) at the beginning of ventricular systole there is a slight outrush of air from the lungs, probably caused by the blow given to the lungs by the suddenness of the systolic movement. (2) This is followed by a marked inrush of air corresponding to the outflow of blood from the ventricles, and caused by the fact that the contracting ventricles draw on and expand the lungs. (3) Succeeding this is a slower outrush of air corresponding to the active filling of the ventricles during the beginning of ventricular diastole. (4) Lastly, during the period of passive diastole, the cardio-pneumatic movements of air are in abeyance (fig. 142).

These cardio-pneumatic movements are of great importance in animals which hibernate. During their winter sleep the ordinary respirations almost stop, but a sufficient gaseous interchange is kept up by these cardio-pneumatic movements.

In the examination of the heart sounds they must be borne in mind, because, if there is any constriction in a small bronchus near the heart, the rush of air through it may give rise to a murmuring sound, in character very like a cardiac murmur and synchronous with the heart's action. On making the patient cough, such a murmur at once disappears.

B. Interchange between the Air breathed and the Blood in the Lung Capillaries

I. Effect of Respiration upon the Air breathed.—To determine this, some method of analysing the air exhaled must be employed. For this purpose the expired air is caught in a graduated vessel in which its amount can be measured; then a measured amount is forced into a chamber containing caustic potash, by which the CO_2 is absorbed and the volume of air is again measured. It is now forced into a chamber containing pyrogallate of soda, which absorbs the oxygen and is again measured. The residue is nitrogen. In this way the amount of the gases present is determined. (*Practical Physiology.*)

The following table shows the average percentage composition of the air inspired and the air expired (fig. 143):—

Per Cent. of	N.	O.	CO_2
Inspired air	79	21	0
Expired air	79	17	4

i.e. about 4 per cent. of oxygen is taken from the air, and *about* 4 per cent. of carbon dioxide is added to it. In man the amount of carbon dioxide given off is smaller than the amount of oxygen taken up. The proportion between the $\frac{CO_2 \text{ given off}}{O \text{ taken up}}$ is called the *Respiratory Quotient*, and it is thus less than unity—usually about ·8 to ·9—that is, for every five volumes of oxygen taken up only four volumes are given off in carbon dioxide, the remainder being combined with hydrogen to form water. The various factors modifying this quotient will be considered while dealing with the extent of the respiratory changes (see p. 320).

Expired air is saturated with watery vapour, and, therefore, it usually contains more *water* than inspired air.

Expired air also contains small amounts of *organic matter*, which may give it an offensive odour. These may possibly be to a small extent formed in the lungs, but they are to a greater extent produced by putrefactive change in the mouth and nose. It is probable that the accumulation of these products in the air is one of the causes of the injurious effect of the "foul air" in overcrowded spaces, but the evidence on this point is inconclusive.

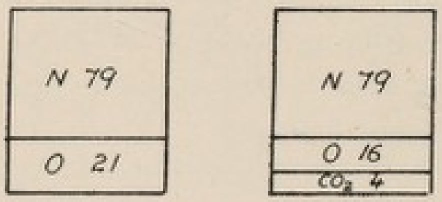


Fig. 143.—Shows the Composition of Inspired and Expired Air.

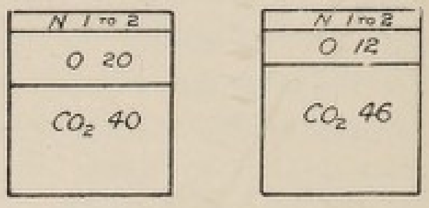


Fig. 144.—Shows the Difference in the Gases of Arterial and Venous Blood.

Expired air is *usually* warmer than inspired air, because usually the body is warmer than the surrounding atmosphere. When, however, the temperature of the air is higher than that of the body, the expired air is cooler than the inspired.

This may be illustrated by the figures of an experiment—

Temperature of Inspired Air.	Temperature of Expired Air.
6·3° C.	30° C.
17–19° C.	37° C.
41° C.	38° C.
44° C.	38·5° C.

II. Effect of Respiration on the Blood.—To understand these changes in the air we must refer to the changes in the gases of the blood in passing through the lungs (p. 215). Analyses show that the blood going to the lungs is poorer in oxygen and richer in carbon dioxide than the blood coming from the lungs (fig. 144). *Oxygen is taken by the blood from the air, carbon dioxide is given by the blood to the air.*

How is this effected? The extensive capillary network in the walls of the air vesicles, if spread out in a continuous sheet, would present a surface of about 75 square metres. Between the blood in the capillaries and the air in the air vesicles are two layers of living cells—

1*st*. The endothelium lining the capillaries.

2*nd*. The flattened cells lining the air vesicles. Through these cells the interchange of gases must take place.

The interchange might take place in two different ways—

1*st*. By simple mechanical diffusion.

2*nd*. By some special action of the cells.

If the process follows strictly the laws of simple diffusion, it is then unnecessary to invoke the activity of the cells as playing a part. But if the gaseous interchange does not *strictly* follow these laws, we must conclude that the cells do play a part.

To determine if the process can be accounted for by diffusion it is therefore necessary to know—

1*st*. The partial pressure or tension of the gases in the blood going to and coming from the lungs.

2*nd*. The partial pressure of the gases in the air in the air vesicles.

I. The Partial Pressure of the Gases in the Blood.—Whether a gas is simply dissolved or whether it be held in loose chemical combination, the amount held will depend upon the *temperature* of the fluid and upon the *pressure* of the gas over the fluid. If the temperature is raised the fluid will hold less of the gas in solution, and any chemical combination will tend to split, as is seen when carbonate of lime is heated and the carbon dioxide is driven off.

If the pressure of any gas over a fluid be increased it will be taken up by the fluid, if it is decreased the gas will tend to come off from the fluid, as occurs when a bottle of soda water is opened. But the same law applies to such chemical compounds as carbonate of lime. If it is heated in ordinary air—*i.e.* under a low pressure of carbon dioxide—the gas is given off; but if the lime is in an atmosphere of CO_2 the gas does not come off, but is taken up and the carbonate is formed.

It will thus be seen that for every temperature there is a certain pressure of the gas at which the solution or chemical combination will neither give off nor take up more of the gas. This may be determined by exposing the material in a series of chambers to air containing different proportions of the gas, and ascertaining by analyses of the air whether the gas has been given off or taken up or has remained unaltered. The presence of a moist membrane between the fluid and the air makes no difference to these interchanges.

For blood some form of ærotonometer is used, an instrument in which blood is allowed to trickle through a tube filled with air of known composition till the tension of the gases in the blood and air have become the same. The tension is then determined by analysis of the proportions of the gases in the air in the tube.

We know that the pressure of gas in an atmosphere depends upon the proportion present. Suppose an atmosphere contains 20 per cent. of oxygen, then the pressure, or partial pressure, of the oxygen is got by multiplying the percentage amount of the gas by 760—*i.e.* a whole atmosphere's pressure—and dividing by 100—

$$\text{Pressure of oxygen} = \frac{20 \times 760}{100} = 152 \text{ mm.}$$

The results obtained by means of the ærotonometer in the hands of different investigators have varied very widely.

Another method of arriving at the tension of oxygen in the blood has been devised by Haldane. It depends upon the fact that if hæmoglobin is exposed to a mixture of air with a trace of carbon monoxide in it, the amount of carbon monoxide taken up depends upon the oxygen tension—the greater the tension of oxygen the less CO will be taken up, and *vice versa*. Therefore if a person be allowed to breathe an atmosphere containing a known amount of CO, the amount of CO taken up by the blood will indicate the oxygen tension in the blood.

By such methods, although the results of different observers vary so greatly, it appears that in blood going to the lungs the O tension may be as low as 20 mm. Hg and the CO_2 tension as high as 40 mm. Hg. And that in blood coming from the lungs the O tension is generally well over 100 mm. Hg, while the CO_2 tension varies enormously, but is, on an average, about 20 mm. Hg.

II. Partial Pressure of Gases in the Air Vesicle.—The air in the alveoli is not renewed by direct ventilation from without, but by a process of diffusion (p. 303). For this reason the amount of oxygen in the alveoli must be much smaller, the amount of carbon dioxide much larger, than in the respired air.

Haldane has devised a method of procuring samples of the alveolar air for analysis. A wide tube is fitted with a measured glass bulb near one end, and this bulb is made a vacuum. The end of the tube near the bulb is put in the mouth and the person under observation breathes through it. At the end of an ordinary inspiration he expires deeply and quickly through the tube, and by opening the upper stop-cock collects a sample of the expired air. A second sample is taken in the same way at the end of a normal expiration. The mean of these samples represents the average composition of the alveolar air.

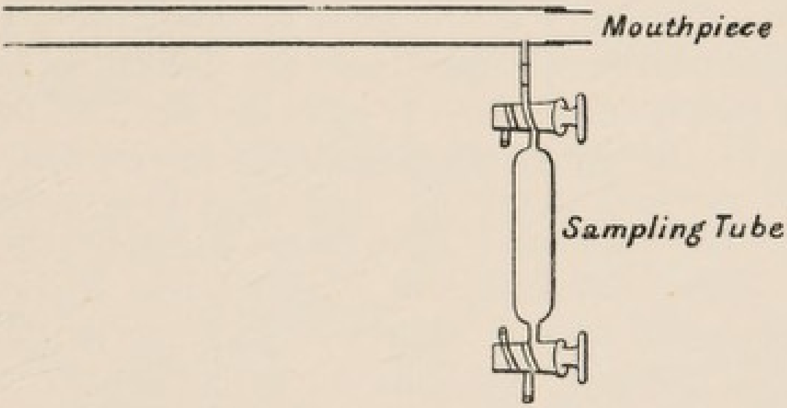


FIG. 145.—Haldane's Apparatus for determining the Composition of Alveolar Air.

By the use of this method it has been found that the partial pressure of the O varies within wide limits, while the partial pressure of the CO_2 remains very constant.

Thus at the top of Ben Nevis the pressure of oxygen was 76 mm. Hg; at the bottom of a mine it was 111; while in both places the pressure of carbon dioxide was about 42 mm.

In spite of these wide variations in the oxygen pressure in alveolar air the tension of oxygen in the blood remains about the same.

The difference in the pressure of these gases in the alveolar air, and in the blood going to and coming from the lungs, may be represented as follows in mm. Hg:—

	Oxygen		Carbon Dioxide	
Alveolar Air	76 to 111		42	
	↙		↗	
Blood	20 Venous	100+ Arterial	46 Venous	0−40 Arterial

This shows that when the blood reaches the lungs the distribution of pressure of the gases is such that, by the laws of diffusion, oxygen will pass from the alveolar air into the blood and carbon dioxide from blood to air; but that, before the blood has left the lungs, the distribution is such that oxygen *should*, by the laws of diffusion, pass *from blood to lungs* and carbon dioxide *from lungs to blood,* which is exactly the reverse of what occurs. The passage of oxygen to the blood and the passage of carbon dioxide from the blood is, in fact, much greater than could be accounted for by diffusion.

We must therefore conclude that the exchange of gases between the alveolar air and the blood *is not due entirely to diffusion, but is in part, at least, brought about by the activity of the cells lining the vessels and the alveoli.*

It should, however, be stated that, in spite of these figures, some physiologists maintain that simple diffusion will explain these interchanges—1*st*, because, when the amount of oxygen in the atmosphere—*i.e.* when the partial pressure of O—falls below a certain point, the gas is no longer taken up by the blood; and 2*nd*, because, when the amount and pressure of CO_2 rises, the CO_2 is not given off from the blood.

The partial pressure of oxygen may be reduced to a half without interfering with the vital processes of the body, and for this reason it is possible for men and animals to live at high altitudes. When men are suddenly subjected to a very marked decrease of pressure, especially if they have to do muscular work, as in climbing, the decreased supply of oxygen leads to shortness of breath, palpitation, and even to sickness **(mountain sickness)**. These symptoms soon pass off, increased pulmonary ventilation and increased heart action increasing the intake of oxygen. Hence residence in high altitudes tends to increase the power of the respiratory muscles and the strength of the heart. It also increases the richness of the blood in erythrocytes and in hæmoglobin.

On the other hand, the atmospheric pressure may be enormously increased without any change in the metabolism. In a diving bell 200 feet under water a pressure of 5120 mm. Hg—seven atmospheres—is sustained. As a result of the high pressure of the gases of the atmosphere they are dissolved in large quantities in the blood and tissues, and there is great danger in too sudden relief of pressure, since this may cause bubbles of gas to be given off in the vessels, and these may lead to air embolism and a plugging of the smaller vessels **(Caisson disease)**.

B. INTERNAL RESPIRATION

1*st*. The Passage of Oxygen from Blood to Tissues.

In studying the physiology of muscle, which may be taken as a type of all the active tissues, it was seen that oxygen is constantly being built up into the muscle molecule, and that the living tissues have such an affinity for oxygen that they can split it off from such pigments as alizarin blue. The tension of oxygen in muscle is therefore always very low. We have seen that the tension of oxygen in arterial blood is nearly 100 mm. Hg; therefore, when the blood is exposed to a low tension of oxygen in the tissues, the oxygen comes off from the blood and passes into the tissues by the ordinary laws of diffusion.

But it must be remembered that this takes place in three stages.

(1) The tissue elements are always taking up oxygen from the lymph, because of the very low pressure of oxygen in the protoplasm and because the protoplasm has an affinity for oxygen as for other nourishing substances.

(2) As a result of this the oxygen pressure in the lymph falls and becomes lower than the oxygen pressure of the blood plasma, and thus the gas passes from the blood through the

capillary walls to the lymph. How far this is simply the result of mechanical diffusion, and how far it is carried on by the vital action of the endothelium of the capillaries, we do not know.

(3) As a result of the withdrawal of oxygen from the plasma, the partial pressure round the erythrocytes is diminished, and the blood being at a high temperature, a dissociation of oxyhæmoglobin takes place, and the oxygen passes out into the plasma, leaving reduced hæmoglobin in the erythrocytes.

2nd. **The Passage of Carbon Dioxide from Tissues to Blood.**

The tissues are constantly producing carbon dioxide, so that it is at a high tension in them—about 60 mm. Hg. In the blood the carbon dioxide is combined with the sodium and is thus at a low tension. Hence there is a constant passage of carbon dioxide from the tissues to the blood.

C. EXTENT OF RESPIRATORY INTERCHANGE

The extent of the respiratory interchange in the lungs is governed by the extent of the internal respiratory changes —*i.e.* by the activity of the tissues. Every factor which increases the activity of the metabolic changes in the tissues increases the intake of oxygen and the output of carbon dioxide by the lungs.

It may be studied by enclosing an animal or a man in an air-tight case or chamber through which air of known composition is passed in measured quantity and analysed as it is withdrawn. This may be done by making the air pass through vessels containing sulphuric acid to absorb the water and caustic potash to fix the CO_2, and absorbing the oxygen by pyrogallate of soda.

In the resting **horse** the average amount of oxygen consumed is about 4 c.cms. per minute per kilo. of body weight, and the amount of carbon dioxide given off about 3·5 c.cms.

1. *Muscular Work.*—Since muscle is the most abundant and active tissue of the body, muscular work more than anything else increases the respiratory changes (see p. 67).

2. *Food.*—The taking of food at once sets up active changes in the digestive apparatus. The muscular mechanism is set in action and the various glands secrete. As a result of these

processes the respiratory interchange is at once increased. That the increase is dependent upon the increased functional activity of the digestive organs is shown by the fact that it is produced by the taking of substances which cannot be absorbed and used in the metabolic processes of the body.

But while the *immediate* increase in the respiratory interchange following the taking of food is due to the increased activity of the digestive structures, there is also an increase due to the utilisation in the body of the food taken. Whether proteins, fats, or carbohydrates, or all of these form the diet, more oxygen is consumed and more carbon dioxide is given off than during starvation. The proportion between the oxygen taken and the carbon dioxide excreted is not, however, the same with all these food-stuffs. If the food is rich in carbon and poor in oxygen, a greater quantity of oxygen must be taken to oxidise it than if it is rich in oxygen.

The chief constituents of the food contain the following percentage amounts of oxygen and of carbon :—

	Oxygen.	Carbon.
Carbohydrates . .	53	40
Proteins	22	52
Fats	12	76

Hence on a carbohydrate diet, such as that of the horse, the respiratory quotient (p. 314) $\frac{CO_2}{O}$ is high, about 0·9 to 1, while on a fatty or protein diet it is low, 0·7 to 0·8.

3. *Temperature.*—If the temperature of the *body* be increased, the metabolic processes become more active and the respiratory interchanges are increased. But if the temperature of the *air* round the body be elevated, the metabolic processes may be diminished in activity, and the respiratory exchange decreased.

4. *Light.*—It has been shown that light increases the metabolic changes and therefore the respiratory activity.

5. *Sleep.*—Since in sleep the animal is in a condition of muscular rest, since light is excluded from the eyes and since food is not taken, the respiratory exchanges are less active during sleep than during the waking hours. Similarly, in

the long winter sleep of certain animals (**hibernation**), these factors, as well as the diminished temperature of the body, cause a great reduction in the intake of oxygen and output of carbon dioxide.

It is thus the internal which governs external respiration. Merely increasing the number or depth of the respirations has only a transient influence on the amount of the respiratory interchanges.

Asphyxia

This is the condition caused by any interference with the supply of oxygen to the blood and tissues. It may be induced rapidly and in an acute form by preventing the entrance of air to the lungs, as in drowning or suffocation, or by causing the animal to breathe air deprived of oxygen, or by interfering with the flow of blood through the lungs, or with the oxygen-carrying capacity of the blood. It is slowly induced in a less acute form when the muscles of respiration fail as death approaches.

In *acute asphyxia* there is an initial stage of increased respiratory effort, the breathing becoming panting, and the expirations more and more forced. The pupils are small, and the heart beats more slowly and more forcibly, while the arterioles are strongly contracted, and a marked rise in the arterial pressure is produced. When the vagi are cut the slowing of the heart does not occur. Within a couple of minutes a general convulsion, involving chiefly the muscles of expiration, occurs. The intestinal muscles and the muscles of the bladder may be stimulated, and the fæces and urine may be passed involuntarily. Then the respirations stop, deep gasping inspirations occurring at longer and longer intervals. The pupils are dilated, and consciousness is abolished. The heart fails, and thus, although the arterioles are still contracted, the pressure in the arteries falls. Finally the movements of the heart cease and death supervenes.

VOICE

In connection with the respiratory mechanism of many animals, an arrangement for the production of sound or voice is developed. This is constructed on the principle of a **wind instrument**, and it consists of (1) a bellows, (2) a windpipe, (3) a vibrating reed, and (4) resonating chambers. In man and other mammals the bellows are formed by the lungs and the thorax. The trachea is the wind-pipe. The vocal cords in the larynx are the vibrating reeds, and the resonating chambers are the pharynx, nose, and mouth.

A. Structure of the Larynx.—The points of physiological importance about the structure of the larynx are the following:—

1. **Cartilages** (figs. 146, 147).—The ring-like *cricoid* (*Cr.*) at the top of the trachea is thickened from below upwards at its posterior part and carries on its upper border two pyramidal cartilages triangular in section—the *arytenoids* (*Ar.*). These articulate with the cricoid by their inner angle. At the outer angle the posterior and lateral crico-arytenoid muscles are attached. From their anterior angles the vocal cords arise and run forward to the thyroid. The *thyroid* cartilage (*Th.*) forms a large shield which articulates by its posterior and inferior process with the sides of the cricoid, so that it moves round a horizontal axis. To the upper and anterior part, the *epiglottis* or cartilaginous lid of the larynx is fixed.

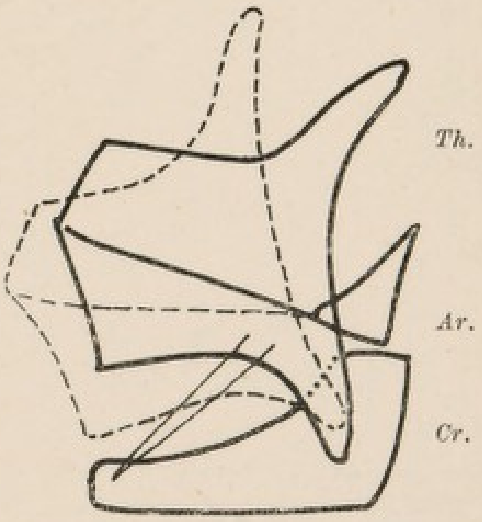


Fig. 146.—Side View of the Cartilages of the Larynx. *Cr.*, cricoid cartilage; *Ar.*, right arytenoid cartilage; *Th.*, thyroid cartilage. The dotted line shows the change in the position of the Thyroid by the action of the Crico-thyroid Muscle, and the stretching of the vocal cords which results.

2. **Ligaments.**—The articular ligaments require no special attention. The true **vocal cords** are fibrous ligamentous structures which run from the arytenoids forward to the posterior aspect of the middle of the thyroid. They contain

many elastic fibres and are covered by a stratified squamous epithelium and appear white and shining.

The vocal cords increase in length as the larynx grows, and in adult life they are generally longer in the male than in the female, and the whole larynx is larger.

3. **Muscles.**—The *crico-thyroids* take origin from the antero-lateral aspects of the cricoid, and are inserted into the inferior part of the lateral aspect of the thyroid. In contracting they approximate the two cartilages anteriorly, and render tense the vocal cords (fig. 146).

The *crico-arytenoidei postici* arise from the back of the cricoid and pass outwards to be inserted into the external or muscular process of the arytenoids. In contracting they pull these processes inwards, and thus diverge the anterior processes and open the glottis (fig. 147).

The *crico-arytenoidei laterales* take origin from the lateral aspects of the cricoid, and pass backwards to be inserted into the muscular processes of the arytenoids. They pull these forward and so swing inwards their anterior processes and approximate the vocal cords (fig. 147).

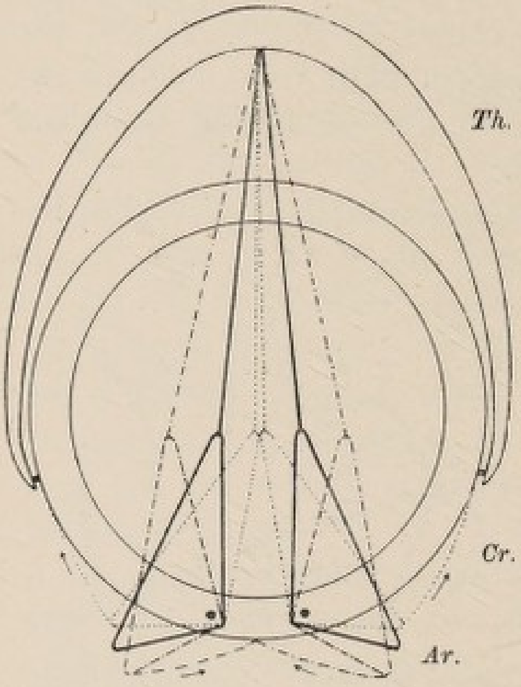


FIG. 147.—Cross Section of the Larynx, to show the cricoid, *Cr.*; thyroid, *Th.*; arytenoid cartilages, *Ar.* The continuous line shows the parts at rest, the dotted line under the action of the Lateral Crico-arytenoid Muscle, and the dot-dash line under the action of the Posterior Crico-arytenoid.

A set of muscular fibres run between the arytenoids—the *arytenoidei*—while others run from the arytenoids up to the side of the epiglottis. These help to close the upper orifice of the larynx.

The *thyro-arytenoid* is a band of muscular fibres lying in the vocal cords and running from the thyroid to the arytenoids. Its mode of action is not fully understood.

4. **Mucous Membrane.**—The mucous membrane of the larynx

is raised on each side into a well-marked fold above each true vocal cord—the false vocal cord. Between this and the true cord on each side is a cavity—the ventricle of the larynx. The other folds of mucous membrane, although of importance in medicine, have no special physiological significance.

The interior of the larynx may be examined during life by the **laryngoscope**. (*Practical Physiology.*)

5. **Nerves.**—The muscles of the larynx are supplied chiefly by the recurrent laryngeal branch of the vagus which comes off in the thorax and arches upwards to the larynx. On the left side, where it curves round the aorta, it is apt to be pressed upon in aneurismal swellings. Paralysis of this nerve causes the vocal cord on that side to assume the cadaveric position, midway between adduction and abduction, and makes the voice hoarse or abolishes it altogether. The superior laryngeal is the great ingoing nerve, but it also supplies motor fibres to the crico-thyroid muscle. Paralysis prevents the stretching of the vocal cords, makes the voice hoarse, and renders it impossible to produce a high note.

Centre.—These nerves are presided over by (*a*) a centre in the medulla. When this is stimulated abduction of the vocal cords is brought about. (*b*) This centre is controlled by a cortical centre situated in the inferior frontal convolution in man and apes. Stimulation of this causes adduction of the cords as in phonation, while destruction leads to no marked change.

B. Physiology.—When a blast of air is forced between the vocal cords they are set in vibration both wholly and in segments like other vibrating reeds, and sounds are thus produced. These sounds may be varied in loudness, pitch, and quality.

The **loudness**, or amplitude of vibration, depends upon the size of the larynx and upon the force of the blast of air acting on the cords.

The **pitch**, or number of vibrations per second, depends upon the length and tension of the vocal cords. The tension of the cords may be varied by the action of the crico-thyroid muscles.

The power of varying the pitch of the voice differs greatly in different animals.

The **quality** of the sound depends upon the overtones which are made prominent by resonance in the pharynx, nose, and mouth. By varying the shape and size of these cavities, and more especially of the mouth, the quality of sound may be considerably altered.

In animals the voice varies with the age and sex, and it may be modified by castration.

II. FOOD AND DIGESTION

I. FOOD

The great use of food is to supply energy to the body. The muscles of the body are constantly active; they are constantly liberating energy by breaking down the complex molecules of proteins, fats, and carbohydrates, and hence a constant fresh supply of such material is necessary to prevent the body living on its own material and wasting away (see p. 69). During the growth of the body, too, the material from which it is to be built up, and the energy used in its construction, must be supplied by the food.

Hence a suitable food is one which will yield the necessary amount of energy, and will supply the materials necessary for repair and for growth.

But food must also supply the water and salts required to keep the various constituents of the body in solution, so that the essential chemical changes may go on.

Nature of Food

Food may be divided into foods not yielding energy and foods yielding energy.

A. Food-stuffs not yielding Energy.—1. Water is the chief constituent. Since it is daily given off in large quantities by the kidneys, lungs, skin, and bowels, it must daily be supplied in sufficient amounts or the chemical changes cannot go on and death supervenes.

2. *Inorganic Salts.*—The most important of these is sodium chloride, which is essential for the maintenance of the chemical changes in the body. When it is not freely supplied in the food, it is retained in the tissues, and hence animals can, when necessary, live with a comparatively small supply.

3. *Salts of Organic Acids.*—The sodium and potassium salts of citric, malic, and tartaric acid, which are found abundantly in various vegetables, when taken into the tissues, are oxidised into carbonates which are strongly alkaline salts. The proteins which are decomposed in the body contain sulphur and phosphorus, and these are oxidised into sulphuric and phosphoric acids. In herbivorous animals the prejudicial effect of such acids is counteracted by the formation of these alkaline carbonates which neutralise the acids. In carnivorous animals these salts are not so necessary, since ammonium is formed from the nitrogen of the proteins in sufficient quantity to neutralise the acids produced. Man occupies a position midway between the herbivora and the carnivora. The amount of energy yielded by the breaking down of these salts into carbonates is so small that it is of no importance.

B. Food-stuffs yielding Energy.—These are complex combinations of carbon, hydrogen, and oxygen, with or without nitrogen, sulphur, phosphorus, and iron. They are of the same nature as the materials which are found on analysis of dead protoplasm. They are commonly spoken of as the **Proximate Principles** of the food, and they may be classified as follows:—

1. Nitrogen-containing—Proteins and Sclero-proteins.
2. Non-nitrogenous—Fats and Carbohydrates.

In studying the value of these food-stuffs it is necessary to consider their **Energy Value**—that is, the amount of energy which can be yielded by the decomposition of a definite quantity of each in the body.

The fats and carbohydrates leave the body as carbon dioxide and water, the proteins leave it partly as carbon dioxide and water, partly as urea $CO(NH_2)_2$.

Such a body as glucose, $C_6H_{12}O_6$, by being oxidised to CO_2

and H_2O, gives off a certain amount of kinetic energy, and the amount of energy liberated is the same whether the oxidation is direct or takes place through any of many possible lines of chemical change.

In whatever ways a chemical substance breaks down into certain final products, the energy set free is always the same, and this principle is taken advantage of in determining the energy value of the food-stuffs. If fats and carbohydrates are changed to carbon dioxide and water in the body, and if the energy given off as they undergo this change can be measured outside the body, their energy value as foods can be ascertained.

Determination of Energy Value.—This is done by burning a definite quantity of the material and finding how many degrees a definite quantity of water is heated. This gives the energy in *heat units*, and, by Joule's law, it can be converted into the equivalent for any other kind of energy, such as mechanical work.

It is known that the energy required to heat one kilogramme of water through one degree Centigrade is sufficient to raise 423 kilograms of matter to the height of one metre against the force of gravity, and thus, if the energy value of any material as a producer of heat is known in heat units—kilogram degrees or **Calories**—by multiplying by 423 we get the value in work units — kilogram metres **(kgms.)**.

The apparatus used for ascertaining the heat produced by the combustion of material is called **a calorimeter**. Many different forms are in use, but the object in the water calorimeter is to secure that *all* the heat is used in raising the temperature of a known volume of water.

The value of the three great proximate principles of the food must be considered in detail.

1. **Proteins.**—The chemistry of these bodies has been already considered (pp. 10–12). They are the "chief substances" of living matter, forming about 80 or 90 per cent. of its dry residue. The molecule is one of great complexity, and contains C, H, O, N, S., and sometimes P and Fe.

It is from the proteins of the food alone that the nitrogen *and sulphur required in the construction and repair of the living tissues* are obtained. The carbon and hydrogen required are also contained in these substances; and, as will be presently shown, they have a considerable energy value. Hence *Proteins form* THE *essential organic constituents of the food.* Theoretically it should be perfectly possible for an animal to live on proteins alone, with a suitable addition of water and salts.

In estimating the actual energy value of proteins in the body a difficulty arises in the fact that, instead of being decomposed to CO_2, H_2O, NH_3, SO_3, as they are during combustion in the calorimeter, in the body the nitrogenous part is not broken down further than to urea—$CO(NH_2)_2$, 3 grms. of protein yielding 1 grm. of urea. If the energy value of the complete combustion of a definite amount of proteins is first ascertained, and then the energy value of the amount of urea derived from the same amount of protein is determined, by subtracting the latter from the former, the energy value of proteins in their decomposition in the body is found (see p. 331).

The combustion of 1 grm. of protein to urea yields 4·1 Calories of Energy.

2. **Sclero-proteins.**—In studying the chemistry of the formed material of the various protecting, supporting, and connecting tissues, these substances have been considered (see p. 12).

Keratin, elastin, and mucin seem to be of no importance as articles of food. If taken in the food they pass through the alimentary canal practically unchanged.

While raw collagen seems also to be of little use, gelatin, formed by boiling collagen, has a certain value. Although it cannot take the place of proteins, because it cannot be used for building up the living tissues of the body, it is nevertheless decomposed into urea, and in decomposing it yields the same amount of energy as the proteins. It has, therefore, a definite though restricted value as a food stuff.

3. **Fats.**—The chemistry of the fats has already been considered (p. 29). From the fact that they contain so little oxygen in proportion to their carbon and hydrogen, a large amount of energy is liberated in their combustion, and therefore they have a high energy value as food-stuffs.

One gramme of fat yields twice as much energy as the same amount of protein or carbohydrate. The combustion of 1 gramme of fat yields 9·3 Calories of Energy.

4. Carbohydrates (*for tests for different carbohydrates, see "Chemical Physiology"*).—The carbohydrates—starches and sugars—form a group of bodies which do not occur largely in animals, but are abundant constituents of plants.

They contain carbon, hydrogen, and oxygen, the carbon atoms of the molecule usually numbering six or some multiple of six, and the hydrogen and oxygen being in the same proportions in which they occur in water. They are aldoses or ketoses and derivations from these, of the hexatomic alcohol, $C_6H_{14}O_6$ (p. 452). A group of carbohydrates having five carbon atoms, and hence called Pentoses, have been found in the animal body, but they are of minor importance.

The simplest carbohydrates are the **monosaccharids,** of which dextrose, the aldose of mannite, is the most important. Dextrose is *the* sugar of the animal body. It has been called glucose, grape sugar, and blood sugar.

Closely allied to dextrose in chemical composition is the ketose *lævulose*, a sugar which, instead of rotating the plane of polarised light to the right, rotates it to the left, but which in other respects behaves like dextrose. It occurs in certain plants, and in the fœtus and fœtal fluids of certain animals.

The other monosaccharid of importance is *galactose*, a sugar produced by the splitting of milk sugar.

These monosaccharids, when boiled with a solution of cupric acetate in acetic acid (Barfoed's solution), are oxidised, taking oxygen from the cupric salt and reducing it to the cuprous state. When boiled with caustic potash, they, along with certain of the double sugars, are oxidised, and if a metallic salt be present which can readily give up its oxygen, it becomes reduced, the sugar appropriating the oxygen. On this depends Fehling's and many other tests for glucose.

Under the influence of yeast they split into ethyl alcohol and carbon dioxide.

They also form crystalline compounds, osazones, with phenylhydrazin. These have proved most useful in distinguishing different sugars.

By the polymerisation of two monosaccharid molecules with the loss of water, **disaccharids**, or double sugars, are formed. Thus, two glucose molecules polymerise to form one *maltose* molecule.

$$\begin{aligned} C_6H_{12}O_6 + C_6H_{12}O_6 &= 2\,(C_6H_{12}O_6) - H_2O \\ &= C_{12}H_{22}O_{11} \end{aligned}$$

Maltose is the sugar formed by the action of malt and other vegetable and animal zymins upon starch. By the action of dilute acids and other agents it can be split into two dextrose molecules. Like the monosaccharids, it ferments with yeast.

Lactose, the sugar of milk, is a disaccharid composed of a molecule of dextrose united to a molecule of galactose with dehydration. It readily splits into these two monosaccharids, but does not ferment with yeast.

Dextrose, polymerising with lævulose, yields *cane sugar*, and this sugar, so largely used as an article of food, can be split into dextrose and lævulose. It does not reduce Fehling's solution, and does not ferment with yeast. Under the action of mineral acids it breaks down into its component sugars.

By further polymerisation of monosaccharids with the loss of water, molecules of greater size are produced and form the set of substances known as the **polysaccharids.** Among the simplest of these are the *dextrins.*

Closely allied to dextrins are the *inulins.* But while dextrin is formed of dextrose molecules, inulin contains lævulose molecules. Both are formed from the splitting of the more complex *starches.* The molecule of soluble starch is built up of no less than thirty dehydrated monosaccharid molecules, and has a molecular weight of 9000. Ordinary starch seems to have a molecular weight of 20,000 or 30,000, and hence must be of still greater complexity.

These polysaccharids are distinguished from the sugars by being precipitated from their solutions by the addition of alcohol. They are not oxidised when boiled with caustic potash, nor do they change to alcohol and carbon dioxide under the influence of yeast. In cold neutral or acid solutions most of them strike a blue or brown colour with iodine. By boiling with a mineral acid and by the influence of various ferments they break down, take up water, and become monosaccharids—the starches yielding the dextroses, and inulins yielding lævulose.

Glycogen is animal starch. It gives an opalescent solution and strikes a brown colour with iodine.

Cellulose, which forms the capsule of vegetable cells, also belongs to the group of polysaccharids. It is characterised by its insolubility and by the fact that it is not acted upon by the starch digesting enzymes of the alimentary canal.

The energy value of the carbohydrates is about the same as that of the proteins.

Energy Value of the Proximate Principles of the Food.—1 gramme of—

Protein yields	4·1	Calories.
Carbohydrate yields . .	4·1	„
Fat yields	9·3	„

The Sources of the Various Proximate Principles of the Food

The proximate principles are in part derived from the *animal*, in part from the *vegetable* kingdoms. While some races procure their food entirely, or almost entirely, from the former, others depend almost entirely on the latter. The vast majority of mankind, however, use a mixture of animal and vegetable foods.

Animal foods may be classified as—

1. Milk and its products, Cream, Butter, and Cheese.
2. Flesh.
3. Eggs.

1. **Milk** (*Chemical Physiology*).—The white colour of milk is due to its being a fine emulsion of fat globules floating in a clear plasma. Hence, when the cream is removed, milk becomes less white and less opaque. Its specific gravity is

about 1030, and in man and herbivorous animals its reaction is alkaline.

The chief *protein* of milk is *caseinogen*, a nucleo-protein with a very small amount of phosphorus, which exists as a soluble calcic compound. It is held in solution in milk, but under the influence of various agents it clots or curds. Its calcic compound is split by the action of acids, and casein is precipitated. Under the influence of rennet caseinogen splits into whey albumin which remains in solution, and calcic paracasein which is insoluble and separates as a curd containing the fat. In cow's milk a small amount of an albumin is also present.

The *fats* of milk occur as small globules of varying size floating in the fluid, each surrounded by a protein envelope which must be removed by means of an alkali or an acid before the fat can be extracted with ether. The fats are chiefly olein with smaller quantities of palmatin and stearin, and still smaller amounts of such lower fats as butyrin, capronin, and caprylin.

The *carbohydrate* of milk is lactose, a disaccharid, which splits into dextrose and galactose. Under the action of various micro-organisms it is split to form lactic acid, thus causing the souring of milk.

Phosphorus Compounds.—In addition to caseinogen, milk contains other organic phosphorous compounds. Among these is *lecithin* and a compound which has been called *phosphocarnic acid*, the constitution of which is not fully understood. In human milk the greater part of the phosphorus is in organic combinations, while in cow's milk the amount in inorganic compounds is much greater.

Milk is specially rich in **calcium** and **potassium**, but the amount of **iron** in milk is very small, and therefore, when the child has used up the store of iron which it has in its body at birth, it is necessary to replace the milk-diet by foods containing more iron.

The *average* composition of the milk of the cow, mare, and bitch is shown in the table on page 334.

Butter and Cream are simply the fats of the milk more or less completely separated from the other constituents.

Cheese is produced by causing the coagulation of the casein, which carries with it a large amount of the fats. If cheese is made before the removal of the cream it is rich in fats, if after the removal of the cream it is poor in fats. Cheese contains between 25 and 30 per cent. of protein, and between 10 and 30 per cent. of fat. It is as a source of protein that it is of chief value.

Percentage Composition of Milk.

	Cow.	Mare.	Bitch.
Water	88·3	91·6	75
Proteins	3·0	1·0	10
Fats	3·5	1·3	11
Carbohydrates	4·5	5·7	3
Salts	0·7	0·4	1

Cheese, when allowed to stand, affords a suitable nidus for the growth of micro-organisms by the action of which the proteins are digested into peptones and simpler bodies, and the fats split up into glycerine and the lower fatty acids. These free fatty acids give the peculiar flavour to ripe cheese. The lactose is in part converted into lactic acid.

2. **Flesh.**—Under this head may be included not only the muscles of various animals, but also such cellular organs as the liver and kidneys.

When free of fat, they contain about 20 per cent. of proteins. These are chiefly native proteins, but a certain amount of collagen is also present which yields gelatin on boiling. The amount of fat may vary from almost *nil* in white fish to about 80 per cent. in fat bacon. In animals specially fed, the amount of fat may be enormously increased and even ordinary butchers' meat may have more fat than protein.

Flesh is thus a source of proteins and sclero-proteins, and to a smaller extent of fats. The extractives include such bodies as creatin, xanthin, inosit, etc. (see p. 40), which may help to give the peculiar flavour to the flesh of various animals.

Flesh may be preserved in various ways—*e.g.* by simply drying, by salting, or by smoking. The result of each of these procedures is to diminish the amount of water, and thus to increase the solids.

3. **Eggs.**—The egg of the domestic fowl need alone be considered. The composition of the white and of the yolk naturally differs considerably. The white of egg is nothing more than a solution of proteins.

In the yolk there is a very large amount of lecithin (p. 397) along with ordinary fats, and a large amount of a phosphoprotein; and the great value of eggs is thus that they contain both proteins, ordinary fats, and the special phosphorus containing protein and fat. The mixed contents of the egg contains a little more than 10 per cent. each of proteins and of fats.

Speaking generally, we may say that the animal food-stuffs are rich in proteins and fats, but are poor in carbohydrates.

Vegetable Food-stuffs.—The peculiarity of special importance in vegetables is the existence of a capsule to the cells, composed of **cellulose**—a substance allied in its composition to starch—or of lignin or allied substances. Cellulose is to a large extent dissolved and decomposed in the alimentary canal of herbivora, while it is practically unacted upon in man and in the carnivora. Lignin or woody matter resists digestive changes even in the herbivora, and its only value is to increase the mass of the fæces, and thus to stimulate intestinal action and to act as a natural purgative.

The chief vegetable foods of the herbivora are grass, hay, oats, maize, and the leguminous plants, such as peas and beans.

These vary considerably in composition according to their character, the ground in which they have been grown, and the season of the year at which they are used. Further, the methods of analysis do not give absolutely definite results. The proteins are generally estimated by determining the nitrogen and multiplying by 6·25. But other nitrogen-containing substances besides proteins occur in plants, amido-acids such as asparagin, which, while they are burned in the body and may yield energy like the fats and carbohydrates, do not seem capable of being used like the proteins in building up the living tissues. The amount of these substances is generally greater in the young than in the older parts of plants. Thus in quite young grass about 70 per cent. of the nitrogen is in proteins, and about 30 per cent. not in proteins; while in old grass about 80 per cent. of the nitrogen exists in proteins. Again, in extracting **fats** with ether, chlorophyll, the green colouring substance of plants and other matters are removed along with the fat. Hence it must be remembered that the proteins and fats in the following table are somewhat too high:—

Average Percentage Composition.

	Water.	Protein.	Fat.	Fibre.	Carbo-hydrate.	Ash.	
Grass .	80	4	1	4	10	1	20 to 30 per cent. of nitrogen not in proteins.
Hay . .	15	10	2	26	40	7	About 10 per cent. of nitrogen not in proteins.
Peas . .	14	22	2	6	53	3	About 10 per cent. of nitrogen not in proteins.
Oats (crushed)	14	12	6	9	57	2	Less than 10 per cent. of nitrogen not in proteins.
Potatoes .	76	2	0	1	20	1	Over 40 per cent. of nitrogen not in proteins.

The soluble **carbohydrates** are determined by taking the difference between the total solids and the proteins, fats, and insoluble fibre combined. But while a rough measure of their amount is thus procured, the presence of *various gummy* substances may somewhat vitiate the results.

For these reasons no attempt is made in the table above to give more than rough approximate results of analysis such as will be found useful in regulating the diet of domestic animals.

Cooking of food for animals has two purposes—First, to soften and burst the cell capsule of vegetable foods so as to render the contents more readily available; and second, to destroy bacteria.

II. DIGESTION

I. Structure of Alimentary Canal

The anatomy and histology of the alimentary tract must be studied practically. We shall here merely give such an outline of the various structures as will assist in the comprehension of their physiology.

The Alimentary Canal (fig. 149) may be divided into the mouth, the œsophagus or gullet, the stomach, the small and large intestines, and three sets of supplementary structures—the salivary glands, the liver, and the pancreas.

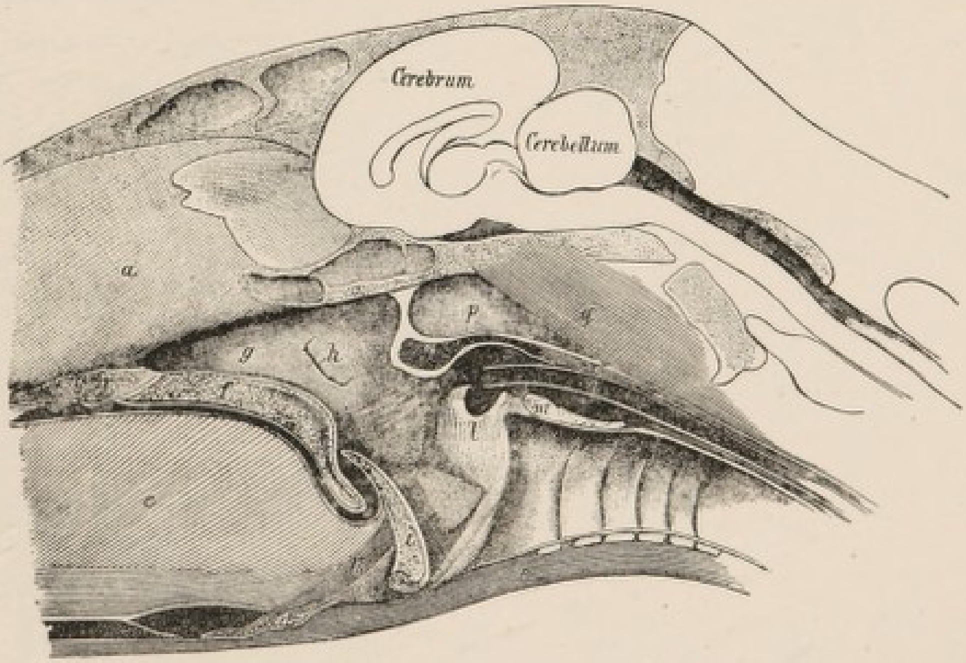


FIG. 148.—Mesial Section through the Head of a Horse, to show the long soft palate, *f*, lying against the front of the epiglottis, *i* ; *c*, the tongue ; *l*, the arytenoids. (ELLENBERGER.)

The **Mouth**, provided with its teeth, and surrounded by its mobile muscular wall, with the muscular tongue lying in its floor, is the part of the canal in which the food is broken up and prepared for digestion. In the horse the lips are long and prehensile, and are essential for the taking of food. Into the mouth three pairs of compound glands—the **Salivary**

Glands—open. The parotid, lined entirely by enzyme-secreting epithelium, opens on the side of the cheek, while the submaxillary gland, composed partly of acini with enzyme-secreting, and partly of acini with mucin-secreting epithelium, and the sublingual, composed entirely of mucin-secreting acini, open under the tongue (*S.C.*).

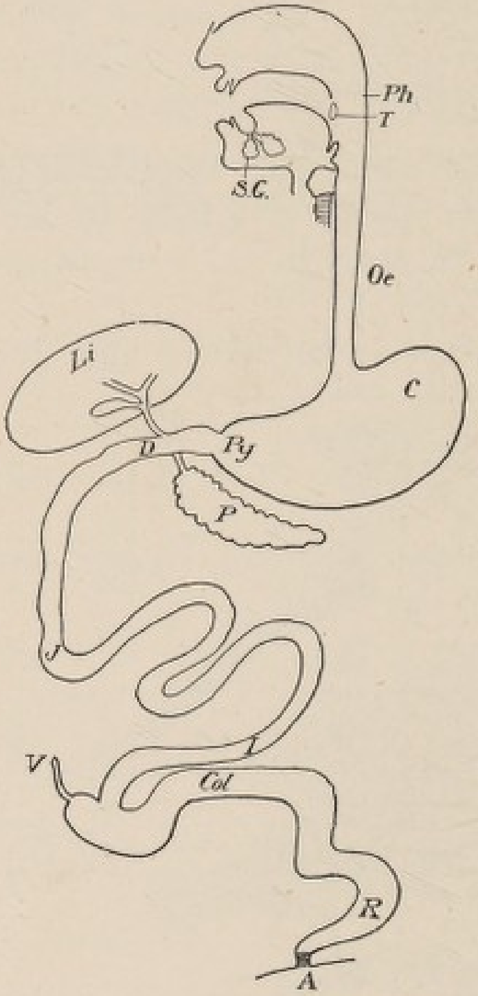


Fig. 149.—Diagram of the Parts of the Alimentary Canal, from Mouth to Anus. *T*, tonsils; *Ph.*, pharynx; *S.G.*, salivary glands; *Oe.*, œsophagus; *C.*, cardiac; *Py.*, pyloric portion of stomach; *D.*, duodenum; *Li.*, liver; *P.*, pancreas; *J.*, jejunum; *I.*, ileum; *V.*, vermiform appendix; *Col.*, colon; *R.*, rectum.

The **tongue** in the horse is smooth, but in the ox, and still more markedly in the cat, it is covered with a fine fur of processes, the *filiform papillæ*, which are of use in passing the food backwards along its surface in the act of swallowing. (For Organs of Taste, see p. 113.)

Posteriorly, the mouth opens into the **pharynx** (*Ph.*) or upper part of the gullet. In the **horse** the soft palate is very long, reaching to the base of the epiglottis, and, unless during swallowing, shutting off the mouth from the pharynx (fig. 148). On each side, between the mouth and the pharynx, is the **tonsil** (*T.*), an almond-like mass of lymphoid tissue. The pharynx is a cavity which can be shut off above from the posterior nares by raising the soft palate, and by pulling forward the posterior pharyngeal wall. It is surrounded by three constrictor muscles, which, by contracting from above downwards, force the food down the gullet towards the stomach.

The **Œsophagus** (*Oe.*) is a muscular walled tube lined by a stratified squamous epithelium. The muscles, below the lowest constrictor of the pharynx, are of the visceral type, and are arranged in two layers, an outer longitudinal layer, and an inner circular layer.

The **Stomach** in carnivora and in the pig is a dilatation of the alimentary canal into which the gullet opens. To the left it expands into a sac-like cardiac end (*C.*), and to the right it narrows, forming the pyloric end (*Py.*). Like the gullet, it is surrounded by visceral muscular fibres, arranged essentially in two sets. At the cardiac orifice, the circular fibres form a not very marked cardiac sphincter, and at the pyloric end they form a very thick and strong pyloric sphincter.

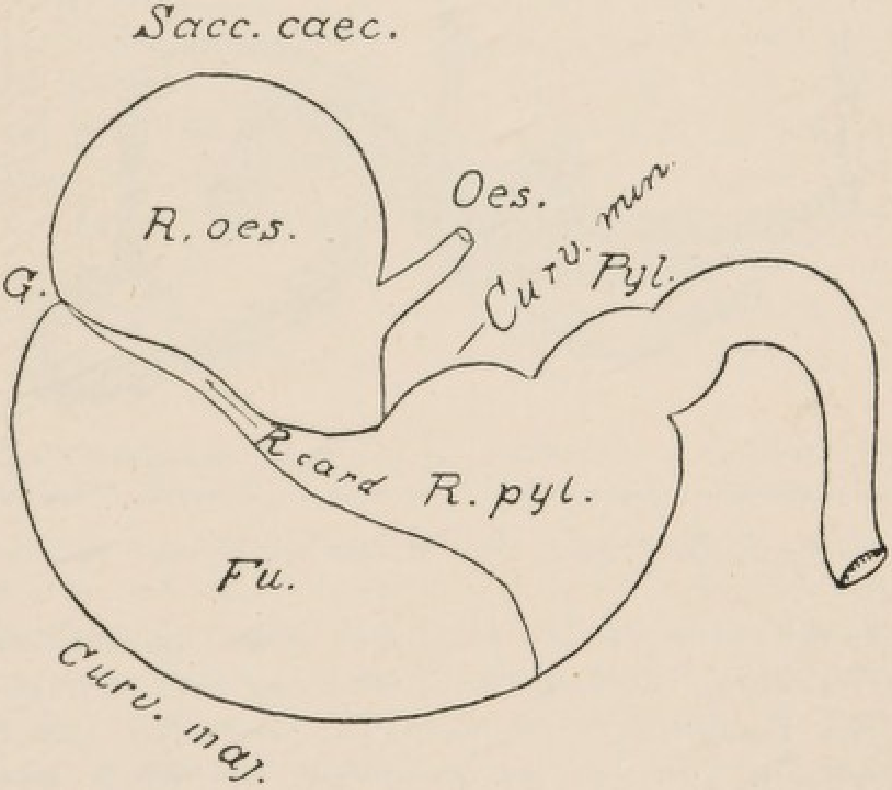


FIG. 150.—Stomach of the Horse to show—*R. œs.*, the œsophageal part ; *Fu.*, the fundus with true gastric glands ; *R. pyl.*, pyloric part.

The mucous membrane, which is covered by a columnar epithelium, is largely composed of tubular glands, those at the cardiac end containing two kinds of cells, the peptic and the oxyntic cells, those at the pyloric end containing peptic cells alone.

In the **horse** the stomach is also a single sac (fig. 150), but the cardiac end is lined by a continuation of the stratified squamous epithelium of the gullet. The opening of this into the stomach is very narrow. The true cardiac mucous membrane is confined to the great curvature. The whole stomach is small when compared with the large intestine, being capable, when distended, of holding about 17 litres.

In **ruminants** the stomach is divided into four parts (fig. 151).

1. The large Rumen or Paunch into which the food is first passed before rumination. It is lined by a stratified squamous epithelium.

2. The Reticulum, which communicates directly with the last, and may almost be considered a part of it, is likewise lined by stratified squamous epithelium. The surface is raised into intersecting ridges, which give it the appearance of a honeycomb.

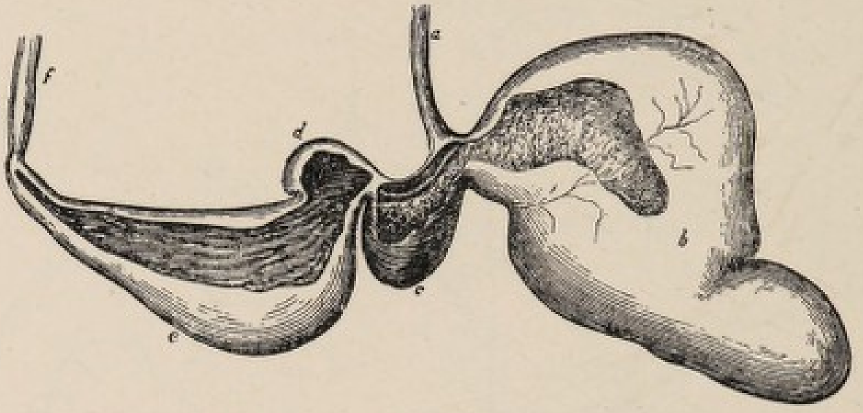


FIG. 151.—Stomach of a Ruminant. *a*, œsophagus ; *b*, rumen ; *c*, reticulum with œsophageal groove above ; *d*, abomasum ; *e*, omasum ; *f*, duodenum.

From the opening of the œsophagus, there pass along the top of the reticulum, two longitudinal muscular folds or pillars.

3. The Psalterium or Omasum has its surface raised into longitudinally disposed leaves, covered by rough stratified squamous epithelium. It opens below into—

4. The True Stomach or Omasum resembles the stomach of the pig in all essential particulars.

The stomach of the ox is about fifteen times as capacious as that of the horse.

The **Small Intestine** has a double muscular coat like the stomach. The mucous membrane, which is covered by a columnar epithelium, is thickly set with simple test-tube-like glands—*Lieberkühn's follicles*—and is projected into the lumen of the tube, as a series of delicate finger-like processes, the *villi*. The tissue of the villi and that between the Lieberkühn's follicles is chiefly lymphoid, and in certain places this lymphoid tissue is massed in nodules which are either placed singly or grouped together in the lower part of the small intestine to form Peyer's patches. In the first part of the small intestine—the upper part of the duodenum (*D.*)—the submucous layer is full of small branching glands lined by an enzyme-secreting epithelium (*Brunner's glands*).

The **Large Intestine**. The small intestine enters it at one side, and the opening is guarded by a fold of mucous membrane which forms the ileo-cæcal valve. Above the opening of the small intestine a cæcal pouch exists, and at the top of this is the vermiform appendix (*V.*), a narrow tube with an abundance of lymph tissue in its wall. This is specially well developed in the rabbit. Below the opening of the small intestine is the colon (*Col.*). This ends in the rectum (*R.*), which opens at the anus. The last part of the rectum is surrounded by a strong band of muscle—the internal sphincter ani—by which it is compressed. The whole large intestine is covered by columnar epithelium, and is studded with Lieberkühn's follicles, in which the epithelium is chiefly mucus-secreting in type. There are no villi.

The cæcum and colon in the **horse** (fig. 152) are enormously developed, holding about 120 litres, or seven times as much as the stomach. The colon is divided into the double colon, which is of immense size and complexity, and the single colon, which is smaller and simpler, and which ends in the rectum.

The large intestine of **ruminants** is much smaller per unit of weight of the animal than that of the horse. In the ox, its capacity is less than 40 litres.

In all animals it is the small intestine which presents the greatest extent of surface for absorption.

Into the duodenum, the bile duct and the duct of the pancreas open. The bile duct is formed by the union of the ducts from the lobes of the liver. Upon its course is a diverticulum, the gall bladder. The **Liver** (*Li.*) is a large solid-looking organ, formed originally as a double outgrowth from the alimentary canal. These outgrowths branch, and again branch, and between them the blood coming from the mother to the fœtus flows in a number of capillary channels. Later, when the alimentary canal has developed, the blood from it is streamed between the liver tubules. In man and other mammals, the fibrous tissue supporting the liver cuts it up into a number of small divisions, the lobules, each lobule being composed of a series of tubules arranged radially with blood vessels coursing between them.

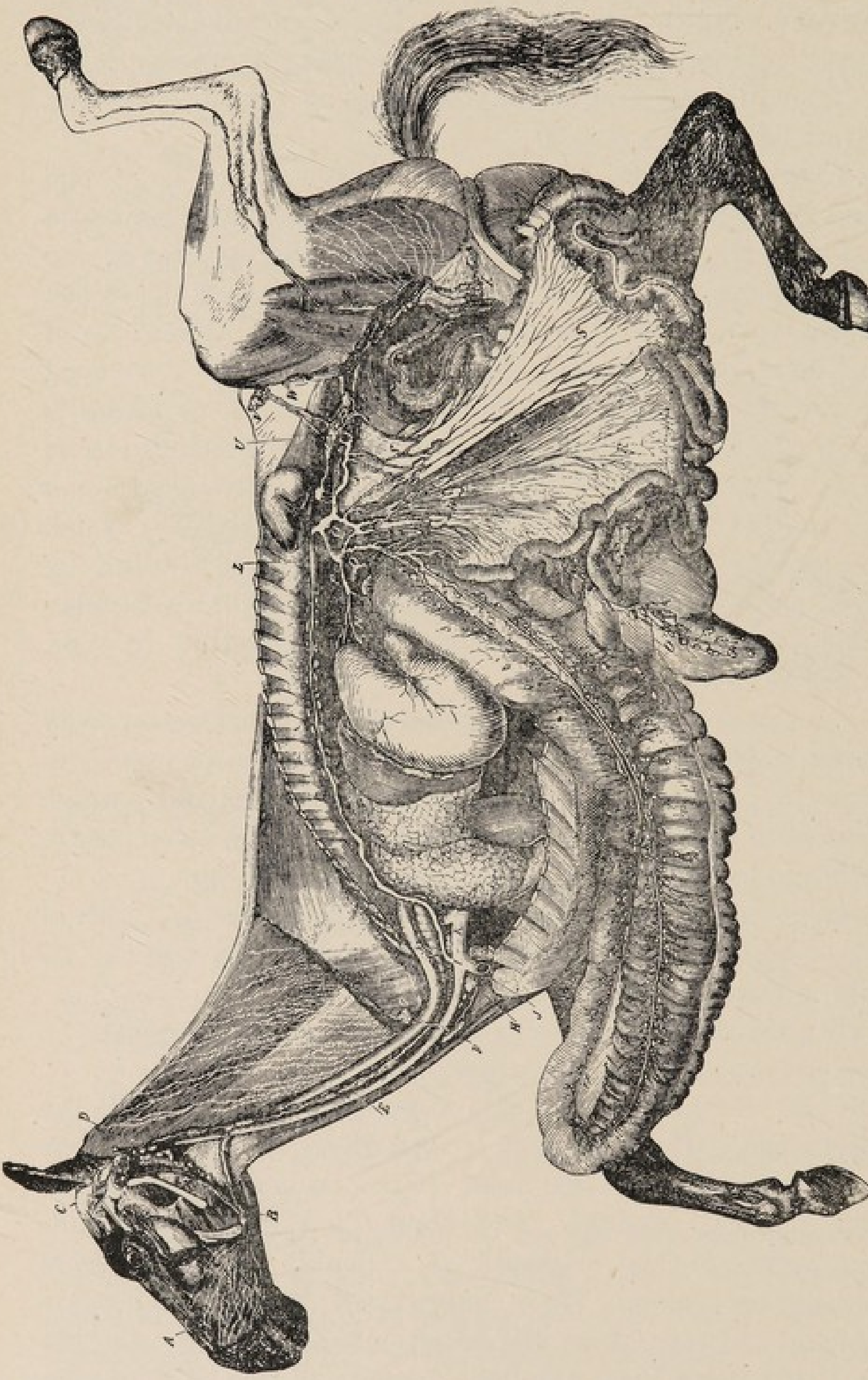


Fig. 152.—Viscera of the Horse, to show the Small Intestine, *R*, ending in the large Colon, *d*, and Cæcum, *O*. The Stomach is seen above the Colon. In the mesentry are seen the lymphatic vessels entering the Receptaculum Chyli and Thoracic Duct. (Chauveau.)

The portal vein which takes blood from the stomach, intestine, pancreas, and spleen breaks up in the liver (fig. 107, p. 225), and carries the blood between the lobules. From the interlobular branches, capillaries run inwards and enter a central vein which carries the blood from each lobule, and pours it into the hepatic veins which join the inferior vena cava. The supporting tissue of the liver is supplied by the hepatic artery; and the terminal branches have a very free communication with those of the portal vein.

The **Pancreas** is essentially the same in structure as the parotid gland. But in the lobules are certain little masses of epithelium-like cells closely packed together, the **Islets of Langerhans** (fig. 153).

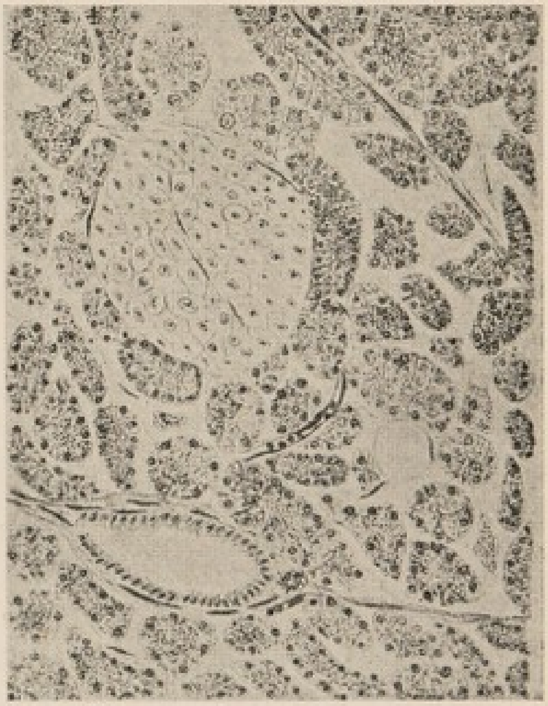


FIG. 153.—Section of Pancreas to show Acini of Secreting Cells; a large duct; and in the centre an Island of Langerhans.

The **Nerve Supply** of the alimentary canal. The muscles round the mouth are supplied by the fifth, seventh, and twelfth cranial nerves. The nerve supply of the salivary glands will be considered later. The pharyngeal muscles are supplied by the ninth and tenth cranial nerves, and the œsophagus is supplied by the tenth.

The stomach and intestine get their nerve fibres from two sources (fig. 76, p. 153)—above the descending colon from the vagus and the abdominal sympathetic, and below this from the nervi erigentes and abdominal sympathetic—the various fibres passing through the abdominal sympathetic ganglia. In the wall of the stomach and intestine, these nerves end by forming an interlacing set of fibres, with nerve cells upon them, from which fibres pass to the muscles and glands. One of these plexuses (Auerbach's) is placed between the muscular coats—the other (Meissner's) is placed in the submucosa.

II. Physiology

I. DIGESTION IN THE MOUTH

A. Prehension of Food.—In the **horse**, solid food is taken up by the lips and bitten by the incisor teeth. If the nerves supplying the lips are cut, it becomes impossible for the horse to graze. Water is sucked into the mouth by a pumping action of the tongue, which acts like a piston, and if air is allowed to get in above the lips, water cannot be sucked up.

In **ruminants** the tongue plays the important part in collecting the hay or grass to be bitten off with the incisors.

B. Mastication.—In the mouth, by the act of chewing, the food is broken up and mixed with saliva.

Mastication in the horse and in ruminants is chiefly a side-to-side movement, by which the food is ground between the molar teeth. It goes on for some time in one direction, and then takes place for some time in the opposite direction. The parotid gland on the side to which the animal is chewing secretes, while the other is less active. In the horse, the process of mastication is very completely performed before the food is swallowed, the animal taking about five to ten minutes to eat a pound of corn, and fifteen to twenty minutes to eat the same amount of hay. The teeth in herbivora grow from a permanent pulp, and hence the changes due to this constant growth give a character to the incisors by which the age may be determined. In ruminants the food is chewed later during rumination.

C. Saliva.—The saliva is formed by the salivary glands (viz., the parotid, submaxillary, sublingual, and various small glands in the mucous membrane of the mouth).

The quantity of saliva secreted by the horse has been measured by making an œsophageal fistula and collecting the boluses of food which are swallowed, and so finding the amount of fluid which has been secreted in the mouth.

In one horse about thirty-six litres of saliva were produced in twenty-four hours.

Characters.—It is a somewhat turbid fluid which, when allowed to stand, throws down a white deposit consisting of shed epithelial scales from the mouth, leucocytes, amorphous calcic and magnesic phosphates, and generally numerous bacteria. Its specific gravity is low—generally about 1003. In reaction it is neutral or faintly alkaline.

Chemically it is found to contain a very small proportion of solids, and the proportion of these varies with the stimulus which causes the secretion. In addition to mucin, traces of proteins are present, and with these proteins in certain animals, but not in the dog, is associated the active constituent or enzyme of the saliva—*ptyalin*.

Saliva generally contains traces of potassium sulpho-cyanide.

The functions of the saliva are twofold:—

1. *Mechanical*, to moisten the mouth and gullet, and thus to assist in speaking, chewing, and swallowing. Since the salivary glands are absent from aquatic mammals, and since in carnivorous animals saliva has no chemical action, it would appear that this is the important function.

2. *Chemical*.—Under the action of the ptyalin of the saliva when this is present, polysaccharids, like the starches, are broken down into sugars. Like other enzyme actions the process requires the presence of water and a suitable temperature, and it is stopped by the presence of strong acids or alkalies, by various chemical substances, and by a temperature of over 60° C., while it is temporarily inhibited by reducing the temperature to near the freezing point. The starch is first changed into the dextrins, giving a brown colour with iodine and hence called *erythrodextrins*, then into dextrins which give no colour with iodine, *achroodextrins*, and lastly into the disaccharid *maltose* (see p. 330). (*Chemical Physiology*).

Physiology of Salivary Secretion.—In order to study the physiology of salivary secretion, a canula may be inserted into the duct of any of the salivary glands and the rate of flow of saliva or the pressure of secretion may be thus measured. In this way it may be shown that the taking of food, or simply the act of chewing, and in some cases the mere sight of food, causes a flow of saliva. This shows that the process of secretion is presided over by the central nervous system.

The submaxillary and sublingual glands are supplied—(1) By branches from the lingual division of the fifth cranial nerve; and (2) by branches of the perivascular sympathetic fibres coming from the superior cervical ganglion. The parotid gland is supplied by the auriculo-temporal division of the fifth and also by sympathetic fibres (fig. 154).

The influence of these nerves has been chiefly studied on the **submaxillary** and **sublingual** glands.

It has been found that, when the lingual nerve is cut, the reflex secretion of saliva still takes place, but that, when the chorda tympani (*Ch.T.*), a branch from the seventh nerve which joins the lingual, is cut, the reflex secretion does not occur. Stimulation of the chorda tympani causes a copious flow of watery saliva, and a dilatation of the blood vessels of the glands. If atropine has been first administered the dilatation of the vessels occurs without the flow of saliva. This indicates that the two processes are independent of one another. The secreting fibres all undergo interruption before the glands are reached; the fibres to the sublingual gland having their cell station in the submaxillary ganglion (*S.M.G.*), the fibres to the submaxillary gland having theirs in a little

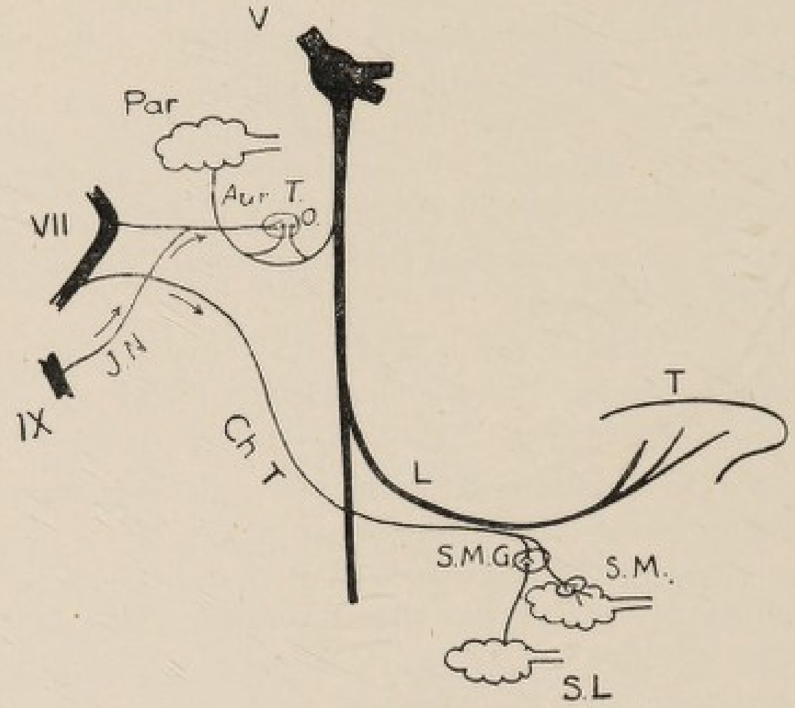


FIG. 154.—Nervous Supply of the Salivary Glands. *Par.*, parotid, and *S.M.* and *S.L.*, the submaxillary and sublingual glands; *VII.*, the seventh cranial nerve, with *Ch.T.*, the chorda tympani nerve, passing to *L.*, the lingual branch of *V.*, the fifth nerve, to supply the glands below the tongue, *T.*; *IX.*, the glossopharyngeal giving off *J.N.*, Jacobson's nerve, to the *O.*, otic ganglion, to supply the parotid gland through *Aur.T.*, the auriculo-temporal nerve.

ganglion at the hilus of the gland (*S.M.*). This was demonstrated by painting the two ganglia with nicotine (p. 154). When applied to the submaxillary ganglion the drug does not interfere with the passage of impulses to the submaxillary gland, but stops those going to the sublingual.

If the duct of the gland be connected with a mercurial manometer, it is found that when the chorda tympani is stimulated the pressure of secretion may exceed the blood pressure in the carotid, showing that the saliva is not formed by filtration.

When the perivascular sympathetics, or when the sympathetic cord of the neck is stimulated, the blood vessels of the gland constrict, and a flow of very viscous saliva takes place.

On the **parotid** gland the auriculo-temporal nerve (*Aur.T.*) acts in the same way as the chorda tympani acts on the other salivary glands. But stimulation of the fifth nerve above the otic ganglion, from which the auriculo-temporal takes origin, fails to produce any effect. On the other hand, stimulation of the glossopharyngeal nerve (*IX.*) as it comes off from the brain, acts upon the parotid gland. Since the glossopharyngeal is united by Jacobson's nerve (*J.N.*) to the small superficial petrosal which passes to the otic ganglion, it is obvious that the parotid fibres take this somewhat roundabout course.

When the sympathetic fibres to the gland alone are stimulated, constriction of the blood vessels but no flow of saliva occurs ; but if, when the flow of watery saliva is being produced by stimulating the glossopharyngeal or Jacobson's nerve, the sympathetic fibres are stimulated, the amount of organic solids in the parotid saliva is very markedly increased.

The nerve fibres passing to the salivary glands are presided over by a centre in the medulla oblongata which acts reflexly. So long as this is intact, stimulation of the lingual or glossopharyngeal leads to a reflex flow of saliva. Other nerves may also act on this centre. Thus, gastric irritation, when it produces vomiting, causes a reflex stimulation of salivary secretion.

According to the investigations of Pavlov the salivary glands react appropriately to different kinds of stimuli through their nervous mechanism. When sand or bitter or saline substances are put in a dog's mouth a profuse secretion of very watery saliva ensues to wash them out. When flesh is given a saliva rich in mucin is produced. When dry food is given saliva is produced in greater quantity than when moist food is supplied. Pavlov further states that the sight of different kinds of food produces a flow of the kind of saliva which their presence in the mouth would produce.

II. SWALLOWING

The food after being masticated is collected on the surface of the tongue by the voluntary action of the buccinators and other muscles, and then, the point of the tongue being pressed against the hard palate behind the teeth, by a contraction of the tongue passing from before backwards, the bolus of food is driven backwards. When the posterior part of the tongue is reached the act becomes purely reflex, and the food is forced through the pillars of the fauces into the pharynx. It is prevented from passing up into the posterior nares by the contraction of the palato-pharyngeus muscle, and of the levatores palati.

The larynx is pulled upwards as a whole by the stylo-hyoid and stylo-thyroid and the thyro-hyoid muscles, and the entrance of food is prevented by the closure of upper part of aperture. The arytenoid cartilages are pulled forward by the thyro-arytenoid muscles, and approximated by the arytenoidei, while a cushion on the posterior surface of the epiglottis becomes applied to their tips, forming a tri-radiate fissure or chink through which food cannot pass. The lateral crico-arytenoids also approximate the vocal cords, and close the glottis.

The constrictors of the pharynx contract from above downwards, and force the food into the grasp of the œsophagus, and this by a slow peristaltic contraction sends the food onwards to the stomach. This peristalsis is abolished by section of the vagi, and it is generally not essential to swallowing. In swallowing liquids it is not brought into play, but the fluid is forced by the tongue down the relaxed œsophagus into the stomach.

The passage of the food into the stomach may be heard as a gurgling sound by applying a stethoscope to the right side of the spinal column, and any delay caused by a stricture may thus be determined.

In swallowing fluids two sounds are heard, one immediately, and one after about six seconds.

III. DIGESTION IN THE STOMACH

Within recent years the most important work on gastric digestion in the dog has been accomplished by Pavlov on dogs. His method is to make a small gastric pouch opening on the surface and separated from the rest of the stomach (fig. 155). This is done by cutting out a V-shaped piece along the great curvature, the apex being towards the pylorus and the base being left connected with the stomach wall. By a series of stitches the opening thus made in the stomach is closed up (top line of ʌʌs in fig. 155), while the cut edges of the V-shaped flap are stitched together to form a tube. The one end of this is made to open upon the skin surface *A*, *A*, and by folding in the mucous membrane the deep end is isolated from the stomach. Thus a pouch is formed still connected with the nerves and vessels of the stomach, the condition of which represents the condition of the whole stomach.

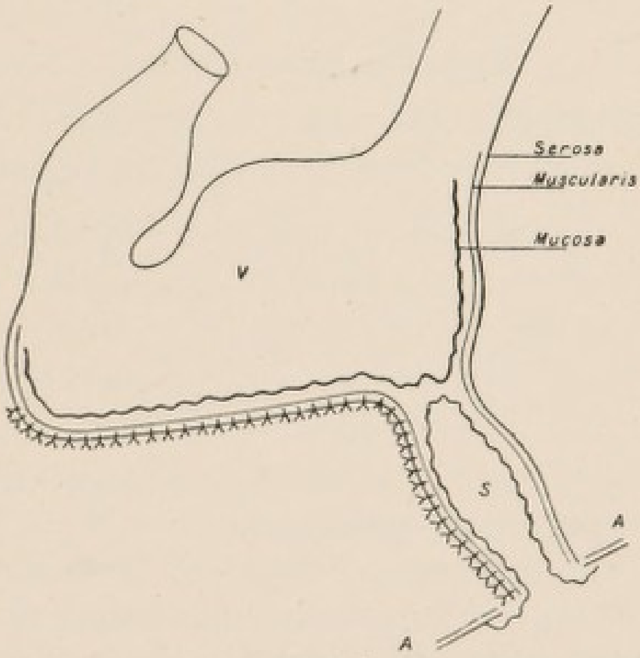


FIG. 155.—Diagram of Pavlov's Pouch made on the Stomach of a Dog.

The condition of the stomach varies greatly in fasting and after feeding.

Gastric digestion in the dog and pig will first be considered.

A. Gastric Digestion in the Dog and Pig

Stomach during Fasting

The organ is collapsed, and the mucous membrane is thrown into large ridges. It is pale in colour because the blood vessels are not dilated. Movements are not marked and the secretion is scanty, only a little mucus being formed on the surface of the lining membrane.

Stomach after Feeding

When food is taken the blood vessels dilate, a secretion is poured out, and movements of the organ become more marked.

1. **Vascular Changes.**—The arterioles dilate, and the mucous membrane becomes bright red in colour. This is a reflex vaso-dilator effect, impulses passing up the vagus to a vaso-dilator centre in the medulla, and coming down the vagus from that centre. Section of the vagi prevents its onset.

2. **Secretion.**—There is a free flow of gastric juice from all the glands in the mucous membrane.

(*a*) *Characters of Gastric Secretion.*—The gastric juice is a clear watery fluid, which is markedly acid from the presence of free hydrochloric acid. In the dog the free acid may amount to 0·2 per cent., but in man it is less abundant, and when the gastric juice is mixed with food the acid rapidly combines with alkalies and with proteins, and is no longer free. In addition to the HCl, small quantities of organic salts are present. Traces of proteins may also be demonstrated, and with these two enzymes are associated—one a proteolytic or protein-digesting enzyme, *pepsin*, the other a milk-curdling enzyme, *rennin*.

(*b*) *Course of Gastric Digestion*—(1) **Amylolytic Period.**—The action of the gastric juice does not at once become manifest. For a short time after the food is swallowed, in the pig the ptyalin of the saliva goes on acting, and the various micro-organisms swallowed with the food grow and multiply, and thus there is a continuance of the conversion of starch to sugar which was started in the mouth, and at the same time the micro-organisms go on splitting the sugar to form lactic acid, which may thus be regarded as a normal constituent of the stomach during the first half-hour after a mixed meal. In the dog ptyalin is absent.

(2) **Proteolytic Period.**—Before the amylolytic period is completed, the gastric juice has begun its special action on proteins. This may be readily studied by placing some coagulated protein in gastric juice, or in an extract of the mucous membrane of the stomach made with dilute hydrochloric acid, and keeping it at the temperature of the body. The protein swells, becomes transparent, and dissolves. The solution is coagulated on boiling—a *soluble native protein* has been formed. Very soon it is found that, if the soluble native protein is filtered off, the filtrate gives a precipitate on neutralising, showing that an *acid proteate* (*meta-protein*) has been produced. If the action is allowed to continue and the acid proteate precipitated and filtered off, it will be found that the filtrate gives a precipitate on saturating with common salt, showing that a *proto-proteose* has been formed. Along with this a certain amount of *hetero-proteose* is also formed. It is characterised by being precipitated on neutralisation and by being insoluble in distilled water. On filtering off these, the filtrate yields a precipitate on saturating with ammonium sulphate, indicating the formation of a *deutero-proteose*, and, if the filtrate from this be tested, the presence of a protein may be demonstrated. *Peptone* has been produced. (*Chemical Physiology.*)

These changes may be represented in the following table :—

Coagulated Protein.
|
Soluble Native Protein.
|
Acid Proteate (Meta-protein).
|

Proto-proteose.	Hetero-proteose.
Deutero-proteose.	Deutero-proteose.
Peptone.	Peptone.

The process is one of breaking down a complex molecule into simpler molecules, probably with hydration.

The object of this was formerly supposed to be to allow of the diffusion of the protein in the form of peptone through the wall of the intestine. It is now known that absorption is not due to diffusion, and it is more probable that the change to the simplest protein molecule is a step to the more complete disintegration of the molecule which seems necessary before it can be built into the special protoplasm of the body of the particular animal.

On certain proteins and their derivatives the gastric juice has a special action. On *collagen* the HCl acts slightly in converting it to gelatin. The gastric juice acts on *gelatin*, converting it to a gelatin peptone.

On *nucleo-proteins* it acts by digesting the protein part and leaving the *nuclein* undissolved.

Hæmoglobin is broken down into hæmatin and globin, and the latter is changed into peptone.

The *caseinogen calcium compound* of milk is first coagulated and then changed to peptone. The coagulation is brought about by the presence of the second enzyme of the gastric juice—**rennin.**

This may be separated from pepsin in various ways, and, unlike pepsin, it acts in a neutral medium.

The change set up by it seems to be due to a splitting of the soluble calcic compound of caseinogen which exists in milk into calcic paracasein, which is insoluble and is thrown down, and a small quantity of whey albumin which remains in solution. The nuclein part of the paracasein remains undigested.

The gastric juice contains an enzyme which splits **Fats** into fatty acids and glycerine if they are in a very fine state of subdivision, as in milk, but it has no action on fats not so subdivided. When fats are contained in the protoplasm of cells, they are set free by the digestion of the protein covering.

On **Carbohydrates** the free mineral acid of the gastric juice has a slight action at the body temperature, splitting the polysaccharids and disaccharids into monosaccharids.

(*c*) **Digestion of the Stomach Wall.**—When the wall of the stomach dies either in whole, as after the death of the animal, or in part, as when an artery is occluded or ligatured, the dead part is digested by the gastric juice and the wall of the stomach may be perforated. In the living condition a substance may be extracted from the mucous membrane which antogonises the action of pepsin and may be called **antipepsin.**

(*d*) **Antiseptic Action of the Gastric Juice.**—In virtue of the presence of free HCl the gastric juice has a marked action in inhibiting the growth of or in killing bacteria. The bacillus of cholera is peculiarly susceptible, and a healthy condition of the stomach is thus a great safeguard against the disease. Other organisms, while they do not multiply in the stomach, pass on alive to the intestine where they may again become active. When HCl is not formed in sufficient quantities to exist free in the stomach, the activity of these bacteria in the organ may lead to various decompositions and to many of the symptoms of dyspepsia.

(*e*) **Source of the Constituents of the Gastric Juice.**—The *hydrochloric acid* is formed at the cardiac end of the stomach. This may be shown by isolating a part of the stomach so that it opens on the surface. Since the parietal or oxyntic cells are confined to this portion of the stomach, it may be concluded that they are the producers of the acid. They manufacture it from the NaCl of the blood plasma. Probably the CO_2 liberated in the cells seizes on some of the Na and turns out HCl.

The *Pepsin* and *Rennin* are produced in the chief or peptic cells which line the glands both of the cardiac and pyloric parts of the stomach. During fasting granules are seen to accumulate in these cells, and when the stomach is active they are discharged. These granules are not pepsin but the forerunner of pepsin—pepsinogen.

(*f*) **Influence of Various Diets upon the Gastric Juice.**—This has been chiefly worked out by Pavlov on dogs with a gastric pouch (p. 349).

He finds that—(1) The amount of secretion depends upon the amount of food taken. (2) The amount and course of secretion varies with the kind of food taken. Thus, with flesh the secretion reaches its maximum at the end of one hour, persists for an hour and then rapidly falls, while with bread it reaches its maximum at the end of one hour, rapidly falls, but persists for a much longer period than in the case of flesh. (3) The digestive activity of the juices varies with the kind of food and with the course of digestion. It is higher and persists longer after a diet of bread, which is difficult to digest, than after a diet of flesh, which is more easily digested. (4) The percentage of acid does not vary markedly. When more acid is required more gastric juice is secreted. (5) The work done by the gastric glands is greater in the digestion of bread than in the digestion of flesh.

(*g*) **Nervous Mechanism of Gastric Secretion.**—It has been proved that in the dog the secretion of gastric juice can go on after the nerves to the stomach have been divided, and this has been ascribed to a reflex stimulation of the nerve plexus in the submucosa. But this mechanism plays a small part compared with the influences of the central nervous system through the vagus. Pavlov finds that, when the vagus is cut below the origin of the cardiac nerves so that they are not acted upon, and the animal left undisturbed for some days, stimulation of the nerve with a slowly interrupted induced current causes, after a long latent period of a minute or two, a flow of gastric juice.

This vagus action may be called into play either by the contact of suitable food with the mouth or by the sight of food. This he demonstrated by making an œsophageal fistula in a dog with a gastric pouch, so that food put in the mouth escaped from the gullet and did not pass into the stomach (fig. 156). Mere mechanical or chemical stimulation of the mouth produces no effect, but the administration of meat produced it. The sight of food in a fasting dog produces after a latent period of five minutes a copious flow of gastric juice. Pavlov calls this "psychic" stimulation. It is an example of how the "distance receptor" in the eye reflexly brings about an appropriate reaction—just as the "non-distance receptor" in the wall of the stomach under certain stimuli brings about an appropriate reaction. It is somewhat rash of a physiologist who can know nothing of the relation of the psychic state to the actions with which it is associated to affirm, as Pavlov does, that the psychic change is causal.

There is some evidence that the formation of gastric juice is also influenced by the action of a chemical substance produced in the mucous membrane of the pyloric end of the stomach. It has been found that the injection into the blood stream of an extract of this membrane made by boiling with acid or peptone causes a production of gastric juice. In all probability the initial secretion of gastric juice is dependent on the nervous mechanism, and the secondary secretion, when food is in the stomach, on the action of this substance. In the case of the pancreas such a chemical stimulant plays a very important part (p. 420). Such substances have been named **Hormones**.

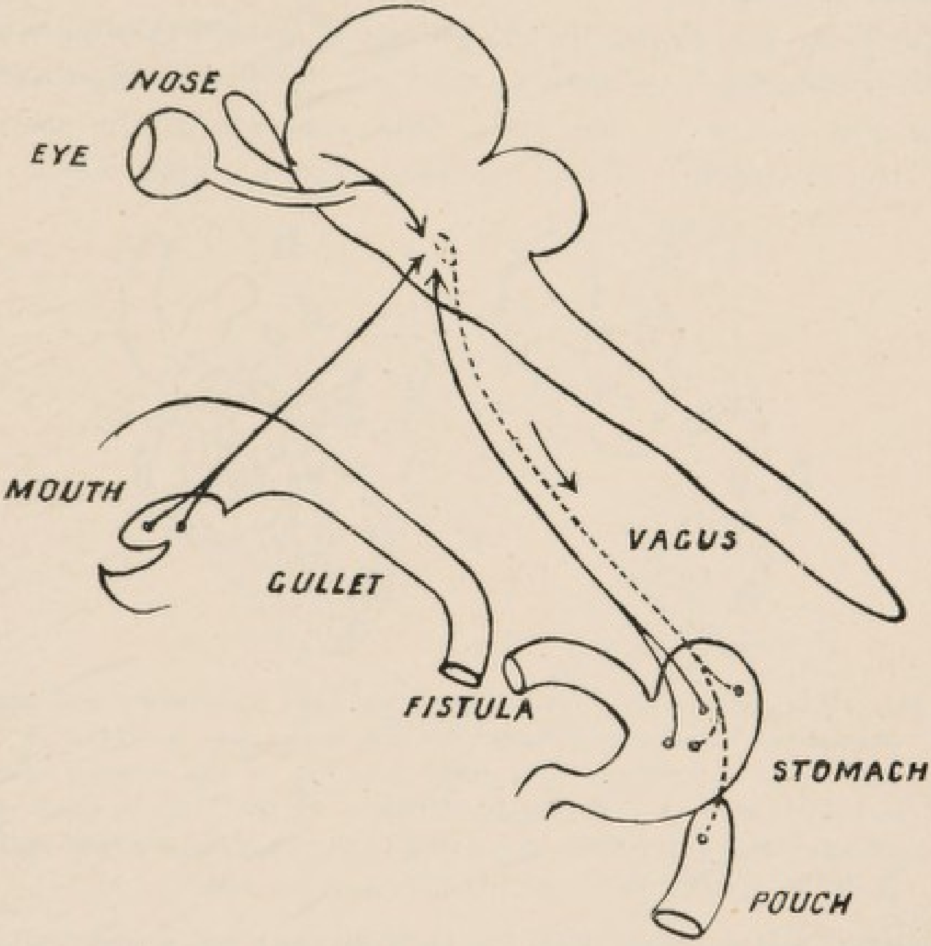


FIG. 156.—To show the nervous mechanism of gastric secretion and how it is reflexly induced through various ingoing channels.

3. **Movements of the Stomach.**—These have been studied by feeding an animal with food containing bismuth, and then applying X-rays, which are intercepted by the coating of bismuth, so that a shadow picture of the shape of the stomach is given (fig. 157).

It is found that, soon after food is taken, a constriction forms about the middle of the stomach and slowly passes on towards the pylorus. Another constriction forms and follows the first, and thus the pyloric part of the stomach is set into active peristalsis. The cardiac fundus acts as a reservoir, and, by a steady contraction, presses the gastric contents into the more active pylorus, so that, at the end of gastric digestion, it is completely emptied.

The pylorus is closed by the strong sphincter muscle, which, however, relaxes from time to time during gastric digestion to allow the escape of the more fluid contents of the stomach into the intestine. These openings are at first slight and transitory, but as time goes on they become more marked and more frequent, and when gastric digestion is complete—usually at the end of five or six hours—the sphincter is completely relaxed and allows the stomach to be emptied. The openings are regulated by a local nervous mechanism which is brought into play by the escape of the acid gastric contents into the duodenum. This leads to an immediate closure of the pylorus, which does not again open till the contents of the duodenum have been neutralised by the alkaline secretions which are poured into it. The rate of passage from the stomach of various kinds of food has been studied by feeding cats with equal amounts of each kind of food mixed with bismuth, and

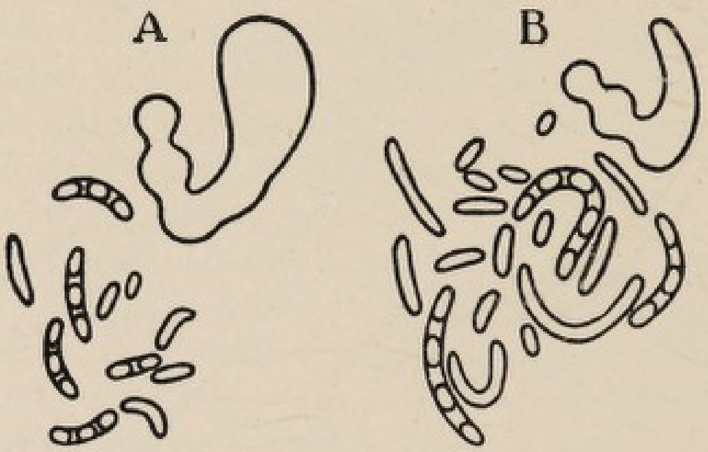


Fig. 157.—Tracings of the shadows of the contents of the stomach and intestine of a cat two hours after feeding (A) with boiled lean beef, and (B) with boiled rice to show the more rapid emptying of the stomach after the carbohydrate food. The small divisions of the food in some of the intestinal loops represent the process of rhythmic segmentation (see p. 375). (Cannon.)

then, by X-rays, getting the outline of the contents of the small intestine at different periods. Carbohydrates were found to pass on most rapidly and fats most slowly (fig. 156). Unless the contents of the stomach are very fluid these movements do not produce a very great mixing of the food taken (fig. 158).

Nervous Mechanism of Gastric Movements.—Even after the section of all the gastric nerves, movements of the stomach may be observed, but the mechanism of these movements has not been fully studied. The action of the vagus and sympathetic fibres is complicated, and their influence on the wall of the stomach and the sphincters requires further investigation. Speaking generally, the vagus seems to increase the movements, while the sympathetic fibres check them. The vagus when stimulated generally causes inhibition of the cardiac sphincter and contraction of the pylorus, but the result is not constant.

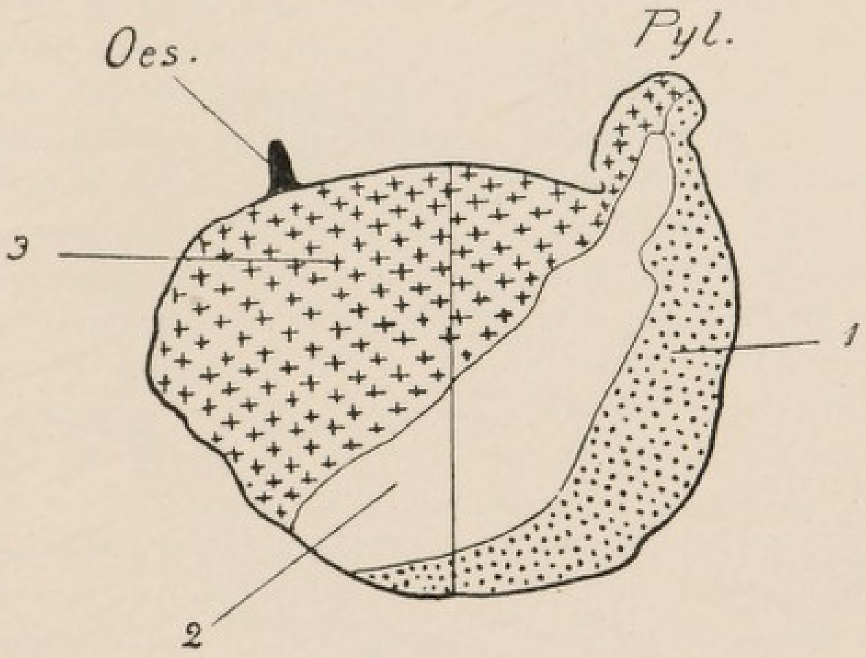


Fig. 158.—Stomach of a Dog fed successively with three different foods to show the absence of mixing. (Scheunert.)

Absorption from the Stomach

By ligation of the pyloric end, it has been found that the stomach plays a very small part in the absorption of food. Its chief function is to act as a reservoir.

Probably the antiseptic action of its secretion is of considerable importance. While it plays a certain part in digestion its action is by no means indispensable, for it has been removed in animals and in men without disturbance of the health.

Vomiting

Sometimes the stomach is emptied upwards through the gullet instead of downwards through the pylorus. This act of vomiting is generally a reflex one, resulting from irritation of the gastric mucous membrane and more rarely from stimulation of other nerves. It is a reaction to nocuous stimuli.

In vomiting, the glottis is closed, and, after a forced inspiratory effort by which air is drawn down into the gullet, a forced and spasmodic expiration presses on the stomach, while at the same time the cardiac sphincter is relaxed through the action of the vagus, and the contents of the stomach are sent upwards. They are at first prevented from passing into the nares by the contraction of the muscles of the soft palate; but, as the act continues, these muscles are overcome, and the vomited matter escapes through mouth and nose. The wall of the stomach also seems to act, but its action is non-essential, since vomiting may be produced in an animal in which a bladder has been inserted in place of the stomach.

The centre which presides over the act is in the medulla oblongata, and while it is usually reflexly called into action, it may be stimulated directly by such drugs as apomorphine.

B. Gastric Digestion in the Horse

In the horse the process of gastric digestion differs from that first described in the following particulars.

In the first place, the horse has to eat a very large quantity of food in proportion to the size of its stomach, and it is found that part of the food begins to pass very rapidly through the stomach into the intestine. Colin found, when he killed a horse which in two hours had eaten 2500 grms. of hay, that the stomach contained only 1000 grms. But while this is the case, a small residue of the meal remains for a very long time in the stomach, and passes out only when the next meal is taken.

The churning action of the stomach is less complete in the horse than in the dog, and hence, when the animal has received hay, followed by oats, these are found lying more or less separate, unless the animal has taken water, when they are more fixed.

In the horse the amylolytic period is well marked, and the percentage of hydrochloric acid is never so high as in the dog. Lactic acid is always formed from the carbohydrate of the food, and on a diet of hay it may exceed the hydrochloric acid.

The proteolytic action of the gastric juice of the horse is slower than that of carnivora, but it is very marked, and peptones are found abundantly in the stomach at the end of digestion. In the stomach of the horse the cellulose of the food is partly decomposed, probably by the action of an enzyme in the grain, which has been described by H. J. Brown.

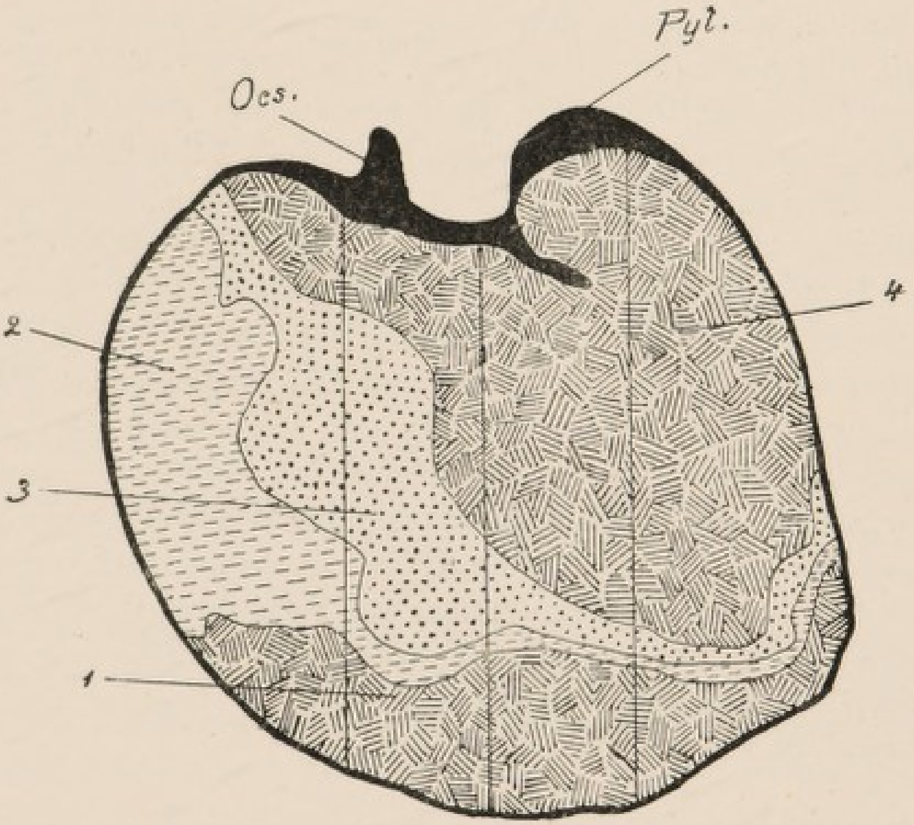


FIG. 159.—Stomach of Horse fed successively on four differently coloured foods to show the distribution of the various foods in the viscus.

Vomiting in the horse is very rare, and only occurs when the stomach is much over-distended. The food passes up the œsophagus in small quantities, and, on account of the length of the soft palate, it cannot get into the mouth, but escapes through the nose (fig. 148, p. 337.)

C. Gastric Digestion in Ruminants

This is complicated by the act of **rumination** or chewing the cud. The food is rapidly cropped and swallowed, being passed into the reticulum and rumen. The more fluid part tends to accumulate in the former cavity. At a convenient opportunity, by contraction of these cavities and of the abdominal walls and diaphragm, a bolus of their contents is regurgitated into the œsophagus, which, by an antiperistalsis, passes it up into the mouth, where it is thoroughly masticated and mixed with saliva. It is then swallowed, and, by a contraction of the walls of the pillars of the œsophageal groove, the third stomach is drawn close up to the œsophagus and receives the bolus. After straining through the leaves of the omasum this enters the abomasum or true stomach, and is there subjected to ordinary proteolytic digestion. This has been studied by making a Pavlov's pouch in the abomasum of the goat. When no food is taken the secretion is alkaline and has no peptic action, but when food is taken hydrochloric acid is secreted and peptic digestion occurs. An amylolytic enzyme converting starch to sugar seems also to be formed, and its presence is confirmed by the demonstration of its occurrence in the stomach of the pig.

As the food lies in the rumen and reticulum, it is subjected to the action of bacteria, by which the cellulose is partly decomposed, and the cell contents thus set free for the action of digestive enzymes.

IV. INTESTINAL DIGESTION

A. In the Dog and Pig

After being subjected to gastric digestion the food is generally reduced to a semi-fluid grey pultaceous condition of strongly acid reaction known as *chyme*, and in this condition it enters the duodenum.

Here it meets three different secretions:—

Pancreatic secretion.
Intestinal secretion.
Bile.

A. Pancreatic Secretion

The secretion of the pancreas may, in the dog, be procured by making either a temporary or a permanent fistula. In the former case the duct is exposed, and a canula fastened in it; in the latter the duct is made to open on the surface of the abdomen, a small piece of the intestinal wall with the mucous membrane round the opening of the duct being stitched to the abdominal opening.

1. **Characters and Composition.**—When obtained immediately from a temporary fistula, the pancreatic juice is a clear, slimy fluid, with a specific gravity of 1030 or less and an alkaline reaction. It contains an abundance of a native protein having the characters of a globulin, and the alkalinity is probably due to sodium carbonate and disodium phosphate. From a permanent fistula a more abundant flow of more watery secretion may be collected.

2. **Action.**—Closely associated with the protein, and precipitated by alcohol along with it, are the enzymes upon which the action of the pancreatic juice depends. (*Chemical Physiology*)

1*st.* *A Proteolytic Enzyme—Trypsin.*—This, in a weakly alkaline or neutral fluid, converts native proteins into peptones, and then breaks these peptones into simpler non-protein bodies.

The pancreatic juice brings about this breaking down of protein in stages. It does not cause solid proteins to swell up but simply erodes them away. Fibrin and similar bodies first pass into the condition of *soluble native proteins* and then into *deutero-proteose,* while boiled egg white appears at once to yield *deutero-proteose.* The deutero-proteose is then changed into peptone, and part of that peptone is then split into a series of bodies which no longer give the biuret test. These consist chiefly of the component amido-acids of which the most important are leucin and tyrosin, and of ammonia compounds (see p. 8).

Amido-acetic acid linked to skatol—tryptophane—is also split off, and if chlorine water is added to a pancreatic digestion, which has proceeded for a long time, a rose-red colour is struck (see p. 430).

On nucleo-proteins trypsin acts by digesting the protein and dissolving the nucleic acid so that it can be absorbed.

On collagen and elastin trypsin has little action; but on gelatin it acts as upon proteins.

2nd. An Amylolytic Enzyme—Amylopsin or *Diastase.*—This acts in the same way as ptyalin, but more powerfully, converting a certain part of the maltose into dextrose. It acts best in a faintly acid medium.

3rd. A Fat Splitting Enzyme—Lipase.—This is the most easily destroyed and the most difficult to separate of the zymins. It breaks the fats into their component glycerin and fatty acids. The fatty acids link with the alkalies which are present to form soaps, and in this form, or dissolved as free fatty acids in the bile, they are absorbed. But the formation of soaps also assists the digestion of fats by reducing them to a state of finely divided particles, an *emulsion*, upon which the lipase can act more freely. This process of emulsification is assisted by the presence of protein in the pancreatic juice and also by the presence of bile.

That these enzymes are independent of one another is shown by many facts.

1. Diastase does not appear till about a month after birth.

2. Diastase is taken up by dry glycerin while trypsin is not.

3. Trypsin may be precipitated and separated by shaking with collodion.

4. Trypsin acts in 0·01 per cent. ammonia while diastase does not.

5. The proportion of the zymins varies with the character of the diet.

This is well shown by experiments carried out in Pavlov's laboratory upon dogs with pancreatic fistulæ. The effects of diets of milk, bread, and flesh were compared, in each case the amount of the food given containing the same amount of nitrogen (protein). The total quantity of ferment unit is got by multiplying the quantity of the juice in c.cm. by the strength of the juice, determined by ascertaining how much of the substance is digested by unit of the secretion in unit of time. The following table and fig. 159 indicate the results obtained:—

Diet.	Quantity of Enzyme.		
	Proteolytic.	Amylolytic.	Fat Splitting.
Bread, 250 grm. . .	1978	1601	800
Milk, 600 c.c. . .	1085	432	4334
Flesh, 100 grm. . .	1502	648	3600

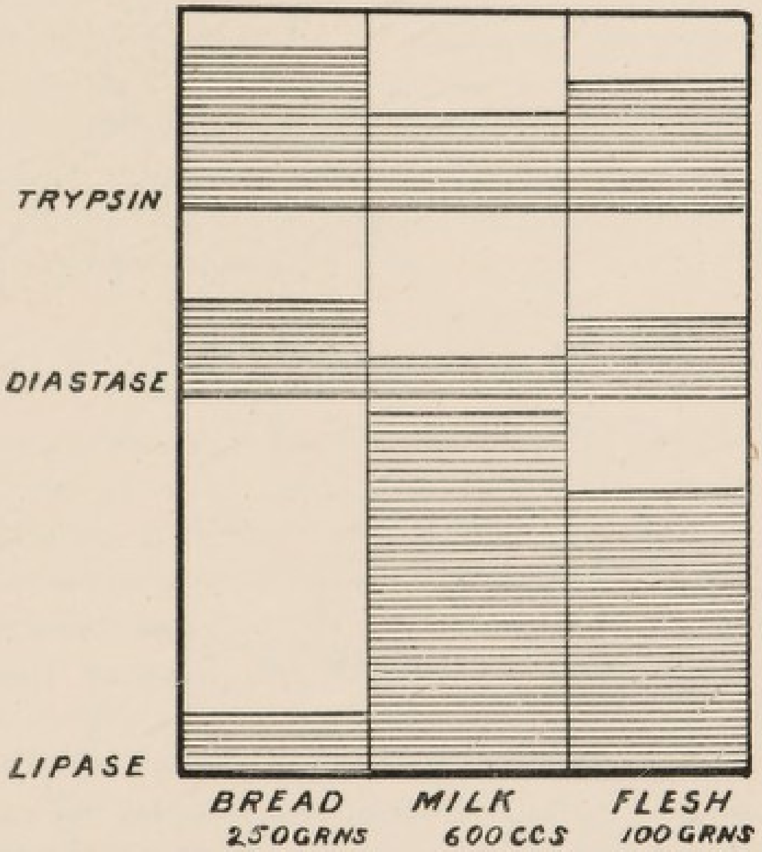


Fig. 160.—To show the relative amounts of the three enzymes of the pancreatic juice formed on different diets.

Bread contains a protein difficult of digestion, plenty of starch, and little fat. Milk contains an easily digested protein, and plenty of fat, but no starch; while flesh contains a comparatively easily digested protein, no starch, and a moderate amount of fat. The first food causes a copious production of trypsin and diastase, and little lipase. The second causes the production of less trypsin, little diastase, but most lipase. The last causes a moderate production of trypsin, little diastase, and a comparatively large amount of lipase.

As to the mode of production of these enzymes, it is known that trypsin is not formed as such in the cells, for the secretion direct from the acini has no tryptic action. A forerunner of trypsin — trypsinogen — is produced, and this changes into trypsin after it is secreted. The intestinal secretion contains something of the nature of an enzyme which has been termed **enterokinase**, which has the power of bringing about this change.

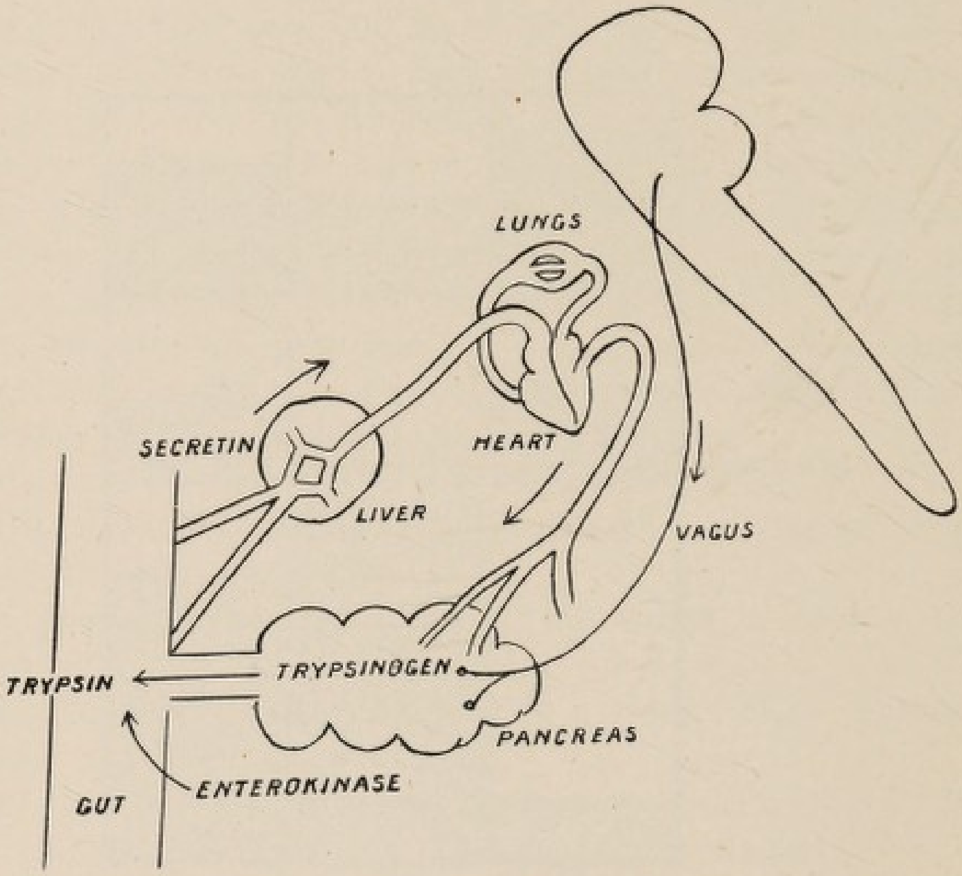


Fig. 161.—To show the mode of action of secretin and the action of the vagus nerve on the secretion of the pancreas and the activation of trypsinogen by enterokinase.

It is doubtful whether the pancreatic secretion contains any true rennin, although it produces a modified clotting of milk, under certain conditions.

3. **Physiology of Pancreatic Secretion.**—The secretion of pancreatic juice is not constant, but is induced when the acid chyme passes into the duodenum. This occurs even when all the nerves to the intestine have been cut, and it appears from

the investigations of Starling to be due to the formation of a material which has been called **secretin**, in the epithelium lining the intestine, under the influence of an acid. This is absorbed, and, on being carried to the pancreas, stimulates it to secrete. It has been shown that the injection into the blood of an extract, made with dilute hydrochloric acid, of the lining membrane of the upper part of the small intestine, leads to a flow of pancreatic juice. This secretin is not destroyed by boiling, and is soluble in strong alcohol. It is therefore not of the nature of an enzyme.

But while secretin seems to play so important a rôle, it has been found that stimulation of the vagus nerve, after a latent period of two minutes, increases pancreatic secretion, so that it must be concluded that the secretion of the fluid is, to a certain extent, under the control of the nervous system.

The influence of the pancreas in the general metabolism will be considered later (p. 410).

B. Secretion of the Intestinal Wall (Succus Entericus)

This is formed in the Lieberkühn's follicles of the intestine, and it may be procured by cutting the intestine across at two points, bringing each end of the intermediate piece to the surface, and connecting together the ends from which this piece has been taken away so as to make a continuous tube. On mechanically irritating the mucous membrane, a pale yellow clear fluid is secreted, which contains native proteins and mucin, and is alkaline in reaction from the presence of sodium carbonate.

Action.—The succus entericus contains: (1) An enzyme which splits some disaccharids, as maltose and cane sugar, into monosaccharids, but does not seem to act on lactose. (2) In the intestine of animals taking milk a special zymin, **lactase**, which splits milk sugar. (3) **Erepsin**, an enzyme which seems to act more powerfully than trypsin in splitting peptones into their component non-protein crystalline constituents such as the di-amino acids and non-amino acids, *e.g.* leucin and tyrosin. The object of this is not at present fully understood. It may be that the nitrogen of the protein is largely treated as a waste product and thrown off. But feeding experiments on dogs and rats seem to show that these non-protein derivatives of proteins can be retained and built into the protoplasm of the animal. Vernon has shown that a similar proteolytic enzyme is widely distributed in the tissues, being specially abundant in the kidney. (4) **Enterokinase**—a zymin which, acting on trypsinogen, converts it into active trypsin (p. 364).

Mechanism of Secretion.—The taking of food leads to a flow of intestinal secretion which reaches its maximum in about three hours ; and this flow is much greater from the upper part of the bowel than from the lower. There is some evidence that the injection of secretin calls forth this secretion, and according to some observers, the injection of succus entericus into the circulation acts in the same way.

As regards the action of nerves very little is known. It has been found that, when the intestine is ligatured in three places so as to form two closed sacs, if the nerves to one of these be divided, it becomes filled with a clear fluid closely resembling lymph. The dilatation of the blood vessels may account for this without secretion being implicated.

C. Bile

1. **Characters and Composition.**—The bile is the secretion of the liver, and it may be procured for examination—(*a*) From the gall bladder, or (*b*) from the bile passages by making a fistula into them. Bile which has been in the gall bladder is richer in solids than bile taken directly from the ducts, because water is absorbed by the walls of the bladder and the bile thus becomes concentrated.

Analyses of gall bladder bile thus give no information as to the composition of the bile when formed. In several cases, where surgeons have produced biliary fistulæ, opportunities have occurred of procuring the bile directly from the ducts during life in man.

Such bile has a somewhat orange-brown colour, and is more or less viscous, but not nearly so viscous as bile taken from the gall bladder. It has a specific gravity of almost 1005, while gall bladder bile has a specific gravity of about 1030. Its reaction is slightly alkaline, and it has a characteristic smell.

It contains about 2 per cent. of solids, of which more than half are organic.

Bile Salts (*Chemical Physiology*).—The most abundant solids are the **salts of the bile acids.** In man the most important is sodium glycocholate, but in the dog sodium taurocholate is the more abundant. These salts are readily prepared from an alcoholic solution of dried bile by the addition of water-free ether, which makes them separate out as crystals.

Glycocholic acid splits into glycin, amido-acetic acid—$H_2N.CH_2.CO.OH$, and a body of unknown constitution, cholalic acid, $C_{24}H_{40}O_5$.

Taurocholic acid yields amido-ethane-sulphuric acid or taurin, $H_2N.CH_2CO.SO_2OH$.—a molecule closely resembling amido-acetic acid linked to sulphuric acid and cholalic acid.

Since both acids contain nitrogen they must be derived from proteins. That they are formed in the liver and not merely excreted by it, is shown by the fact that, while they accumulate in the blood if the bile duct is ligatured, they do not appear if the liver is excluded from the circulation.

Action of Bile Salts.—1. The bile salts are solvents of fats and fatty acids, and they thus assist in the digestion and absorption of fats. When bile is excluded from the intestines no less than 30 per cent. of the fats of the food may escape absorption and appear in the fæces. When this is the case, as in jaundice from obstruction of the bile duct, the fæces have a characteristic white or grey appearance from the abundance of fat.

2. These salts keep cholesterin in solution.

3. They lower the surface tension of solutions, and in this way they may bring the fat particles into more intimate contact with the mucous membrane.

4. While the salts have no action on proteins, free taurocholic acid precipitates native proteins and acid proteate. In the human intestine this is an action of no importance.

5. These salts are powerful hæmolytic agents, and rapidly dissolve hæmoglobin out of the erythrocytes.

Bile Pigments.—These amount to only about 0·2 per cent. of the bile. In human bile the chief pigment is an orange-brown iron-free substance, *bilirubin*, $C_{32}H_{36}N_4O_6$, while in the bile of herbivora, *biliverdin*, a green pigment somewhat more oxidised than bilirubin, $C_{32}H_{36}N_4O_8$, is more abundant. By further oxidation with nitrous acid, other pigments—blue, red, and yellow—are produced, and this is used as a test for the presence of bile pigments (Gmelin's test). (*Chemical Physiology.*)

The pigments are closely allied to hæmatoporphyrin and hæmatoidin (see p. 213), and they are derived from hæmoglobin. Their amount is greatly increased when hæmoglobin is set free or injected into the blood. That they are formed in the liver is shown by the fact that, when the liver is excluded from the circulation, the injection of hæmoglobin does not cause their formation.

The liver has the property of excreting not only these pigments formed by itself, but also other pigments. Thus the liver of the dog can secrete the characteristic pigment of sheep's bile when this is injected into its blood.

Cholesterin is a monatomic alcohol — $C_{27}H_{45}OH$ — which occurs free in small amounts in the bile. It is very insoluble and is kept in solution by the salts of the bile acids. It readily crystallises in rhombic plates, generally with a notch out of the corner. On account of its insolubility, when it is in excess in the bile or when the bile salts are decreased, it may form concretions or biliary calculi—gall stones—which may accumulate in the gall bladder and may get caught in the bile passages, obstructing the flow of bile and leading to its absorption throughout the system. Jaundice is thus produced. When these stones are passed by the rectum, their nature is readily demonstrated by breaking them up in a mortar, dissolving in hot alcohol, and allowing the solution to cool, when the characteristic crystals separate out. (*Chemical Physiology.*) The source of the cholesterin of the bile is not definitely known. It is not an excretion of cholesterin formed elsewhere, because the injection of cholesterin does not lead to an increase in the amount in the bile. According to Naunyn's observations it is most abundant in cases of inflammation of the bile passages, and he therefore thinks that it is formed by the breaking down of the epithelium lining these ducts.

Fats and Lecithin.—The true fats and the phosphorus containing lecithin are present in small amounts in the bile, and apparently they are derived from the fats of the liver cells, and they may be increased in amount by the administration of fatty food.

Nucleo-protein and Mucin.—The bile owes its viscosity to the presence of a mucin-like body, which, however, does not yield sugar on boiling with an acid and which contains phosphorus. It is precipitated by acetic acid, but the precipitate is soluble in excess. It is therefore a nucleo-protein. In some animals a certain amount of mucin is also present. (*Chemical Physiology.*)

Inorganic Constituents.—The most abundant salt is calcium phosphate. Phosphate of iron is present in traces. Sodium carbonate, calcium carbonate, and sodium chloride are the other chief salts.

2. **Flow of Bile.**—The bile, when secreted by the liver cells, may accumulate in the bile passages and gall bladder to be expelled under the influence of the contraction of the muscles of the ducts or of the pressure of the abdominal muscles upon the liver. The flow of bile into the intestine thus depends upon—1st, The secretion of bile; 2nd, the expulsion of bile from the bile passages. It is exceedingly difficult to separate the action of these two factors. The flow of bile in the human subject has now been studied in several cases in which the surgeon has had to make a fistula into the gall bladder through which all the bile secreted escaped and could be collected.

The flow of bile begins in intra-uterine life before the twelfth week, and it continues without intermission throughout the whole of life, even during very prolonged fasts.

The taking of food increases the flow of bile, and the extent to which it is increased depends largely on the kind of food taken. In the dog a protein meal has the most marked effect, a fatty meal a less marked effect, and a carbohydrate meal hardly any effect. The increased flow of bile following the taking of food does not reach its maximum till six or nine hours after the food is taken, and some observers have found that the period of maximum flow is even further prolonged.

Pavlov found in dogs, in which a biliary fistula had been made leaving the opening of the bile duct in the mucous membrane of the intestine, that an *expulsion* of bile follows the taking of food and the secretion of pancreatic juice, and Starling finds that the flow of bile is increased by the injection of secretin. It thus tends to run parallel with the flow of pancreatic juice.

When the individual is taking a liberal diet the secretion of bile appears to be greater than when the diet is low.

In fever there is a very marked fall in the secretion, the fluid flowing from a fistula becoming colourless and almost devoid of bile salts and pigments.

Certain drugs markedly modify the formation of bile—the salts of the bile acids stimulating the liver to form more solids and to secrete more water, the salicylates acting in much the same way, and all drugs which cause hæmolysis—*i.e.* the solution of the pigment of the erythrocytes—producing an increased formation of bile pigments.

Influence of Nerves upon the Flow of Bile—(*a*) *Expulsion of Bile.*—There is good evidence that nerve fibres pass to the muscles of the bile passages and that they may cause an expulsion of bile by stimulating them to contract.

(*b*) *Secretion of Bile.*—There is no evidence that nerve fibres act directly upon the secretion of bile. This appears to be governed by the nature of the material brought to the liver by the blood and by the activity of the liver cells. It is an example of function regulated by chemical substances rather than by a nerve mechanism.

3. **Mode of Formation of Bile.**—It has been seen that the bile salts and pigments are actually formed in the liver cells, and there is good evidence that the water of the bile is not a mere transudation but is the product of the living activity of these cells. The pressure under which bile is secreted may be determined by fixing a canula in the bile duct or in a biliary fistula and connecting it with a water manometer. In man the pressure is as much as 20 to 30 mm. Hg, while the pressure in the portal vein of the dog is only 7 to 16 mm. Hg.

4. **Nature and Functions of Bile.**—Bile is not a secretion of direct importance in digestion. It has practically no action on proteins or carbohydrates, and its action on fats is merely that of a solvent, and possibly by its action on the surface tension of the intestinal contents. Pavlov maintains that it activates the lipase of the pancreatic juice, and others have found that it increases the activity of trypsin and diastase. It may thus be considered as an adjuvant to the action of

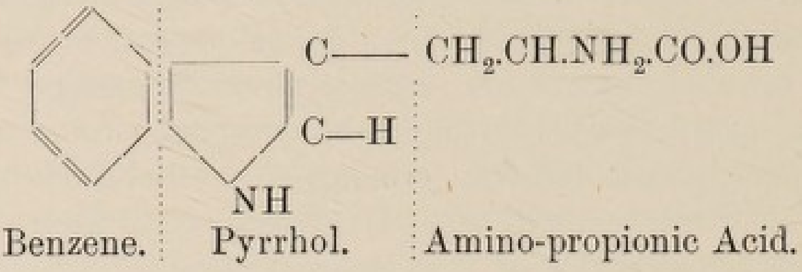
pancreatic juice. Its secretion in relationship to food does not indicate that it plays an active part in digestion. It is formed during intra-uterine life and during fasting, and it is produced many hours after food is taken, when digestive secretions are no longer of use in the alimentary canal. Digestion can go on quite well without the presence of bile in the intestine, except that the fats are not so well absorbed. The composition of bile strongly suggests that it is a waste product. The pigment is the result of the decomposition of hæmoglobin and the acids are the result of protein disintegration.

All these facts seem to indicate that bile is the medium by which the waste products of hepatic metabolism are eliminated, just as the waste products of the body generally are eliminated by the kidneys.

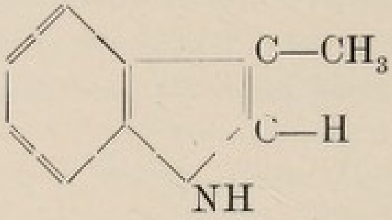
Bacterial Action in the Alimentary Canal

With the food and saliva numerous micro-organisms of very diverse character are swallowed. It has been suggested that the leucocytes formed in the lymphoid tissue at the back of the mouth and pharynx attack and destroy such organisms, but so far definite proof of this is not forthcoming. When the food is swallowed, the micro-organisms multiply for some time in the warm moist stomach, and certain of them, by splitting sugars, form lactic and sometimes acetic acid. But when sufficient gastric juice is poured out for the hydrochloric acid to exist free, the growth of micro-organisms is inhibited, and some of them, at least, are killed. Others pass on into the intestine, and, as the acid in the chyme becomes neutralised, the acid-forming organisms begin to grow, and, by splitting the sugars, form lactic or acetic acid, and render the contents of the small intestine slightly acid. Towards the end of the small intestine, and more especially in the large intestine, the alkaline secretions have neutralised these acids, and in the alkaline material so produced the putrefactive organisms begin to nourish and to attack any protein which is not absorbed—splitting it up and forming among other substances a series of aromatic bodies, of which the chief are indol, skatol, and phenol.

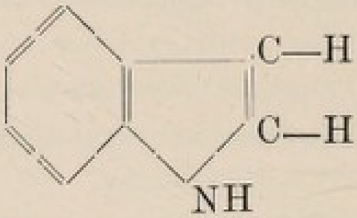
This splitting probably occurs through the liberation of tryptophane—in which amido-propionic acid is linked to a pyrrhol-benzene.



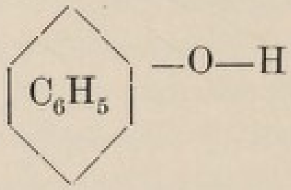
By the breaking down of the amino-propionic acid, skatol—



is formed, and by the removal of the methyl, indol is produced—



Phenol—



is a further stage of disintegration.

By taking embryo guinea-pigs at full time from the uterus and keeping them with aseptic precautions, it has been shown that the absence of micro-organisms from the intestine does not interfere with digestion.

The most important and abundant organism present in the intestinal tract is the *bacillus coli communis*, which has a certain power of splitting proteins and a marked action in producing acids from sugars. Its presence in water is generally indicative of sewage contamination.

Fate of the Digestive Secretions

1. *Water.*—Although it is impossible to state accurately the average amount of the various digestive secretions poured into the alimentary canal each day, it must be very considerable, probably not far short of 3000 c.cms., or something considerably more than one-half of the whole volume of the blood. Only a small amount of this is given off in the fæces, and hence the greater part must be re-absorbed. There is thus a constant circulation between the blood and the alimentary canal, or what may be called an *entero-hæmal circulation.* One portion of this is particularly important. The blood vessels of the intestine pass to the liver, and many substances, when absorbed into the blood stream, are again excreted in the bile and thus are prevented from reaching the general circulation. Among these substances are the salts of the bile acids and their derivatives, many alkaloids such as curarine, and in all probability a set of animal alkaloids called *ptomaines* formed by putrefactive decomposition of proteins in the gut. If, from disturbances in the functions of the liver, these are allowed to pass through that organ, the feelings of lassitude and discomfort which are associated with intestinal dyspepsia are produced. The liver thus forms a protective barrier to the ingress of certain poisons.

2. *Enzymes.—Ptyalin* appears to be destroyed in the stomach by the hydrochloric acid. *Pepsin* is probably partly destroyed in the intestine, but it seems also to be absorbed and excreted in the urine; for, on the addition of hydrochloric acid, the urine has a peptic action on proteins. *Trypsin* appears to be destroyed in the alimentary canal; but the fate of the other pancreatic enzymes and of the enzymes of the succus entericus is unknown.

3. *Bile Constituents.*—1. The *bile salts* are partly reabsorbed from special parts of the small intestine—sodium glycocholate being taken up in the jejunum and taurocholate in the ileum. The acids of these salts are also partly broken up. The glycocholic acid yields amido-acetic acid, which is absorbed and passes to the liver to be excreted as urea; while the taurocholic acid yields amido-isethionic acid which goes to the liver and yields urea and probably sulphuric acid. The

fate of the cholalic acid is not known, but it is supposed to be excreted in the fæces. 2. The *pigments* undergo a change and lose their power of giving Gmelin's reaction. They appear in the fæces as what may be called *stercobilin*. It is probably formed by reduction of bilirubin in the intestines as the result of the action of micro-organisms. 3. The *cholesterin* is passed out in the fæces.

Fæces

The materials not absorbed from the intestine, whether these are derived from the food or from the alimentary canal, are thrown off from the rectum as the fæces. In *fasting animals* these are passed at long intervals, and consist of mucin, shed epithelium, the various products of the bile constituents, and inorganic salts. In *feeding animals* the amount and character of the fæces depends largely upon the amount and character of the food, and upon the bacteria which are growing in the large intestine. The unabsorbed material, as it passes down the large intestine, becomes inspissated from the absorption of water, but, if much undigested matter is present, water may also be added, and the consistence of the fæces may thus be varied. The colour is normally brown, from the hæmatin of the flesh eaten, while the sulphide of iron formed by the splitting of the hæmatin compounds in the intestine may make them darker in colour. On a milk diet they are light yellow in colour, and if a large excess of fatty food is taken, or if fat is not absorbed, as in jaundice, they become clay coloured. The derivatives of the bile pigments play but a small part in colouring the fæces.

The reaction of the fæces varies. Usually the outside of the mass is alkaline from the alkaline secretion of the intestine, while the inside is acid from the free fatty acids and other acids formed by the action of such acid-forming bacteria as the bacillus coli communis. The amount of solid fæces depends on the amount of food, and on a vegetable diet, from the presence of undigested cellulose, the amount is very much greater.

The solids of the fæces of a feeding animal consist of the same constituents as the fæces in a fasting animal, with the addition of all the undigested constituents of the food—elastic and white fibrous tissue, remains of muscle fibres, often fat and the earthy soaps of the fatty acids, and, when a vegetable diet is taken, the cellulose of the vegetable cells, and frequently starch. The cellulose, by stimulating the intestine, is a valuable natural purgative.

The odour is due to the presence of aromatic bodies such as indol and skatol.

Meconium is the name given to the first fæces passed by the child after birth. It is greenish-black in colour, and consists of inspissated bile and shed epithelium from the intestine.

Movements of the Intestine

These are of two kinds—**myogenic** and **peristaltic**. The *myogenic* movements are slight rhythmic contractions which pass rapidly along the intestine, and are insufficient to drive on the contents, but are probably of use in churning and mixing them. By feeding with food mixed with bismuth, and employing X-rays, Cannon finds that the contents of the small intestine get broken up into small segments. This is possibly due to these myogenic movements (fig. 157, p. 356). These movements occur when all the nerves have been divided, and when the ganglia in the intestinal walls have been poisoned with nicotine, and they are therefore due to the muscle fibres alone.

The *peristaltic* movements are much more complex and powerful. They consist of a constriction of the muscles, which seems to be excited by the passage of the food, and may be caused by inserting a bolus of cotton-wool covered with vaseline. Starting at the upper end of the intestine, they pass slowly downwards. In front of the contraction the muscular fibres are relaxed, and thus the contracting part drives its contents into the relaxed part below. These peristaltic movements go on after the nerves to the gut are cut, but they are stopped when the ganglia in the wall of the intestine are poisoned with nicotine. It has therefore been concluded that the nerve ganglia in the intestinal wall form a local reflex mechanism, which is stimulated by the presence of foreign matter in the intestine, and which brings about the co-ordinated contraction and relaxation, which together constitute a true peristalsis.

But while peristalsis is thus independent of the central nervous system, it is nevertheless controlled by it. The splanchnic nerves inhibit, while the vagus to the small intestine and upper part of the large gut, and the nervi erigentes to the lower part of the large gut are augmentor nerves, increasing the peristalsis. Stimulation of the sympathetic fibres which inhibit the peristalsis causes contraction of the sphincter between the small and large intestine.

As the contents of the small intestine are forced through the ileo-cæcal valve, the **large intestine** relaxes to receive them, and then a series of contractions passing from below upwards —an anti-peristalsis—sets in by which the contents are very thoroughly churned. Afterwards they are forced downwards by tonic peristaltic waves.

Defæcation

By the peristalsis of the intestine, the matter not absorbed from the wall of the gut is forced down and accumulates in the part of the rectum which passes horizontally forward to end in the vertical anal canal. It is prevented from escaping into this by the sharp fold which the last part of the bowel makes, and by the contraction of the strong sphincter ani muscle.

Defæcation depends primarily on the intestinal peristalsis, without which it cannot be performed. When fæces accumulate in the rectum, the mucous membrane is stimulated, and impulses are sent up to inhibit a centre in the lumbar region of the cord which keeps the sphincter ani contracted, and the sphincter is relaxed, and the escape of fæces made possible. In some diseases of the cord this centre is stimulated and cannot be inhibited, and thus defæcation is interfered with, while in other diseases, when this centre has been destroyed, the sphincter does not contract, and fæces may escape continuously.

Normally the act of defæcation is partly voluntary and partly involuntary. The voluntary part of the act consists in closing the glottis, and making a forced expiration so as to press upon the contents of the abdomen ; while at the same time the perineal muscles are relaxed, and the rectum straightened, and thus the contents are allowed to pass into the anal canal. The act is completed by the emptying of the canal by the contraction of the levatores ani muscles.

B. Intestinal Digestion in the Horse and other Herbivora

In the horse intestinal digestion is of great importance.

In the small intestine the processes which go on are much the same as in the carnivora, but in the huge large intestine important changes occur.

1. In the **cæcum** some of the food remains for a very considerable time—as much as twenty-four hours. It is mixed with the secretion of the intestine and with water which the horse has drunk, and which passes rapidly to the cæcum. The reactions of the contents are alkaline, and bacteria are abundant. Here a considerable quantity of protein is digested and cellulose disappears. This disappearance of cellulose is probably largely due to the action of bacteria, and it results in the production of:—

(1) *Lower fatty acids*, such as acetic and butyric acid, which combine with the alkalies present, and, being absorbed, are oxidised to carbonates, yielding possibly a small amount of energy, and being partly excreted by the lungs as CO_2 and partly by the urine as carbonates of sodium and potassium, which help to give the fluid its alkaline reaction. It is said that 100 parts of cellulose in decomposing will yield about 60 parts of these acids.

(2) *Gases*, of which carbon dioxide, CO_2, and marsh gas, CH_4, are the chief.

2. In the **double colon**, which has a mean capacity of no less than 80 to 100 litres, the same processes go on as in the cæcum, and when the **single colon** is reached, a very rapid absorption of fluid and of the products of digestion held in solution takes place, and the residue of the food is formed into the desiccated balls of fæces. So rapid is absorption from the lower bowel in the horse, that the animal is readily killed by rectal injection of strychnine, and may be easily anæsthetised by giving ether per rectum. The rapid absorption also allows of life being maintained on nutritive enemata.

The time taken for food to pass right along the alimentary canal of the horse is considerable—probably about four days. But solid bodies given by the mouth have been found in the fæces after twenty-two to thirty hours. Some idea of the distribution of the contents of the alimentary canal is afforded by an observation of Colin's :—

In the Stomach	5 kilos.
,, Small Intestine	7·5 ,,
,, Cæcum	11 ,,
,, Colon	36·2 ,,

Some interesting observations have been made upon the removal of a great part of the large intestine in the rabbit. It has been found that the digestion and utilisation of proteins is not decreased, but that the digestion of the cellulose is markedly decreased.

The **fæces** of the horse are passed in rounded yellow masses. They contain about 76 per cent. of water, 3 per cent. of ash, largely composed of silica from the husks of grain and partly of phosphates of soda, potash, lime and magnesia, and about 21 per cent. of organic matter, such as cellulose, lignin, and other undigested vegetable remains, unabsorbed proteins, carbohydrates, and fats, indol and skatol, and the various constituents of the fæces of a fasting animal.

They are acid, from the presence of organic acids, and they contain so much gas that they float in water.

The amount of fæces depends upon the food taken—on an average about 15 kilos are passed per diem.

The question of how far **cellulose** is available as a food, of how far it acts like other carbohydrates, has not been satisfactorily demonstrated. But the most recent experiments upon rabbits and upon sheep seem to show that pure cellulose may replace starch as a protein sharer. When, however, it is eaten mixed with the encrusting substances of the cell wall, the work of digestion seems to be so great that little of its potential energy is available.

C. Intestinal Digestion of Ruminants

Intestinal digestion is not so important in ruminants as it is in horses, for digestion in the stomach is much more complete. It is essentially the same in character, and cellulose is more completely dissolved in these animals than it is in the horse.

The **fæces** in the ox and cow are more fluid than in the horse, while in the sheep they contain a smaller proportion of water. In the ox the average weight of the fæces per diem. is about 30 kilos.

Food takes about five days to pass completely through the alimentary canal of ruminants.

III. ABSORPTION OF FOOD

1. **State in which Food leaves the Alimentary Canal.**—The *carbohydrates* generally leave the alimentary canal as monosaccharides; but some resist the action of digestion more than others. Lactose seems to be broken down in the intestine only when the special *lactase* is present in the succus entericus, but in all cases it is broken down before it reaches the liver. Cane sugar when taken in large excess may also be absorbed, and it is then excreted by the kidneys.

The *proteins* are absorbed as peptones, possibly as proteoses, and as the amino-acids and other crystalline compounds formed by the action of trypsin and erepsin (p. 8). Native proteins may be absorbed unchanged from the lower bowel, since it has been found that when egg white is injected into an isolated part of the rectum it disappears to a very considerable extent.

The *fats* are chiefly absorbed as soaps and as fatty acids.

2. **Mode of Absorption of Food.**—That absorption is not due merely to a process of ordinary diffusion or osmosis is clearly indicated by many facts.

(1) Heidenhain has shown that absorption of water from the intestine takes place much more rapidly than diffusion through a dead membrane.

(2) The relative rate of absorption of different substances does not follow the laws of diffusion. Grübler's peptone passes more easily through the intestine than glucose, but glucose passes more readily through parchment paper, while sodium sulphate, which is more diffusible than glucose, is absorbed much less readily. Again, as shown by Reid, an animal can absorb its own serum under conditions in which filtration into

blood capillaries or lacteals is excluded. In such a case osmosis cannot play a part. Absorption is stopped or diminished when the epithelium is removed, injured, or poisoned with fluoride of sodium, in spite of the fact that this must increase the facilities for osmosis and filtration.

3. **Channels of Absorption.**—There are two channels of absorption from the alimentary canal (see fig. 107, p. 225)—the veins which run together to form the portal vein of the liver, and the lymphatics which run in the mesentery and, after passing through some lymph glands, enter the *receptaculum chyli* in front of the vertebral column. From this, the great lymph vessel, the thoracic duct, leads up to the junction of the subclavian and innominate veins, and pours its contents into the blood stream. The lymph formed in the liver also passes into the thoracic duct.

(1) **Proteins.**—Peptones and the further products of their digestion are formed from proteins in digestion, but they seem to undergo a change in the intestinal wall before passing to the tissues, since they are not found in the blood. That in some altered condition they leave the intestine by the blood and not by the lymph is shown by the fact that their absorption is not interfered with by ligature of the thoracic duct.

During the digestion of proteins the number of leucocytes is enormously increased, sometimes to more than double their previous number, and in all probability it is they which carry the products of digestion from the intestine. According to the observations of Pohl, the leucocytes are derived from the lymph tissue in the intestinal wall, but more recent experiments tend to show that they come from the bone marrow, being probably attracted to the intestine by a positive chemiotaxis. By breaking down in the blood stream they probably set free the proteins for use in the tissues.

When an excess of proteins is taken in the food, it is broken down in the lining membrane of the gut, and the nitrogen is rapidly excreted in the urine as urea, and thus the entrance of an excess of nitrogen to the tissues is prevented. Its non-nitrogenous part remains available as a source of energy.

It has been pointed out that gastric juice does not dissolve the nucleo-proteins, but that the pancreatic juice does so.

Phosphorus is undoubtedly absorbed in organic combination, but the mode of absorption and the channels by which it passes from the intestine have not been investigated.

(2) **Carbohydrates.** — Although the chief monosaccharid formed in digestion is dextrose, others are also produced—lævulose from cane sugar and galactose from milk sugar. All these are absorbed in solution, and are carried away in the blood of the portal vein.

(3) **Fats.**—After being split up into the component acids and glycerin, fats pass, as soluble soaps or as fatty acids soluble in the bile, through the borders of the intestinal epithelium. Here they appear to be again converted into fats by a synthesis of the acid with glycerin. Fine fatty particles are found to make their appearance in the cells at some distance from the free margin and to increase in size. A similar synthesis occurs even when free fatty acids are given, so the cells must be capable of producing the necessary glycerin to combine with the acids. The fats are sent on from the cells, through the lymph tissue of the villi, into the central lymph vessels, and thus on, through the thoracic duct, to the blood stream. Unlike the proteins and carbohydrates, they are not carried directly to the liver.

IV. FATE OF THE FOOD ABSORBED

The food absorbed may be—

(*A*) used immediately as a source of energy, for (1) the Construction or Reconstruction of Tissues; (2) the Production of Mechanical Work; (3) the Production of Heat;

Or (*B*) it may be stored for future use in the body.

The processes of construction and repair of the tissues and the production of mechanical work have already been considered (p. 13 *et seq.*), and the production of heat and the regulation of temperature may now be dealt with.

I. PRODUCTION OF HEAT AND REGULATION OF TEMPERATURE

1. Production of Heat

A. Muscle.—The production of heat in muscle has been already studied (p. 61). It has been shown that muscle, from its great bulk and constant activity, is the main source of heat in the body. Not only may it be demonstrated that the temperature of contracting muscle rises, but it has been found that the temperature of blood coming from the muscles is slightly higher than that of blood going to them. Muscular exercise raises the temperature of the body. The shivering fit which is induced by exposure to cold is really a reflex reaction by which heat production is increased. Drugs which interfere with muscular contraction, such as curare, diminish the temperature, and young animals, before their muscular tissues become active, have a low temperature unless kept in a warm atmosphere.

B. Glands.—Wherever chemical change goes on in protoplasm, heat is liberated. Therefore in glands during activity a certain amount of heat is produced. But the production in them is trivial when compared with the production in muscle. During the period of active digestion the temperature of the blood coming from the liver may be nearly 1° C. higher than that of the blood going to the organ. The liver alone among glandular structures contributes an appreciable amount of heat to the body, since the amount of blood passing through the organ is large, and thus a considerable amount of heat is derived from it.

C. Brain.—Some physiologists have maintained that the fact that the temperature of the brain rises during cerebral activity indicates that the chemical changes going on are sufficient to yield a certain amount of heat. But it is more probable that the rise of temperature is due to the increased flow of blood through the organ, since a study of the gases in the blood coming from the brain gives no indication of any marked increase of chemical change during periods of increased cerebral action.

2. Regulation of Temperature

Since heat is constantly being produced, the temperature of the body would tend to rise higher and higher, were there not some arrangement by which just as much heat is eliminated as is produced, and by which the temperature is thus kept constant.

Elimination of Heat.—Heat is got rid of by three channels. **A. Skin.**—Since the body is generally warmer than the surrounding air, heat is constantly lost by *conduction*, *convection*, and *radiation*, and the extent of this loss depends mainly upon the difference between the temperature of the body and that of the air. Radiation plays the most important part when a person is sitting quiet in still air ; conduction and convection when the exchange of air over the surface is rapid. The temperature of the skin is increased when, from dilatation of the cutaneous vessels, more blood is brought to the surface and conversely it is lowered by constriction of these vessels. The influence of variations in the temperature of the air is generally minimised in man by the covering of clothes, and in animals by the covering of fur or feathers, which retains a stationary layer of air at about 25° to 30° C. over the skin. It has been calculated that in man over 70 per cent. of all the heat is lost by conduction and radiation.

The loss of heat by radiation may be determined by finding to what extent a thin metal grill fixed at a definite distance from the surface of the body is heated. This can be done by determining the change produced in its electric conductivity.

By the *evaporation of sweat*, heat is rendered latent, and is taken from the body, which is thus cooled just as the hand may be cooled by allowing ether to evaporate upon it. If the amount of sweat vaporised is known, it is possible to calculate the amount of heat removed from the body in this way. The loss is comparatively small—in man only about 14 per cent. of the whole. The extent depends upon the rapidity with which evaporation goes on, and this is governed by the amount of sweat secreted, and by the dryness and temperature of the atmosphere. Thus a warm dry climate is better borne than one which is warm and moist, since in the former the loss of heat by evaporation is so much greater. Of the various factors increasing sweat secretion, heat is probably the most important.

In the lower animals the loss of heat by evaporation is much increased if the skin is wet, and the temperature of the horse may fall distinctly if the coat remains moist.

Since the temperature of the skin is governed by the state of the cutaneous vessels and the amount of sweat produced by the state of the sweat glands, and since both of these are under the control of the nervous system, the elimination of heat from the skin is presided over by a nervous mechanism.

B. Respiratory Passages.—By conduction and radiation and by evaporation from the respiratory passages, about 10 per cent. of the heat is got rid of in man. In the dog and some other animals, the proportion of heat eliminated in this way is considerably greater.

C. Urine and Fæces.—Since these are warmer than the surrounding air, a certain amount of heat is lost through them. The amount is small—something less than 2 per cent. of the whole.

Temperature.—In all higher animals, the loss of heat and the production of heat are so nicely balanced that the temperature of the body remains fairly constant under all conditions. If an extra amount of heat is produced, say in muscular exercise, it is at once eliminated by the skin, and, if the body is exposed to a low temperature, loss of heat is rapidly checked by contraction of the cutaneous vessels and diminished activity of the sweat glands.

Since heat is constantly being given off, the temperature at the surface of the body is always lower than the temperature in the interior. The temperature of the rectum may be taken as a measure of the internal temperature.

The mean daily temperature of the **horse** is 37° to 38° C.

Under all normal conditions the temperature undergoes only small variations, because the balance between production of heat and elimination of heat is so well maintained. But under abnormal conditions the balance is frequently upset. Thus severe muscular work causes a temporary rise of temperature, because heat elimination does not quite keep pace with heat production. Exposure to very high temperatures may cause a slight rise of temperature, while exposure to excessive cold may cause a slight fall; but, unless in the case of those unable to use their muscles, the change is small.

While the higher "warm-blooded animals," mammals and birds, maintain a constant temperature, the lower vertebrates, "cold-blooded animals," reptiles, amphibia and fishes, do not do so, and their temperature varies with that of the surrounding medium.

But even in mammals the mechanism for the regulation of temperature is not absolutely perfect, and in every species of animal there is a limit to the power of adjustment.

Mammals which hibernate become for the time "cold-blooded animals," and lose their power of regulating their temperature.

The **regulation of temperature** may be effected either by modifying heat production, or by altering the rate of elimination. **Heat production** is voluntarily modified when muscular exercise is taken during exposure to cold, and involuntarily when muscles are set in action by a shivering fit. There is, however, no evidence of the existence of a special nervous mechanism presiding over heat production in muscle.

But it is not so much by changes in the rate of heat production, as by alteration in **heat elimination** through the skin, that the temperature is kept uniform. The nerves to the cutaneous vessels, and to the sweat glands, are the great controllers of temperature. It is through failure of this mechanism under the action of the toxins of micro-organisms that heat elimination is diminished, and the temperature is raised in fevers.

It is not necessary to assume that there is a special heat regulating nervous mechanism, since the nervous arrangements presiding over the vessels and glands of the skin are capable of immediately responding to change of condition calling for their intervention.

II. STORAGE OF SURPLUS FOOD

A. Since bulk for bulk fat has more than twice the energy value of proteins or carbohydrates, it is an advantage to store surplus food as **Fat.**

This storage takes place chiefly in three situations: (1) Fatty tissue; (2) liver; (3) muscle.

1. **In Fatty Tissues.**—In most mammals the chief storage of surplus food is in the fatty tissues.

That the **fat** of the food can be stored in them is shown by the fact that the administration of large amounts of fats different from those of the body leads to their appearance in those tissues.

Fats are also formed from the **carbohydrates** of the food. Feeding experiments upon pigs and other animals, carried out in this country by Laws and Gilbert, have definitely proved that sugary foods are changed to fat in the body and stored in that form. The following may be given as an example of such experiments. Two young pigs of a litter were taken, and one was killed and analysed. The other was fed for weeks on maize, the amount eaten being weighed and the excretion of nitrogen by the pig being determined. The animal was then killed and analysed, and it was found that the fat gained was more than could be produced from the fat and protein of the food eaten. It must therefore have been formed from the carbohydrates.

The evidence that fats may be formed from the *proteins* of the food is conflicting. In the ripening of cheese it is undoubted that under the influence of micro-organism proteins are changed to fats, and in all probability the same thing occurs in the formation of the fatty adipocere in the muscles of the dead body during putrefaction. At one time it was supposed that under the influence of such poisons as phosphorus the proteins of the cells of the mammalian tissues are changed to fat. But careful chemical examination has shown that the so-called fatty degeneration is due to accumulation of already existing fats in the affected organs. Voit fed dogs on lean beef, and found that, while all the nitrogen was discharged from the body, the carbon was retained, and he concluded that it was retained as fat. But he failed to recognise that even lean flesh contains both fat and glycogen from which the fat can be formed. At present we have no direct evidence that the fats of the body are formed from proteins.

2. **In the Liver.**—The liver is a storehouse of carbohydrates and fats (p. 387). Lecithin is always present in the liver, even in prolonged fasting.

3. **In Muscle.**—Some animals, as the salmon, store fats within their muscle fibres; but in mammals such a storage is limited in amount.

B. Proteins may, to a small extent, be stored in muscle, especially after a fast or a prolonged illness. But in the healthy mammal it is difficult to get such a storage, except in athletic training, where the muscles may be enormously increased by the building up of the protein-derivatives of the food into their protoplasm.

C. **Carbohydrates** are stored to a small extent in the liver and in the muscle.

III. THE LIVER IN RELATIONSHIP TO ABSORBED FOOD AND TO THE GENERAL METABOLISM

The liver develops as a couple of diverticula from the embryonic gut, and is thus primarily a digestive gland, and in invertebrates it remains as a part of the intestine both structurally and functionally. But in mammals, early in fœtal life, it comes to have important relationships with the blood going to nourish the body from the placenta (see p. 440). The vein bringing the blood from the mother breaks up into a series of capillaries in the young liver, and in these capillaries the development of the cells of the blood goes on for a considerable time. Soon the liver begins to secrete bile, while animal starch and fat begin to accumulate in its cells. Gradually the formation of blood cells stops, and the mass of liver cells become larger in proportion to the capillaries. As the fœtal intestine develops, the vein bringing blood from it—the portal vein—opens into the capillary network of the liver, so that, when at birth the supply of nourishment from the placenta is stopped, the liver is still associated with the blood bringing nutrient material to the tissues.

1. **Relation to Carbohydrates—Glycogenic Function.**—Claude Bernard discovered that sugar is formed in the liver. This formation of sugar goes on throughout life, and on account of this constant supply the amount of sugar in the blood does not diminish, even when an animal undergoes a prolonged fast. In starvation there are only two possible sources of this glucose—the fats and the proteins of the tissues. There is no conclusive evidence that **fats** can be changed to sugar in the liver, although it is difficult to explain the large amount of sugar which is sometimes excreted in phloridzin poisoning, unless it is formed from fats. That it is not all formed from proteins is shown by the fact that the sugar which appears is sometimes greater than could be produced by the proteins broken down, as indicated by the output of nitrogen.

That **proteins** are a source of sugary substances is shown by the amount of sugar which is produced by an animal rendered diabetic by removal of its pancreas and fed exclusively on proteins. It is therefore probable that in starvation the proteins of the body are broken down and their non-nitrogenous part changed to sugar.

But not only does the liver manufacture sugar for the tissues in starvation, but, when the supply of sugar is in excess of the demands of the tissues, it stores it as a form of starch—**glycogen**—and gives it out as sugar as that substance is required. On a carbohydrate diet the accumulation of glycogen in the liver is very great; but even on a protein diet, in dogs at least, a smaller accumulation takes place. The observation that the various monosaccharids are all stored as the same form of glycogen shows that they must first be assimilated by the liver protoplasm and then converted to glycogen, the process being one of synthesis.

The way in which glycogen is again changed to sugar is doubtful. The fact that the liver, after treatment with alcohol, can change glycogen to glucose, has induced some physiologists to believe that it is by an enzyme that this conversion goes on during life. But it has been shown (1) that the injection of methylene blue, which poisons protoplasm but does not interfere with the action of enzymes, checks the conversion, and (2) that stimulating the splanchnic nerves going to the liver increases the conversion of glycogen without increasing the amylolytic enzyme in the liver and blood. It is therefore probable that the conversion results from chemical changes in the protoplasm which are controlled by the nerves of the liver.

If more sugar is taken than the liver can deal with, it passes on into the general circulation, and is excreted in the urine. Every individual has a certain power of oxidising and storing sugar, and most persons can dispose of about 200 grms. at a time. But the carbohydrate capacity varies greatly, and even in the same individual it is different under different conditions. When the glycogen stored in the liver is changed to glucose more quickly than is required by the tissues, the glucose may be to a certain extent again stored in the muscles as glycogen, or it may accumulate in the blood and be excreted in the urine (glycosuria). This condition is seen when the posterior part of the floor of the fourth ventricle in a rabbit is punctured. If glycogen be abundant in the liver, glycosuria results, the stimulation of the nervous system producing a too rapid conversion of the glycogen.

Another way in which sugar may be made to appear in the urine is by injecting phloridzin. Under the influence of this drug the sugar in the blood is not increased. It must be concluded that it acts by causing the kidneys to excrete glucose too rapidly, so that it is not available for the tissues. But even when carbohydrates are withheld and cleared out of the body, phloridzin causes glycosuria. Hence the kidneys must be made to form glucose from the protein of the blood plasma.

The injection of large doses of extract of the suprarenal bodies causes a glycosuria with an increase of sugar in the blood ; but so far it is not known whether the condition is one of increased production or of diminished utilisation of sugar (p. 406).

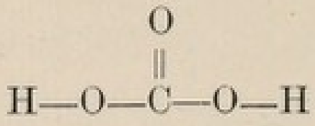
Removal of the pancreas also causes glycæmia and glycosuria (p. 410).

2. **Relation to Fats.**—Although the fats are not carried directly to the liver, as are proteins and carbohydrates, they are stored in large amounts in the liver of some animals—*e.g.* the cod among fishes and the cat among mammals. Animals which have little power of storing fat throughout the muscles and other tissues generally, seem to have a marked capacity for accumulating it in the liver. Even in starvation the fats do not disappear from the liver, and throughout all conditions of life a fairly constant amount of **lecithin**—a phosphorus and nitrogen containing fat (see p. 76)—is present in the liver cells. Lecithin, in the yolk of the egg, is an intermediate stage in the formation of the more complex nucleins of living cells, and the formation of lecithin in the liver by the synthesis of glycerin, fatty acids, phosphoric acid, and cholin is probably a first step in the construction of these nucleins. If this be so, the fat of the liver must play an important part in retaining and fixing phosphorus in the body.

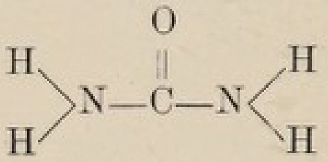
3. **Relation to Proteins.**—Along with the intestinal wall, the liver regulates the supply of proteins to the body. A

study of the chemical changes in muscle has shown that the waste of protein is normally small in amount, and that a great part of the nitrogen is capable of being used again if a supply of oxygen and carbonaceous material is forthcoming (see p. 69). Hence the demand for nitrogen in the muscles is small, and for this reason, apparently, any excess of protein in the food is decomposed, either by trypsin and erepsin or by the intestinal wall, into simple nitrogenous compounds, which are changed into urea in the liver.

Urea, the chief waste substance excreted in the urine, is the bi-amide of carbonic acid.



$$H-O-\overset{O}{\overset{\|}{C}}-O-H$$



It contains 46·6 per cent. of nitrogen. It is a white substance crystallising in long prisms. It is very soluble in water and alcohol—insoluble in ether. With nitric and oxalic acids it forms insoluble crystalline salts. It is readily decomposed into nitrogen, carbon dioxide and water by nitrous acid and by sodium hypobromite in excess of soda. (*Chemical Physiology.*)

Urea is chiefly formed in the Liver.—That it is not produced in the kidneys is shown by the following facts:—(1) When these organs are excised, urea accumulates in the blood. (2) When ammonium carbonate is added to blood artificially circulated through the kidney of an animal just killed, no urea is formed.

That it is not formed in the muscles is shown—(1) By the absence of a definite increase in urea formation during muscular activity; (2) by the fact that when blood containing ammonium carbonate is streamed through muscles, urea is not produced.

That it is formed in the liver is indicated—(1) By the fact that when an ammonium salt such as the carbonate dissolved in blood is streamed through the organ, it is changed to urea; (2) by the observation that, when the liver is cut out of the circulation, the urea in the urine rapidly diminishes, and ammonia and lactic acid take its place.

The exclusion of the liver from the circulation in mammals is difficult, because, when the portal vein is ligatured, the blood returning to the heart tends to accumulate in the great veins of the abdomen. But this difficulty has been overcome by Eck, who devised a method of connecting the portal vein with the inferior vena cava, and finally occluding the portal vein, and of thus allowing the blood to return from the abdomen to the heart.

Source of Urea.—Urea is produced from the decomposition products of proteins of the food and tissues (see p. 216). The manner in which excess of protein in the *food* is broken down into ammonia compounds in the intestine and sent to the liver has been already considered (p. 380). But the fact that even in starvation urea is produced seems to indicate that the initial stages of decomposition of proteins may go on elsewhere than in the intestinal wall. The fate of hæmoglobin tends to show that the whole process may be conducted in the liver cells. When hæmoglobin is set free from the corpuscles, the nitrogen of its protein part is changed to urea, while the pigment part is deprived of its iron and excreted as bilirubin. Whether the proteins of muscle and other tissues are thus directly dealt with, or whether the initial stages of decomposition go on outside the liver, is not known. But the wide distribution of erepsin through the tissues may indicate that the initial splitting of the protein goes on in them.

The nitrogen excreted is not all in the form of urea, but some is combined in ammonia salts, in uric acid and other purin bodies (see p. 427), and in creatinin. In the mammalian body ammonia and the purin bodies can be changed into urea, and it is probable that the small amounts of these substances which appear in the urine have simply escaped this conversion. Certain drugs (alcohol, sulphonal, etc.) and toxins (diphtheria) markedly decrease their conversion into urea and so increase their quantity in the urine. Although urea may be prepared from creatin, there is no evidence that the process goes on in the body. Creatin yields the creatinin of the urine.

It is probable that after the nitrogenous portion of the protein molecule is split off and got rid of, the liver has the further power of turning the non-nitrogenous part into sugar and either sending it to the tissues or storing it as glycogen.

Summary of the Functions of Liver.—The functions of the liver may be briefly summarised as follows:—(1) It regulates the supply of glucose to the body (*a*) by manufacturing it from proteins when the supply of carbohydrates is insufficient, and (*b*) by storing it as glycogen when the supply of carbohydrates is in excess, and giving it off afterwards as required. (2) Along with the intestinal wall it regulates the supply of proteins to the body, by decomposing any excess, and giving off the nitrogen as urea, etc. (3) It regulates, in many animals at least, the supply of fat to the body by storing any excess. (4) It regulates the number of erythrocytes by getting rid of waste hæmoglobin and retaining the iron for further use (see p. 213). (5) From the part it plays in the entero-hepatic circulation, it protects the body against certain poisons by excreting them in the bile.

V. GENERAL METABOLISM

Having considered how the food is digested and absorbed, and how it is then either stored or at once used (*a*) for building up and repairing the tissues, or (*b*) as a source of energy, *the rate at which the various chemical changes go on and the factors modifying them* may be dealt with.

The changes in the two great constituents of the body—proteins and fats—have to be separately studied.

1. Method of Investigating

A. Protein Metabolism. — The amount of protein used in the body is readily calculated from the amount of nitrogen excreted, since, under normal conditions, unless nitrogen in some unusual combination is being taken, it is derived entirely from the proteins in the body. Proteins contain 16 per cent. of nitrogen, and hence each grm. of nitrogen excreted is derived from 6·25 grms. of protein.

The nitrogen is almost entirely excreted in the urine. Only a small amount escapes by the bowels and skin, and hence only when very accurate observations are desired is it necessary to analyse the fæces and sweat.

B. Metabolism of Fats.—Proteins contain nearly three and a half times as much carbon as nitrogen, and hence, when they are broken down, for each grm. of nitrogen excreted, 3·4 grms. of carbon are given off.

The carbon is chiefly excreted from the lungs as carbon dioxide, and in this form it may be collected and estimated.

Any excess of carbon excreted, over the 3·4 times the amount of nitrogen given off, must be derived from the fats of the body or from the fats and carbohydrates taken in the food. Any carbon retained in the body, apart from that in proteins, is stored ultimately as fat. Since carbon constitutes 76·5 per cent. of fats, the amount of fat is calculated by multiplying the carbon by 1·3.

The following tabular example of an investigation of the metabolism may be given :—

	Intake in Grams.			Output.	
		C.	N.	C.	N.
Proteins . . .	100	54	16	...	...
Fats	100	76	...	...	...
Carbohydrates . .	400	200	...	...	...
		330	16	300	14

Two grms. of nitrogen are retained as protein ; that is, 2 × 6·25 = 12·5 grms. of protein—are being daily laid on. Thirty grms. of carbon are also retained in the body, and of this 3·4 × 2 = 6·8 grms. are combined with the nitrogen in the protein. The remainder, 23·2 grms., go to form fats, the amount of which is 23·2 × 1·3 = 30·16 grms. of fat.

2. Metabolism during Fasting

When the usual supply of energy in the food is cut off, the animal liberates the energy required by oxidising its own stored material and its tissues. This is shown by the fact that the animal loses weight and goes on excreting carbon dioxide, urea, and the other waste products of the activity of the tissues.

Several prolonged fasts have been undertaken by men, and, in one or two of these, careful observations have been made by physiologists. It has been found that during the first day or two of a fast, the individual goes on using proteins and fats at something like the same rate as he did while taking food, but that gradually he uses less and less protein each day. This is well shown in the case of Succi, who underwent a fast of thirty days.

Day of Fast.	Protein used in Grms.	Fat used.
1st	104	Not estimated.
10th	51	170
20th	33	170
29th	31	163

It is from the stored fats that the energy is chiefly derived, and the result of this is that before death the fats of the body are largely used up. The protein-containing tissues waste more slowly and waste at different rates, the less essential being used up more rapidly than the more essential, which, in fact, live upon the former. In cats deprived of food till death supervened the heart and central nervous system had hardly lost weight; the bones, pancreas, lungs, intestines, and skin each had lost between 10 to 20 per cent. of their weight, the kidneys, blood, and muscles between 20 to 30, and the liver and spleen between 50 to 70.

The *rate of waste* during a fast depends upon the amount of energy required, and it is therefore increased by muscular work and by exposure to cold. When a man is kept quiet and warm and supplied with water, a fast of thirty days may in some cases be borne without injury.

3. **Effect of Feeding**

When food is given to a fasting animal or man, the first effect is to increase the rate of wasting by calling into action the muscles and glands concerned in digestion. The result is an immediate increase in the excretion of nitrogen and carbon, indicating an increased breaking down of proteins and fats. It has been found that in the dog a diet of white bread and butter increased the metabolic processes by an amount equivalent to about 10 per cent. of the energy value of the diet. For this reason, to give an animal which is fasting a diet containing just the amount of nitrogen and of carbon which the animal is excreting, will not at once stop the loss of weight. Suppose, for instance, that to a fasting animal using daily 30 grms. of the proteins and 160 grms. of the fats of his body, a diet containing these amounts is given, the disintegration of proteins and of fats will at once rise, say, to 50 grms. of protein and 280 of fat. Thus the result will be that, instead of his losing 30 grms. of protein, he will lose only 20 grms. per diem, and instead of 160 grms. of fat, only 120 grms. But, if the diet is sufficient to supply the energy required, in a few days the intake and output will balance, and the individual is then said to be in **metabolic equilibrium**, and he neither gains nor loses weight. The following table and fig. 168 give an idea of how this adjustment of the metabolism is reached:—

Day.	Intake.		Disintegrated.		Waste diminished to.	
	Protein.	Fat.	Protein.	Fat.	Protein.	Fat.
1	0	0	30	160	...	...
2	30	160	50	280	20	120
3	30	160	40	240	10	60
4	30	160	30	200	0	40
5	30	160	30	160	0	0
6	30	160	30	160	0	0

If the amount of food be further increased, a small proportion of the proteins and a larger proportion of the fats are retained, and weight is gained. As already indicated, the power of storing proteins is generally small (see p. 386).

Protein Diet.—Proteins contain all the chemical elements required for the building and repair of the tissues, and from the complexity of their molecules they also supply latent energy. It is therefore theoretically possible for an animal to sustain life on proteins, and certain animals can be fed exclusively upon them. Thus Pflüger kept a dog for many months upon a purely protein diet without injury to its health. But to supply the necessary energy in proteins alone requires the consumption of excessively large quantities, and herbivorous animals are unable to digest and use such quantities. Further, when large quantities are taken, the greater portion is broken up in the intestinal wall and formed into urea by the liver and excreted by the kidney, and thus excessive work is thrown upon these excretory organs.

It is therefore not advantageous to adopt a too purely protein diet. The great use of proteins is as muscle-builders. When the muscles are in a state of constant activity they have a certain power of laying on protein as they grow. Hence the value of proteins in muscular training.

Gelatin, although undergoing digestion and absorption like the proteins, is not available as a muscle-builder. Its sole use is as an energy yielder, and in this respect it has a value equal to the proteins.

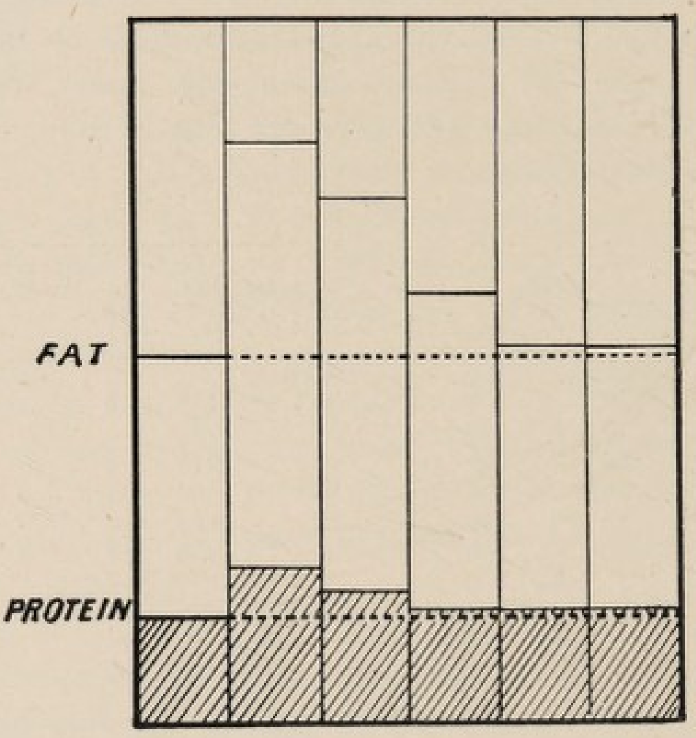


FIG. 162.—To show the effects on the metabolism of proteins and fats of feeding a fasting animal. The continuous horizontal lines indicate the amount of material metabolised, the broken horizontal lines the amount taken. The differences between the levels of these indicate the amount of protein and of fats of the animal body which are metabolised. The first column represents the condition in fasting—the succeeding columns the intake and output each day when food is given.

Carbohydrate Diet.—Carbohydrates are of equal value with proteins as a source of energy, but they contain no nitrogen, and they are not available alone for building up and repairing the protoplasm of muscles and other tissues. Carbohydrates alone will not support life, but when added to proteins they enable the animal to do with smaller quantities of the latter. They are thus sometimes termed *protein sparers.* Their use in diminishing the consumption of proteins is, however, strictly limited.

Fat Diet.—Fats, like carbohydrates, will not support life, because they cannot be used for building up protoplasm; but, like carbohydrates, they are a source of energy, and they have more than twice the energy value of proteins or of carbohydrates. They are thus *protein sparers.* But experiment has shown that, in spite of their higher energy value, they have not the same power as carbohydrates of sparing proteins, since their digestion and absorption is more difficult. Thus while theoretically 1 grm. of carbohydrate yields 4·1 Calories of energy, 1 grm. taken in the food, since it is not all absorbed and used, yields 4·03 Calories of energy. But fat, which theoretically yields 9·3 on account of its less availability, yields in the body only 8·93 Calories. That is, while carbohydrates yield 97 per cent. of their energy, as determined by the calorimeter, fats yield only 92 per cent. of their energy.

When once absorbed, fats are iso-dynamic with the equivalent amount of carbohydrates. This has been determined by replacing the carbohydrates in a diet with the equivalent amount of fat.

A knowledge of the part played by proteins, carbohydrates, and fats in the animal body is the groundwork of the study of *Dietetics.*

VI. DIETETICS

The object of Dietetics is to fit the supply of matter and energy in the food to the requirement of the body under different conditions.

In all animals the great essentials of a diet capable of maintaining health are:—

1*st.* That it should be capable of digestion, absorption, and assimilation, *i.e.* that it should be available.

2*nd.* That it should supply the energy required.

3rd. That it should contain sufficient proteins to make good the waste of these substances.

1. Diet must be capable of Digestion, Absorption, and Assimilation.—The constituents of the food, to be of use in the body, must be capable of being acted on by the digestive juices. For this reason young vegetables, in which the cells have only a thin capsule of cellulose, which is easily broken up in mastication or by maceration in the rumen of the ox or colon of the horse, yield more of their nutritious constituents than do the older vegetables, where the capsule has become indurated, and possibly in part converted to lignin and other encrusting substances. A food that is capable of proper digestion is also capable of absorption, provided the cells lining the intestine are active.

Lastly the food, to be of use, must consist of proteins, carbohydrates, and fats, which alone are capable of being taken up—assimilated—by the tissues, so that they can be broken down and their energy liberated. Various matters may be absorbed from the food into the blood merely to be again excreted by the kidneys, without serving any purpose in the body.

The investigation of the extent to which food is digested is more difficult in herbivorous than in carnivorous animals, because the process of digestion is so much slower. In the ruminants it takes nearly five days for the contents of the alimentary canal to be cleared out. In the horse it takes about four days.

To determine the extent to which digestion has been carried out, analyses of the food and of the fæces during a somewhat prolonged period have to be made. It has been found that digestion of various plant foods goes on to about the same extent in the various ruminants, but that in the horse it is less complete. When fed on hay, 11 or 12 per cent. less of the solids are digested in the horse than in the sheep. The proteins are digested about as well, the fats much less well digested, sometimes as much as 50 per cent. less well; the carbohydrates about 10 per cent. less well. The crude fibre of the hay, which is well digested in the ruminants, is not so perfectly dissolved in the horse.

Some examples of the extent to which some of the commoner foods are digested by ruminants may be given in per cent. of total amount taken.

	Protein.	Fibre.	Fat.	Carbo-hydrate.
Meadow grass	75	75	66	78
Hay	61	57	53	64
Oats	78	20	83	76
Peas	89	66	75	93

The following table gives the results of some recent observations upon the availability of the proximate principles of oats in the horse and sheep:—

Per cent. digested.

	Horse.	Sheep.
Raw protein	68·2	63·8
„ fat	54·0	62·6
„ fibre	7·1	40·3
N free extractives	69·3	72·0

Only about 58·7 per cent. of the energy of the oats was thus available.

This shows very clearly that the diet must contain far more energy than is actually required by the animal, that the *gross energy* of the diet must greatly exceed the *nett* energy requirements of the animal.

With these general considerations we may now take up the feeding of the various kinds of animals.

2. **The energy requirements** vary enormously in animals of different species, and even in animals of the same species.

1. Size must obviously have a marked effect. A big animal requires a greater supply of energy than a small one. But, since in small animals the loss of heat is greater than in large animals, the metabolic processes in these are more active, and more food in proportion to their size is required.

In this connection it must be remembered that, in considering the influence of size on the energy requirements, we should really consider only the weight of the living tissues, and should neglect the weight of mere practically dead matter, such as fat, skin, hair, hoofs, and the contents of the alimentary canal. This, however, is not easily ascertained.

Mode of Life.—An animal kept warm and at rest requires much less energy than one doing muscular work and exposed to cold.

The variations in the amount of material used in different conditions is well illustrated by the experiments of Zuntz on the excretion of carbon dioxide in the dog.

	CO_2 excreted per minute in c.cms.
Resting lying	124·7
„ standing	170·2
Forward movement (unloaded) . .	525·0
„ „ (drawing weight) .	798·9

Muscular Work.—The influence of the activity of the muscle upon the metabolism has been considered on p. 67 *et seq.*

In the horse the question has been very carefully studied by Zuntz and Lehmann, especially as regards the intake of oxygen and output of carbon dioxide. The gaseous exchange was estimated either by putting a mask over the nose and mouth or by performing tracheotomy, while various forms of exercise without change of position were rendered possible by placing the horse on a platform which could be moved at any speed required, and which could be placed in the horizontal or in a sloping position.

3. Protein Requirements.—The minimum amount of proteins necessary to maintain health varies in different animals, but a review of the ordinary dietaries of different herbivorous animals indicates that it should rather exceed one grm. per diem per kilo of animal weight, and that, if muscular work is to be done, its amount must be increased.

1. **The Horse.**—The great object of feeding the horse is to get work out of him, and the more work that is required the more food must be given to supply the energy, or the animal will draw upon the tissues of its body, and will emaciate and lose the power of doing work. Since horses vary so much in size and weight, it is necessary to state the dietary requirements in terms of units of weight, and the unit here taken is the kilo.

It has been found that, to maintain the weight of a horse standing in its stall and doing no work, something like the following combination of proximate principles must be absorbed per kilo of body weight :—

		Grms.		Calories of energy.
Protein	about	1·200	yielding about	4·920
Carbohydrates		5·000	,,	20·500
Fats		0·400	,,	3·720
				29·140

That is, the horse when resting requires about 30 Calories of energy per diem per kilo.

When hard muscular work has to be done by the horse, the diet may have to be increased to something like the following :—

	Grms.		Calories.
Proteins	2·300	about	9·500
Carbohydrates	12·500	,,	50·000
Fats	0·800	,,	7·500
			67·000

which, in proportion to the weight, is about the same as that required by a man doing hard muscular work.

The consideration of the manner in which this supply of nutritious matter is to be given in hay, oats, and straw, etc., must be left to the teacher of stable management.

2. **Ruminants.**—In feeding ruminants, three different objects may be aimed at. In this country oxen are fed to fatten them for food ; cows are fed to yield milk ; while sheep are fed with the object of obtaining their wool, and, in the second place, of preparing them for food.

Feeding of Oxen.—The main purpose here is to make the animal convert the cheap vegetable proteins and carbohydrates as rapidly and completely as possible into the more expensive animal proteins and fats. As we have already seen (p. 386), it is much more difficult to get an increase of protein in a full-grown animal than an increase of fat, because of the tendency on the part of the animal to decompose any excess of protein in the intestinal wall and liver and to excrete the nitrogenous part. But in growing animals the power of laying on protein is very much greater. Therefore the diet of young cattle, say from two to three months old, and weighing about 75 kilos, should contain no less than 4 grms. of protein per kilo per diem, and this should be to the non-protein as 1 to 4·7, while, at the age of two years, the proteins need not exceed 1·6 grms. per kilo per diem, and be to the non-protein food as 1 to 8, and if an older ox is being kept at rest in the stall it may maintain health on a diet containing only about half this amount of protein.

When, however, the animal is being fed for market, the supply of food must be largely increased:—

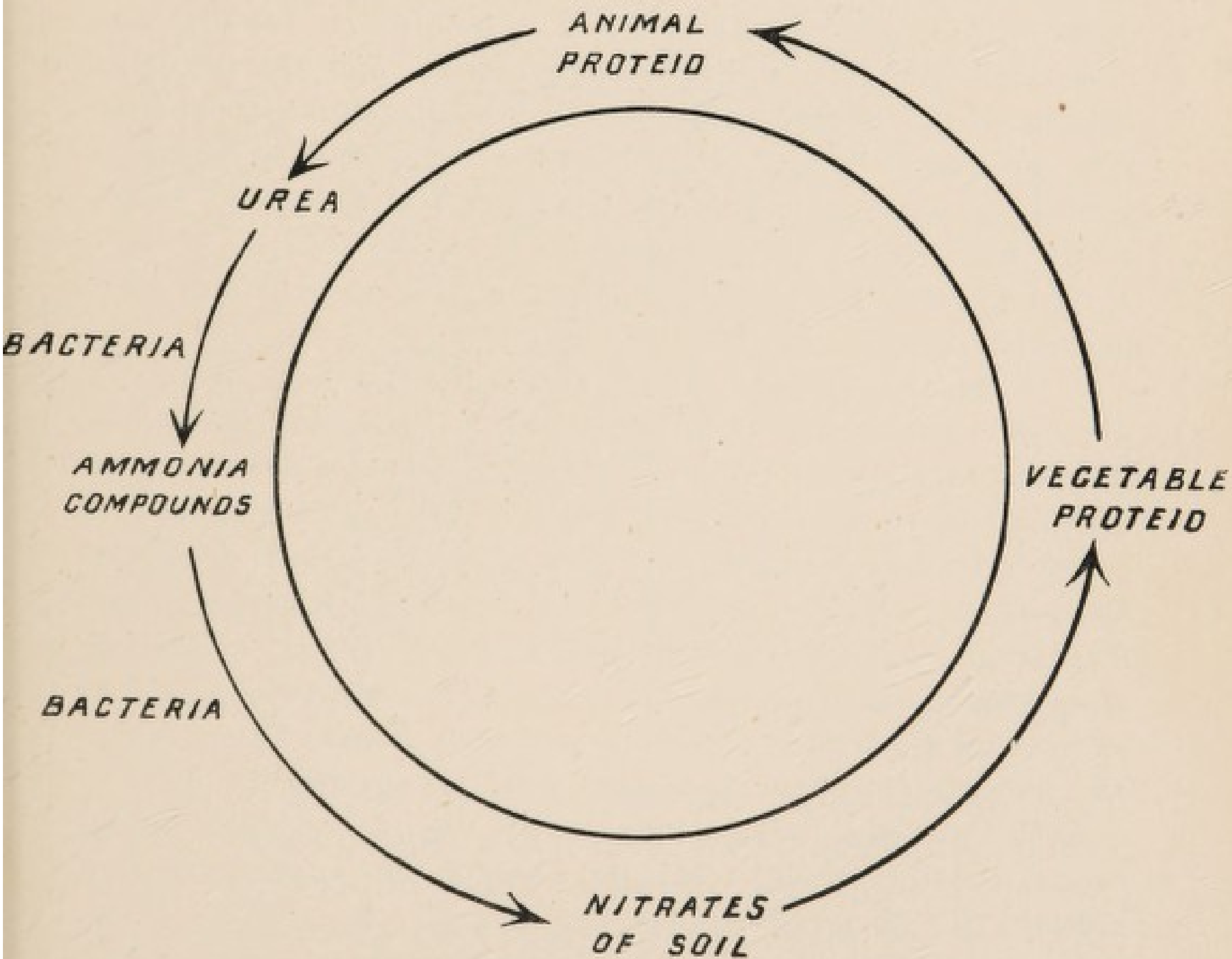
Proximate Principles of Diet of Ox per Kilo, in Grms.

	Proteins.	Carbo-hydrates.	Fats.	Energy in Calories.
Resting in stall . . .	0·7	8	0·15	37
Feeding for market . .	3·0	15	0·7	80

Feeding of Sheep.—While those which are being kept for the purpose of producing the slowly growing wool require a comparatively small diet with only a small proportion of protein, animals which are being rapidly fattened require the diet to be nearly doubled, and the proportion of protein increased.

Feeding of Milk Cows.—Since the various constituents of the milk are manufactured in the udder and not merely extracted from the blood, the activity of the udder is the first factor to be considered in the production of milk. The activity of this organ, like that of others, seems to be influenced very markedly by the supply of protein food, and hence it is desirable to give to milk cows a higher proportion of protein food than is given to oxen. A cow may produce about 20 grms. of milk per kilo of body weight per diem, and this contains about 0·6 grm. of protein and 0·7 grm. of fat. Such a cow should have a diet containing, in a form capable of absorption, about 2·5 grms. of protein and 13·0 grms. of carbohydrates per kilo of body weight per diem. A milk cow, in fact, should have a diet as abundant in proportion to its weight as a horse doing hard muscular work.

In domestic animals the further question of the **manurial value** of the food has to be considered. The constituents of the excreta which are of special manurial value are the nitrogen and phosphorus. Since so little nitrogen is fixed in the body of the adult animal as proteins, the greater quantity of the nitrogen of the food is recoverable in the urine and fæces. In ruminants the phosphorus is chiefly excreted in the fæces. Hence, by careful storage of the excreta and its proper disposal, a large return to the land may be made. This cycle between animal and plant may be illustrated by the following diagram :—



SECTION VII

INTERNAL SECRETIONS OR HORMONES—THEIR PRODUCTION AND ACTION

THE products of the metabolism of the various organs are carried away in the lymph and blood, and certain of these products exercise an important influence upon other structures in the body. Thus, the carbon dioxide produced in muscle acts upon and stimulates the respiratory centre, and the secretion formed in the lining membrane of the duodenum stimulates the pancreas. These products have been termed Internal Secretions, while more recently the name Hormones or "Activators" has been suggested for them.

Among the structures which are known to yield such hormones are :—

1. **Suprarenal Bodies.**—These structures lie just above the kidneys. Each consists of a tough *cortex* composed of epithelial-like cells arranged in columns, and a soft *medulla* consisting of cells derived from neuron cells which stain of a peculiar brown colour with chromic acid. The medulla is developed from the sympathetic chain of ganglia. The cortex is a perfectly independent structure derived from the surrounding mesoblast, and in teleostean fishes it is quite apart from the representative of the medullary part. A suprarenal body is thus two distinct and independent organs combined with one another (fig. 163).

Long ago Brown-Séquard found that removal of these bodies causes great muscular weakness, loss of tone of the vascular system, loss of appetite, and finally death in a short time. Addison had already pointed out that a similar set of symptoms, accompanied by pigmentation of the skin, is associated with diseased conditions of these organs in man. The injection of small quantities of the medullary portion of the bodies or of extracts of it exercises a powerful effect on the endings of the thoracico-abdominal visceral nerves. The most marked result is to cause contraction of the arterioles and an enormous rise in the blood pressure. That the action is upon the endings of these nerves is shown by the fact that McFie found no action on the heart of the chick in which the nerves are not yet developed, while Brodie has failed to get any effect on the vessels of the lungs in which the sympathetic nerve terminations are said to be absent. Further, apocodeine, which poisons the nerve endings, abolishes the effect of suprarenal extracts.

Cardiac inhibition is produced—but this may be due to the rise of blood pressure. It is abolished by the administration of atropin.

These extracts also cause a dilatation of the pupil in the cat and it inhibits intestinal peristalsis. Their action on the bladder varies according to the action of the sympathetic fibre, which is different in different animals. In those in which these fibres cause contraction, extract of the suprarenal acts in this way; in those in which relaxation is caused, the extract causes relaxation. With blood vessels which are not supplied with vaso-constrictor fibres, *e.g.* those of the lungs and heart, the extract does not act, and hence a rush of blood to the lungs is caused.

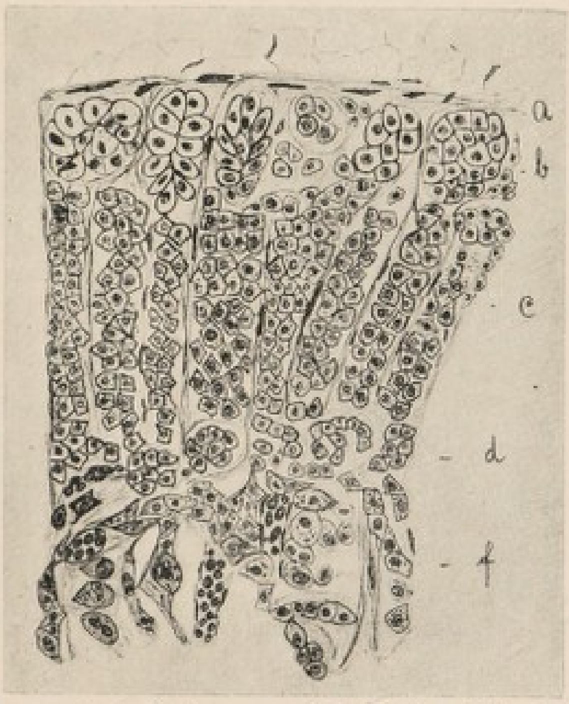


Fig. 163.—Section through Cortex and Medulla of the Suprarenal Body of a Mammal ; *a*, *b*, *c*, *d*, cortex ; *f*, medulla.

As already indicated (p. 389), injections of extracts of the suprarenal bodies profoundly modify the metabolism, leading to an increase of sugar in the blood and to its excretion in the urine. This is best marked when the animal is well fed and has a store of glycogen in its liver, but since it occurs in fasting animals, after the stored carbohydrates have been cleared out by the administration of phloridzin (p. 385), it would appear to be due, in part at least, either to a non-utilisation of sugar by the tissues or to an increased production of sugar from proteins. A decrease in the nitrogen in the form of urea and an increase of that in ammonia, similar to that found in cases of true diabetes, have also been observed. It has been suggested that the suprarenal secretion acts through the pancreas by preventing the formation of the internal secretion which has been supposed to act on the liver (see p. 410). But the evidence is not satisfactory.

Its continued administration produces atheroma of the aorta.

The essential principle of the suprarenals is a substance, *adrenalin*, which is of the nature of a secondary alcohol linked to a benzene ring. Various more or less successful attempts have been made to prepare it synthetically.

The functions of the cortex of the suprarenals are unknown.

2. **Pituitary Body.**—This lies at the base of the mid-brain, and consists of an anterior part of nervous tissue, somewhat resembling the medulla of the suprarenals, and a posterior part derived from the alimentary canal, and consisting of masses of epithelial-like cells.

Removal of this body causes in cats and dogs a fall of temperature, lassitude, muscular twitchings, dyspnœa, and ultimately death. Injection of extracts of the substance is said to diminish these symptoms. In the healthy animal the injection of extracts of the posterior or nerve parts of the pituitary causes a rise of arterial blood pressure, a dilatation of the kidney, and an increased flow of urine. A repetition of the injection may cause a fall of blood pressure, but the dilatation of the kidney and the increased flow of urine are produced.

3. **Thyroid Gland** (fig. 164).—This structure is formed as a hollow outgrowth for the anterior part of the alimentary canal, which branches and again branches. It early loses its connection with the alimentary canal, and becomes cut up by fibrous tissue into a number of small more or less rounded cysts or follicles, each lined with epithelium, and filled with a mucus-like substance, which contains a nucleo-protein, and

a substance with a marked power of combining with iodine. This has been called **iodothyrin**. It contains about 3·6 per cent. of iodine, and it seems to be the active constituent of the internal secretion of the gland.

The removal of the thyroid usually leads to a train of symptoms which varies somewhat in different animals, but is essentially the same in nearly all. The connective tissues tend to revert to the embryonic conditions, and the amount of mucin increases. The temperature falls, muscular tremors appear, and in dogs these may go on to convulsions. They do not disappear on removing the cortex cerebri, but are stopped by section of the nerves to the muscles, and thus they appear to be spinal in origin. The functions of the higher nervous system become sluggish, and the animal frequently dies. By administering the substance of the thyroid, or by giving extracts of the thyroid, most of these symptoms may be delayed or prevented. When thyroid gland or extract is given to healthy animals in moderate doses it causes an increased metabolism of both fats and proteins, and may thus induce emaciation. These phenomena seem to indicate that one function of the organ is to produce an internal secretion

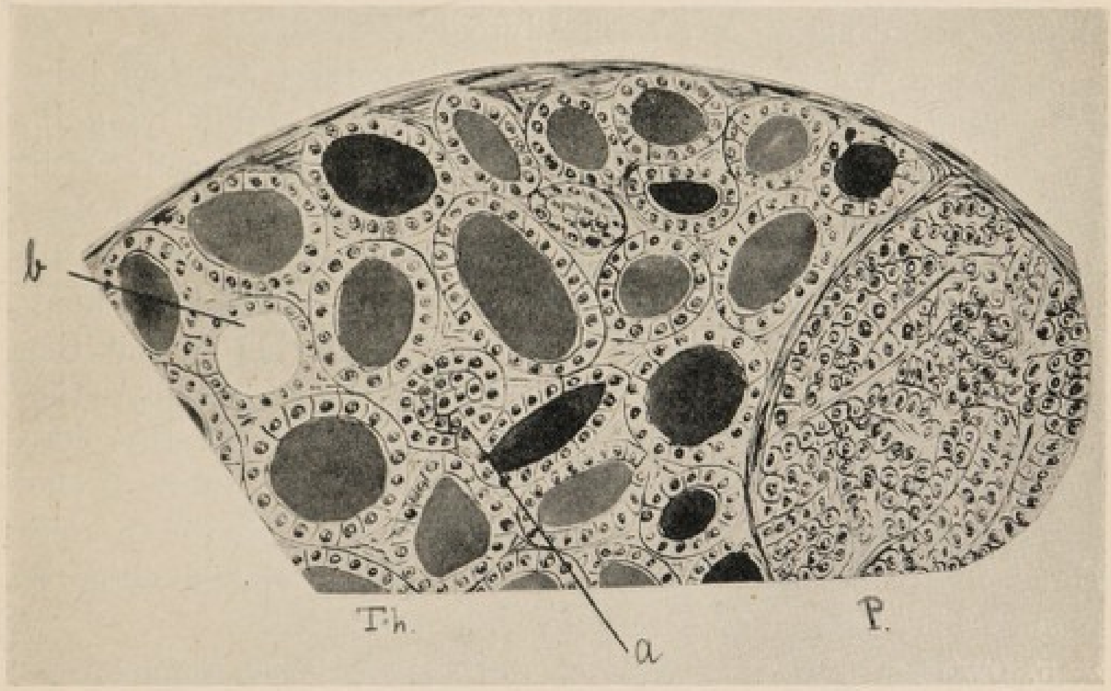


FIG. 164.—Section through part of the Thyroid (*Th.*) and a Parathyroid (*P.*) of a Mammal.

which regulates the rate of the metabolic processes in the body by increasing them when such an increase is desirable. When the thyroid is not developed, the growth and development of the individual are partially arrested, and the condition of *cretinism* is produced. Atrophy of the structure in adult life causes a train of symptoms somewhat resembling those produced by its removal, and constituting the disease, *myxœdema*. It has been suggested that a condition of increased activity of the action of the heart, usually accompanied by prominence of the eyes and swelling in the region of the thyroid—*exophthalmic goitre*—may be due either to increased activity of the structure, or to deficient action of the parathyroids.

4. **Parathyroids.**—Two to four small nodules are found in close relationship to each lobe of the thyroid, often lying in its substance, and these are formed of columns of cells with capillary blood vessels between them (fig. 164). More or less successful attempts have been made in different animals to remove them without the thyroid, or the thyroid without them, and the general result of these experiments is that the nervous symptoms which follow ordinary thyroidectomy—the tremors, etc.—seem to be due to the loss of the parathyroids, while the metabolic changes are probably due to want of the internal secretion of the thyroid. After removal of the thyroid some observers have found that the parathyroids undergo a change and become like the thyroid.

5. **Ovaries and Testes.**—It is well known that removal of these organs causes characteristic changes in the animal: a tendency to the deposition of fat being produced, the activity of the central nervous system being somewhat modified, the voice in the male losing its masculine character, and the thymus persisting, in the male at least, for a considerably longer period than in the normal. That it is not the tubules of the testes but some product of the interstitial cells which act in this way is demonstrated by the fact that ligature of the vasa deferentia which causes atrophy of the tubules does not prevent the development of sexual characters. Several years ago Brown-Séquard maintained that the general effects of atrophy of these organs might be obviated by the administration of testicular substance; and more recently, as a result of clinical experience, the administration of extracts of the

ovaries has been described as relieving certain of the nervous symptoms which supervene on their removal or atrophy. It has further been found that ovarian substance, when given to dogs whether male or female, causes an increase in the rate of protein metabolism, although no similar action is found with testicular substance. There is thus evidence that the ovaries, like the thyroid, form an internal secretion having an important action in accelerating the metabolism. It is at least probable that the testes produce a similar substance.

6. **Thymus.**—This structure develops as an epithelial outgrowth from one or more of the branchial arches of the embryo. Round these outgrowths masses of lymph-like tissue collect, and thus a much lobulated structure lying in the front of the neck and upper part of the thorax is formed. As development goes on the epithelial core of each lobule breaks up and forms nests of cells which are often disposed concentrically and form the corpuscles of Hassall. These lie in the loose lymph-like tissue, the medulla of the lobule, the meshes of which are formed from the epithelial cells, and this is surrounded by a cortex of more dense lymph-like tissue. The thymus is largest in relationship to the body weight about the time of birth, but it continues to grow, although not in proportion to the growth

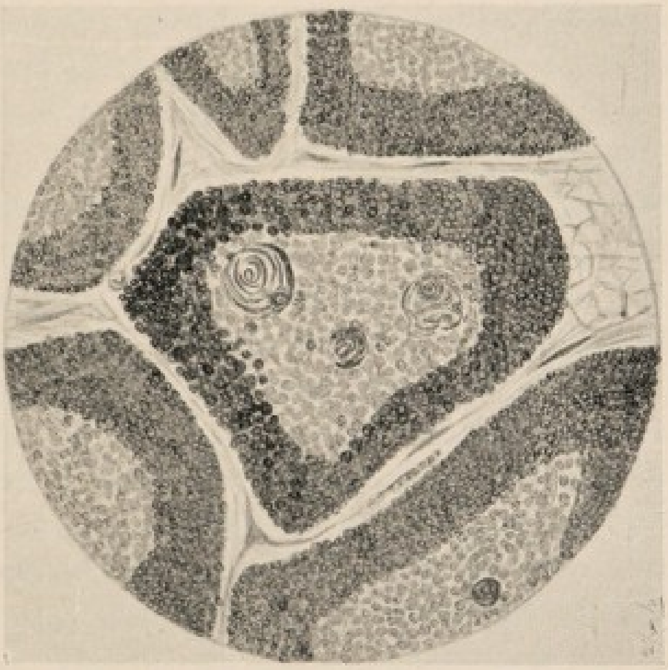


FIG. 165.—Section of the lobules of the Thymus to show the lobules, with Hassall's corpuscles in the central part.

of the body, till about the age of puberty. After about twenty-four years of age it atrophies and is replaced by a mass of fatty tissue. The Hassall's corpuscles seem to atrophy earlier than the lymph-like tissue.

Castration in cattle and guinea-pigs markedly retards the onset of atrophy, so that the thymus of the ox is much larger than that of the bull of the same age. Not only so, but removal of the thymus in young guinea-pigs seems to be followed by a more rapid growth of the testes. It is therefore probable that the thymus yields an internal secretion which controls the growth of the male genital organs.

The only other effect of its removal in young guinea-pigs is a transient diminution in the number of leucocytes. This seems to lead to a diminished power of resisting the invasion of those micro-organisms—*e.g.* staphylococci—which are normally combated by the leucocytes.

7. **Pancreas.**—Excision of the pancreas in dogs and other mammals produces a condition of diabetes—an increase of sugar in the blood, its appearance in the urine, an increased excretion of nitrogen, and a general emaciation. These symptoms do not occur when the duct is tied or occluded until degeneration has developed, but they are invariable and immediate when a sufficient amount of the gland is removed. They are not prevented by the administration of pancreas, either fresh or as extracts. The sugar is formed from the proteins, since it appears in amounts proportionate to the amount of nitrogen excreted, after all the glycogen has been removed. The pancreas seems therefore to form a hormone which either controls the production of sugar in the liver or causes its utilisation by the muscles.

It has been suggested that adrenalin causes diabetes by checking the production of this hormone in the pancreas. But the facts that, in ducks and geese, in which removal of the pancreas does not cause diabetes, the injection of suprarenal extracts causes glycosuria, and that its administration increases the output of sugar in dogs without a pancreas, are opposed to the view that it acts through the pancreas, and suggests that it must act directly on the liver or other tissues.

Since the only respect in which the pancreas differs in histological character from the parotid gland—removal of which has no effect on the metabolism—is in the presence of the islets of Langerhans, it has been suggested that they are related to this function of the organ. Some recent observations, however, tend to show that these islets are not permanent structures, but that they are formed from and revert to the ordinary secreting tissue.

8. **Duodenum.**—As already pointed out the duodenum yields a hormone (*secretin*), which acts directly upon the pancreas to stimulate its secretion.

Toxic Action and Immunity

It is not definitely known how each of these internal secretions performs its special action, but light seems to be thrown upon the question by the study of the mode of action of various toxic substances, and the mode of production of a condition of immunity against them. As will be presently shown, a process of the same nature as the production of internal secretions is involved.

Snake and Diphtheria Toxins.—The question may be most simply approached by considering first the probable mode of action of the toxin or poison of snake venom, or of that produced by the diphtheria bacillus, and the way in which protection against these is established by the development of antitoxins.

By injecting under the skin of the horse increasing doses of such toxins the animal becomes quite resistant to the poison. A certain quantity of its serum can then neutralise a definite quantity of the toxin, so that if the mixture of serum and toxin be injected the animal is uninjured. Something has been formed in the horse which seizes on the molecules of the toxin and makes them harmless, just as when soda is added to sulphuric acid it forms a neutral salt.

The two molecules have a definite chemical affinity for one another, so that the toxin is no longer free to seize upon the protoplasm of the animal's body. To explain this Ehrlich has suggested that the protoplasm molecule, like the protein molecule (p. 7), is to be considered as made up of a central core with a number of side-chains, hands, or *receptors*, which play an important part in taking up nourishment of different kinds, for each variety of which special side-chains have a special affinity (fig. 166). He supposes that some of these side-chains fit the toxin molecule, and are thus capable of anchoring it to the cell and allowing it to exercise its toxic action, and he explains the production of antitoxin by supposing that, as these side-chains get linked to the toxin and are thus, as it were, thrown out of action, others are produced to take their place, since they are necessary for the nourishment of the protoplasm. If the toxin is continually administered in small doses this production of side-chains may be so increased that they get thrown off into the blood and in it are capable of linking to the toxin and so preventing it from fixing itself to the cells. If, therefore, some of the blood be injected into an animal which afterwards receives a dose of the toxin, that toxin will not act, and the animal will be immune.

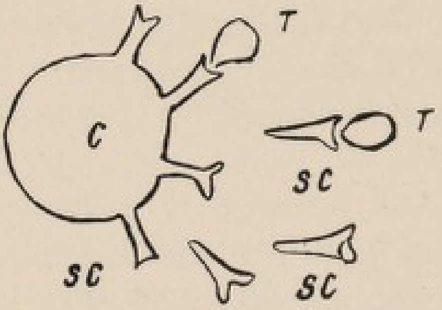


FIG. 166.—To illustrate the formation of side-chains or receptors, *sc*, by which the toxin molecules, *T*, are either anchored to the cell or neutralised. When the side-chains are set free an anti-toxin is formed.

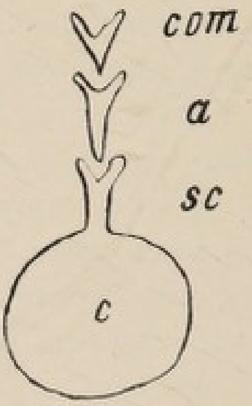


FIG. 167.—To illustrate the anchoring of the anti-body or amboceptor, *a*, to the cell by a side-chain or receptor, *sc*, and the action upon it of complement, *com*.

Typhoid Toxin.—But immunity may also be established not against toxins separate from organisms, but against organisms which hold their toxin, as in the case of the bacillus of typhoid fever. Here repeated injections of increasing doses produce a serum which has the power of destroying the organism when added to it even outside the body. But this is not a simple combination, because if the serum be heated to 55° C. it loses its power, but if a few drops of the fresh serum of an unimmunised animal be added, the power is restored. Obviously the anti-body which destroys the organism—the *bactericidal* or *bacterilytic body*, often called the *amboceptor*—requires the co-operation of another body to enable it to act, and this body has been called the *complement* or *activator*. Ehrlich supposes that the immune body does link to the protoplasm of the organism, but that it must in its turn be linked to the complement. The figure may help to explain this (fig. 167).

Cytotoxins.—Similar anti-bodies, acting upon the cells of the animal body, may be produced by injecting the particular kind of cell into an animal of another species. Thus, if human blood be repeatedly injected into a rabbit the serum of the rabbit's blood becomes *hæmolytic*—*i.e.* acquires the power of dissolving the erythrocytes in *human* blood. In this case too, the immune body requires the presence of a complement, readily destroyed at a comparatively low temperature, to enable it to act. If such hæmolytic serum be injected into another animal an anti-hæmolysin may be developed—a body which will antagonise the action of the hæmolysin. Possibly this is a body which links with the amboceptor to prevent its linking to the complement.

Precipitins.—By the injection of the proteins of the blood of any particular animal into an animal of another species a serum is developed which precipitates the proteins of the blood of the first species and of no others.

In these various cases the active body is produced by the throwing off of side-chains from protoplasm, and as these products are carried away in the blood the process is exactly analogous to the formation of internal secretions.

Opsonins.—Many bacteria after treatment with the serum of the animal are taken up by the leucocytes, but if not treated with serum are not taken up. Apparently the serum contains something which has been called an opsonin which prepares the bacteria to be devoured. The action of opsonins is destroyed by temperatures between 55° and 65° C. The opsonic power of the serum is often increased by the injection of small quantities of dead bacteria (Vaccines).

SECTION VIII

EXCRETION OF MATTER FROM THE BODY

1. EXCRETION BY THE LUNGS (see Respiration, p. 294)

2. EXCRETION BY THE KIDNEYS

URINE

THE water and waste nitrogen of the body are chiefly eliminated in the urine, which is secreted by the kidneys.

The tests for the various constituents of the urine must be studied practically. (*Chemical Physiology.*)

I. Physical Characters

The characters of the urine depend largely on the relative proportion of water and of solids which are excreted in it: at one time it may be very concentrated, while at another time it may be very dilute indeed. For this reason its **specific gravity,** which depends upon the percentage of solids in solution, varies within wide limits. But the average specific gravity in the horse is about 1036. It is possible from the specific gravity to form a rough idea of the amount of solids present, for by multiplying the last two figures by 2·22 the amount of solids per 1000 parts is given.

Since the percentage of pigments in the urine varies like that of the other constituents, the **colour** of the urine shows wide divergence in the normal condition. A concentrated urine has a dark amber colour, while a dilute urine may in some animals be almost colourless. Under average conditions the urine has a straw-yellow colour.

The **reaction** of urine is normally acid in dog and other carnivora.

In herbivora, when suckling or when fasting, the urine is acid, but when on their normal diet it is alkaline.

The alkalinity is due to the presence of alkaline carbonates formed from the citrates, malates, and tartrates of the vegetable foods, and also from the acetates, etc., produced by the decomposition of cellulose in the rumen and intestine.

Urine in carnivora is normally **transparent**; but when it has stood for a few hours, a cloud of a mucin-like substance is seen floating in it. In herbivora, as the urine cools, it rapidly becomes turbid and throws down a white precipitate composed chiefly of carbonate of lime.

The **smell** of urine is characteristic, and it may be modified by the ingestion of many different substances.

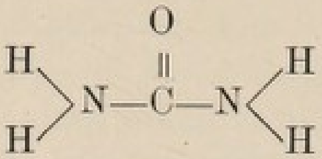
II. Composition

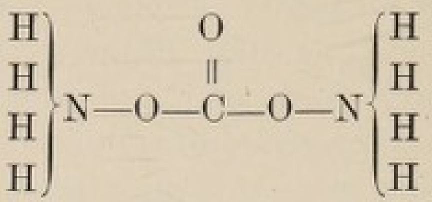
Since the relative amounts of water and solids vary within such wide limits, the percentage composition of urine is of little moment. Of the solids, rather more than half are organic, rather less than half are inorganic. Since water and solids are derived from the water and solids taken by the individual, the amounts excreted depend upon the amounts taken, and must be considered in connection with them. Thus if an animal takes little fluid, it will pass little water in the urine. If it takes little food, a small quantity of solids will be excreted by the kidneys. Since excretion and ingestion must be studied in relationship to one another, it is convenient to compare them during a definite period of time, and the natural division into days of twenty-four hours is generally adopted.

I. Nitrogenous Substances

A. Urea.—The chemistry and mode of formation of urea have been discussed on p. 390. Since it is as urea that, on an ordinary diet, nearly 90 per cent. in the dog, and probably about 80 per cent. in the horse, of the waste nitrogen is eliminated in the urine, the amount excreted affords a measure of the amount of proteins taken in the food.

When the urine is allowed to stand, certain micro-organisms are apt to get into it, and to cause a hydration of the urea, whereby it is changed into ammonium carbonate—



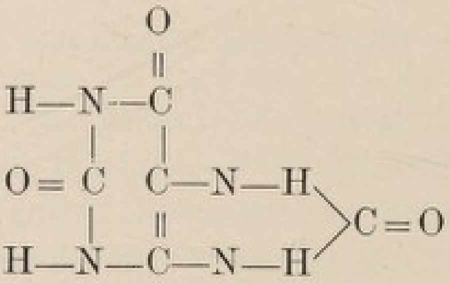


The urine if acid is thus made alkaline, and in carnivora the phosphates of the earths are precipitated. The phosphate of magnesium combines with the ammonia to form ammonio-magnesium-phosphate, $NH_4MgPO_4+6H_2O$, which crystallises in characteristic prism-like crystals. In the horse and other herbivora it is the carbonate of lime which is precipitated.

B. **Non-Urea Nitrogen.**—The 10 to 20 per cent. of nitrogen which on an ordinary diet is not excreted as urea is distributed in :—

1. **Ammonium Salts.**—About 4 or 5 per cent. of the total nitrogen is normally excreted as ammonium salts in the dog, but in the horse the proportion is much smaller. But under certain conditions the proportion is greatly increased. Anything which causes an increased breaking down of protein and an increased formation of acids in carnivora, leads to an increased excretion of ammonia—the ammonia being formed from the proteins to neutralise the acids.

2. **Diureides.**—The members of this series of bodies consist of two unmodified or modified urea molecules, linked together by an acid nucleus. The most important of the series have acrylic acid as the linking molecule, and they constitute the **purin bodies.**



In birds and reptiles they replace urea as the substances in which nitrogen is chiefly eliminated. In these animals they are formed in the liver from lactate of ammonia derived from proteins, but in mammals they appear to be very largely derived from the decomposition of nucleic acid. Even when all supplies from without of nucleins and purin bodies are cut off, a certain amount of these purin bodies is daily eliminated. These have been called the "endogenous" purins, while those derived from the constituents of the food are termed the "exogenous" purins. A certain amount of the purins formed are changed to urea before being excreted, and, therefore, when disturbances of the chemical processes in the liver occur, the purins appear to be increased at the expense of the urea.

Uric Acid is the most important member of the series in man, but in the dog, horse, and ox its amount is very small. Its constitution is shown on p. 416.

It is an exceedingly insoluble substance which tends to crystallise in large irregular crystals, and in the urine these are generally coloured brown by the urinary pigment. It occurs as salts of sodium and potassium.

From their insolubility, uric acid and the urates tend to form calculi or concretions in the urinary passages. The presence of uric acid in such concretions is recognised by the murexide test, which depends upon the fact that uric acid heated with nitric acid is oxidised to alloxantin, which strikes a purple colour with ammonia, yielding murexide—the ammonium salt of purpuric acid.

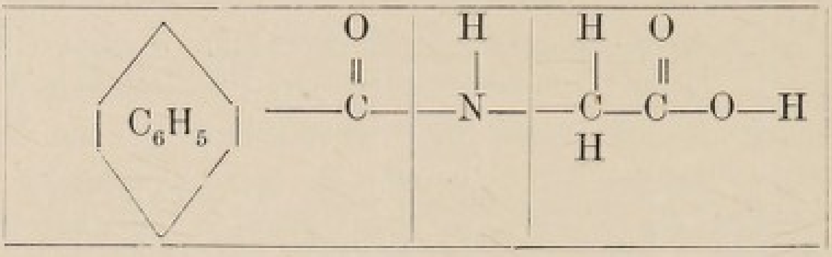
Other members of the series, such as **xanthin** and **hypoxanthin**, occur in the urine in small quantities.

Allantoin, which occurs in the urine of the fœtus, in the urine of cows, and possibly of other herbivora, and in the urine of dogs both before and after the administration of nucleic acid, is a diureide in which glyoxylic acid with two carbon atoms is the linking band.

3. **Creatinin.**—Creatinin is the form in which the creatin of muscle is excreted.

Creatin is methyl-guanidin-acetic acid (see p. 43). By dehydration creatinin is produced. The amount excreted is always small, and depends upon the amount of muscular tissue broken down in the body. According to the investigations of Folin the amount of creatinin excreted per diem on a flesh-free diet is very constant in each individual, and does not vary with the amount of protein food taken.

4. **Hippuric Acid.**—This is benz-amino-acetic acid—



It is formed from benzoic acid taken in the food by linking it to glycocoll—amino-acetic acid. This synthesis appears to take place in the kidneys, for it has been found that hippuric acid is not formed when these organs are excised, and that, when blood containing benzoates is circulated through them, hippuric acid is produced. Its chief interest is in the fact that it is one of the first organic compounds which were demonstrated to be formed synthetically in the animal body. Normally it is absent from the urine of carnivora, but in the urine of herbivora its amount is considerable. It is formed from the benzoic acid in the food, and it is therefore abundant upon a diet of grass or hay and smaller in amount when oats or beans are given.

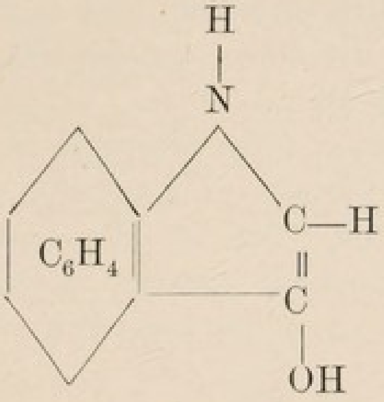
II. Sulphur-containing Bodies

The sulphur excreted in the urine is derived from the sulphur of the protein molecule, and the amount of sulphur excreted may be taken as a measure of the amount of protein decomposed. This is sometimes used as a check upon an estimation from the excretion of nitrogen.

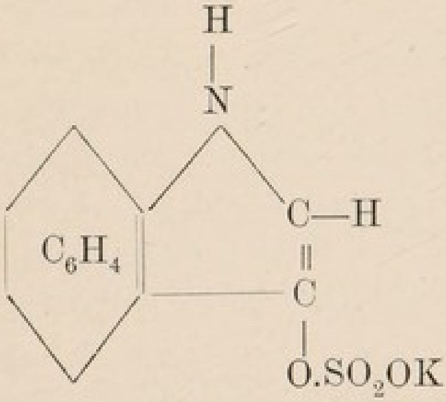
A. Acid Sulphur.—The greater part of the sulphur is fully oxidised to SO_3. (*a*) *Preformed Sulphates.* The greater quantity of this is linked with bases to form ordinary sulphates.

(*b*) A small quantity is in organic combination, linked to benzene compounds, *Ethereal Sulphates.* The **indol**, **skatol**, and **phenol** (see p. 372), formed by the putrefaction of proteins in the bowel or from the benzene compounds in the food of herbivora, being excreted in the urine in an oxidised form linked with sulphuric acid. Indol, as already shown, is related to amido-ethyl-benzene.

It is oxidised into indoxyl thus—



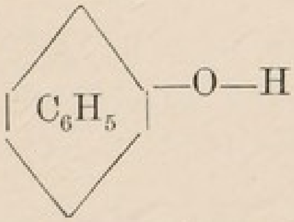
This when linked to sulphate of potassium forms **indoxyl-sulphate of potassium** or **indican.**



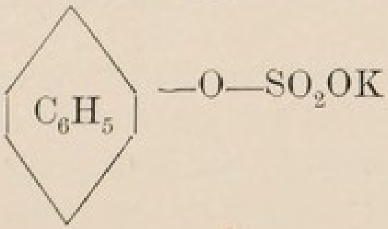
From skatol, which is methyl-indol, skatoxyl-sulphate of potassium is formed in the same way.

These bodies are colourless, but when oxidised they yield pigments—indican yielding indigo blue, skatoxyl-sulphate of potassium yielding a rose colour.

Phenol—



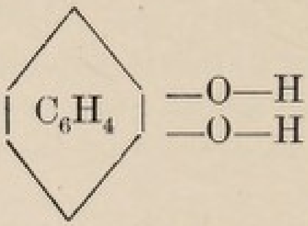
This is also linked to sulphate of potassium—



and excreted in the urine.

In carnivora their amount of these depends upon the activity of putrefaction in the intestine, and is a good index of its extent. In herbivora they are formed from the aromatic compounds in the food.

When **Dioxybenzene** or **Pyrocatechin** is formed in the body, it too is linked to sulphate of potassium and excreted. It is always present in the urine of the horse, and when urine containing this substance stands, it becomes oxidised and yields a greenish brown or black pigment.



B. Neutral Sulphur.—A small quantity of sulphur is excreted in a less oxidised state, in the form of *neutral sulphur.* In man the most important compound of this kind is *cystin,* the disulphide of amino-propionic acid, two molecules of amino-propionic acid linked by sulphur—

Amino-propionic acid.
|
Sulphur.
|
Sulphur.
|
Amino-propionic acid.

In some individuals and in certain conditions of the metabolism not yet fully understood, the amount of cystin is increased, and it then tends to crystallise out in peculiar hexagonal plates.

III. Phosphorus-containing Bodies

In herbivorous animals phosphates are practically absent from the urine. They are excreted from the mucous membrane of the bowel. Hence, in the horse, crystals of triple phosphates are found in the fæces, not in the urine.

In carnivores the phosphorus in the urine is derived partly from phosphates taken in the food, and partly from the nucleins of the food and tissues and from the bones.

(*a*) Normally the phosphorus is fully oxidised to P_2O_5, which is linked to alkalies and earths, and excreted in the urine. The most important phosphate is the phosphate of soda, NaH_2PO_4, which is the chief factor in causing the acidity of the urine. About *one quarter* of the phosphoric acid is linked to *calcium* and *magnesium*, and it is these earthy phosphates which precipitate when the urine becomes alkaline. When the urine becomes ammoniacal, triple phosphate is formed (p. 416).

(*b*) It is probable that a small quantity of the phosphorus is excreted in organic compounds, such as glycero-phosphates; but so far these have not been fully investigated.

IV. Chlorine-containing Bodies

Chloride of sodium is the chief salt of the urine. It is entirely derived from the salt taken in the food, and its amount varies with the amount ingested. In the horse it is present in very small quantities.

In starvation, and still more in fever, the tissues of the body have an extraordinary power of holding on to the chlorine, and the chlorides may almost disappear from the urine.

V. Bases of the Urine

Sodium, potassium, calcium, and magnesium occur in the urine in amounts varying with the amounts taken in the food. On a flesh diet and in starvation potassium is in excess of the others. Calcium and magnesium are present in much smaller quantities. In herbivora potassium is the chief salt, and in the horse calcium is also abundant.

VI. Pigments

A brown hygroscopic substance, which gives no bands in the spectrum, may be extracted from urine. This has been termed **urochrome.** By reducing this, another pigment, **urobilin**, is produced, which gives definite bands, and which is frequently present in the urine. It is probably identical with the hydrobilirubin which has been prepared from the bile pigments, and it contains C. H. O. and N.

The pigment which gives the pink colour to urates has been called **uroerythrin**, and its chemical nature is unknown.

Hæmatoporphyrin (see p. 213) is normally present in small traces in the urine, but in certain pathological states it is increased in amount and gives a brown colour to the urine.

VII. Nucleo-protein

A mucin-like nucleo-protein derived from the urinary passages is always present in small amounts, and forms a cloud when the urine stands.

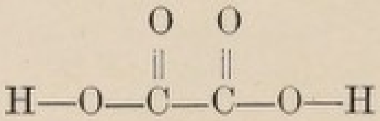
VIII. Carbonic and Oxalic Acids

1. **Carbonic Acid.**—Small amounts of this are present in urine of carnivores.

In herbivora it is present in large amounts, combined with potassium, lime, and magnesia, and also free. The carbonate of lime readily crystallises out in large dumb-bell-like crystals which may be confused with crystals of oxalate of lime, but which are quickly soluble, with effervescence, on the addition of an acid.

The differences between the urines of different herbivora are not important. The urine of the ox and cow is more abundant and more dilute than the urine of the horse, while the urine of the sheep is considerably more concentrated and contains a very high proportion of hippuric acid.

2. **Oxalic acid**



$$\mathrm{H{-}O{-}\overset{\overset{O}{\|}}{C}{-}\overset{\overset{O}{\|}}{C}{-}O{-}H}$$

is a substance in a stage of oxidation just above that of carbonic acid. It is frequently present in the urine linked with lime, and the lime salt tends to crystallise out in characteristic octohedra, looking like small square envelopes under the microscope. Under certain conditions these crystals assume other shapes. The oxalic acid of the urine is chiefly derived from oxalates in vegetable foods, but it has been detected in the urine of animals on a purely flesh diet.

SECRETION OF URINE

Structure of the Kidney

(*This must be studied practically.*) The kidney (fig. 168) is a compound tubular gland, consisting of innumerable tubules, each made up of—

(1) A closed extremity or Malpighian body (*M.B.*), consisting of an expansion at the end of the tubule—Bowman's capsule—into which a tuft of capillary vessels—the glomerulus—projects.

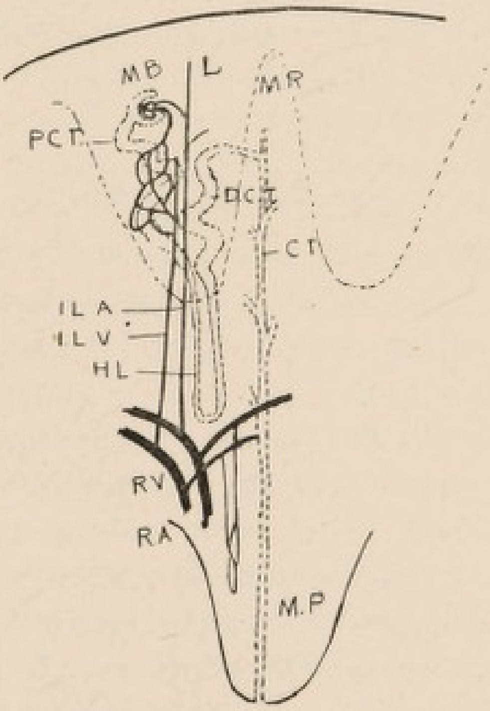


FIG. 168.—Diagram of the Structure of the Kidney. *M.P.*, Malpighian pyramid of the medulla ; *M.R.*, medullary ray extending into cortex ; *L.*, labyrinth of cortex ; *M.B.*, a Malpighian body consisting of the glomerular tuft and Bowman's capsule ; *P.C.T.*, a proximal convoluted tubule ; *H.L.*, Henle's loop on the tubule ; *D.C.T.*, distal convoluted tubule ; *C.T.*, collecting tubule ; *R.A.*, branch of renal artery, giving off *IL.A.*, interlobular artery, to supply the glomeruli and the convoluted tubules ; *IL.V.*, interlobular artery bringing blood back from the cortex.

(2) Extending away from this is a *proximal convoluted tubule* (*P.C.T.*) lined by pyramidal and granular epithelial cells. This dives into the medulla, becomes constricted and lined by a transparent flattened epithelium, and is known as the *descending limb* of the looped tubule of Henle. Turning suddenly upwards

and becoming lined by a cubical granular epithelium, it forms the *ascending limb*, and reaching the cortex expands into the *distal convoluted tubule*, which exactly resembles the proximal (*D.C.T.*). It opens into a *collecting tubule* (*C.T.*) lined by a low transparent epithelium, which conducts the urine to the pelvis of the kidney.

The renal artery breaks up and gives off a series of straight branches—the interlobular arteries (*IL.A.*)—which, as they run towards the surface, give off short side branches which terminate in the glomeruli. The efferent vein passing from these breaks up again into a series of capillaries between the convoluted tubules, and these pour their blood into the interlobular veins (*IL.V.*). This arrangement helps to maintain a high pressure in the capillary loops of the glomerular tuft.

Physiology of Secretion

The marked difference in the structure and vascular supply of the Malpighian bodies and of the different parts of the renal tubules make it probable that they perform different functions.

Malpighian Bodies.—(*a*) It has been shown by injecting into the blood vessels acid fuchsin, which is colourless in alkaline solution and red in acid solution, that the urine formed in these bodies is alkaline in reaction and that it becomes acid as it passes down the convoluted tubules.

(*b*) It is also known that these bodies are thrown out of action by decreasing the flow of blood through the kidneys. The rate of flow of blood depends upon the blood pressure in the renal arteries and the dilatation of the renal arterioles. It may be measured by measuring the amount of blood passing out by the renal vein or by enclosing the kidney in an oncometer—a closed vessel connected with a recording tambour—so that changes in the volume of the kidney are recorded (see p. 249), or by a combination of these methods.

Section of the renal nerves derived from the 11th, 12th, and 13th dorsal nerves causes a dilatation of the renal arterioles, an expansion of the kidney, and an increased flow of urine. Stimulation of these nerves has the opposite effect. A fall in the general arterial pressure to about 50 mm. Hg in the dog generally causes a decreased flow of blood through the kidney and practically stops the flow of urine, although the tubules, as will be presently shown, still act.

(*c*) In the frog the renal arteries supply the Malpighian bodies, while portal veins from the posterior end of the animal supply the convoluted tubules. Ligature of the renal arteries stops the flow of urine, but the flow may be again induced when urea is injected.

(*d*) Even when this flow is induced, if dextrose or egg albumin or peptone are injected into the blood, substances which in the normal frog appear in the urine, they are not excreted.

These observations seem to show that the Malpighian bodies have to do chiefly with the excretion of water and of certain abnormal constituents of the blood, and that their activity depends upon the rate of blood-flow through them. That it is not due to a mere physical filtration under pressure is indicated by experiments, in which the blood pressure in the kidneys of a dog was raised by injecting large quantities of blood from another dog, without the flow of urine being increased. That it is a selective action of the epithelium seems to be proved by the passage into the urine of such large molecules as those of egg albumin and hæmoglobin and of various pigments such as carmine.

The fact that, if a cannula connected with a manometer be placed in the ureter, the secretion of urine stops when a pressure of about 50 mm. Hg is reached, is not opposed to the view that the formation of urine from the glomeruli is an active secretion. In the salivary gland, where the formation of saliva is undoubtedly due to the vital action of the cells, the same result follows obstruction of the duct.

The point of practical importance is that *the secretion of water takes place chiefly through the Malpighian bodies*, and that this is reduced or stopped by a fall in the general arterial pressure, such as occurs in heart failure. The decreased excretion of water may lead to the development of dropsy.

The Tubules.—The alkaline urine formed in the Malpighian bodies undergoes changes as it passes along the tubules. It becomes acid and the various solids are increased, for urine contains a higher proportion of these than does the blood, *e.g.* the blood contains only about 0·03 per cent. of urea, but the urine usually contains 2 per cent. The addition of solids in the tubules is further proved by the following facts:—

(*a*) Uric acid crystals are frequently found in the cells of the convoluted tubules of the kidney of birds. (*b*) Heidenhain, by injecting a blue pigment—sulph-indigotate of soda—into the circulation of the rabbit, demonstrated that the cells of the convoluted tubules take it up and pass it into the urine. In the normal rabbit the whole of the kidney and the urine become blue. But, if the formation of urine in the Malpighian bodies be stopped by cutting the spinal cord in the neck so as to lower the blood pressure, then the blue pigment is found in the cells of the convoluted tubules and of the ascending limb of Henle's tubule. (*c*) When the Malpighian bodies of the frog have been thrown out of action by ligaturing the renal arteries, the injection of urea still causes a flow of urine and the excretion of urea by the tubules. When the portal veins which supply the tubules were ligatured on one side, it was found that less urine was formed on the ligatured than on the unligatured side.

These last experiments show that the cells of the convoluted tubules are capable of secreting **water** as well as solids, and that they can do so is further demonstrated by the fact that, if by cutting the spinal cord in the neck the formation of urine in the Malpighian bodies of a dog is stopped, the administration of caffeine and of some other substances causes an increased flow of urine, although the blood pressure in the kidneys is not raised. This is taken advantage of in cases of heart disease, when the secretion of urine is almost arrested from low arterial pressure, and when dropsy is rapidly advancing. Until the heart is toned up, the kidneys may be stimulated to get rid of water by means of such diuretics as caffeine.

It is quite possible that under certain conditions the cells of the renal tubules absorb water and possibly the other constituents of the urine, but the weight of the evidence we at present possess is against the idea that they exercise the function to any great extent.

EXCRETION OF URINE

1. **Passage from Kidney to Bladder.**—The pressure under which the urine is secreted is sufficient to drive it along the ureters to the bladder. If these are constricted the pressure behind the constriction rises, and may distend the ureters and the pelvis of the kidney, but when it reaches about 50 mm. Hg in the dog, the secretion of urine is stopped. The muscular walls of the ureters show a rhythmic peristaltic contraction, which must also help the onward passage of the urine to the bladder.

2. **Micturition.**—As the urine accumulates in the urinary bladder the rhythmic contraction of the non-striped muscle becomes more and more powerful. These contractions are chiefly excited by the fibres of the nervi erigentes of the second and third sacral nerves, although fibres passing down from the inferior mesenteric ganglion also probably act either in exciting or inhibiting them in certain animals. The backward passage of the urine into the ureters is prevented by the oblique manner in which these tubes pass through the muscular coat of the bladder.

The passage of urine into the urethra is at first prevented either by the oblique manner in which the urethra leaves the bladder, or more probably by the contraction of a strong band of non-striped muscle, the *sphincter trigonalis.* This muscle or the striped fibres which surround the membranous part of the urethra are under the control of a centre in the lumbar enlargement of the spinal cord, and the expulsion of urine must be preceded by their relaxation. In some cases of inflammation of the spinal cord the increased activity of the centre may prevent the expulsion of urine, while later in the disease, when the nerve structures have been destroyed, the urine is not retained and dribbles away on account of the absence of the tonic contraction of the muscles.

The expulsion of the last drops of urine is carried out by the rhythmic contraction of the bulbo-cavernous muscle, while the peristaltic contraction of the bladder wall is assisted by the various muscles which press upon the contents of the abdomen and of the bladder.

In man, in early life, micturition is a purely reflex act, and in the dog it is perfectly performed when the spinal cord is cut in the back. As age advances the reflex mechanism comes to be more under the control of the higher centres, and the activity of the sphincters may be increased or abolished as circumstances indicate.

3. EXCRETION BY THE SKIN

The skin is really a group of organs, and some of these have been already studied. (*The structure of the skin and its appendages must be studied practically.*)

(1) The **Protective** functions of the horny layer of epidermis, with its development in hair and nail, and of the layer of subcutaneous fat, are manifest.

Hair.—Attached to each hair follicle is a band of non-striped muscle, the *arrector pili,* which can erect the hair by contracting. These muscles are under the control of the central nervous system, and the nerve fibres have been demonstrated in the cat to take much the same course as the vaso-constrictor fibres of somatic nerves (see p. 280). A hair after a time ceases to grow, and the lower part in the follicle is absorbed and the hair is readily detached. From the cells in the upper part of the follicle a new down-growth occurs, a papilla forms, and the hair is regenerated. In many of the lower animals this process occurs twice a year.

(2) The **Sensory** functions have been studied under the Special Senses.

(3) The **Respiratory** action of the skin in mammals is of little importance.

(4) **The Excretory Function of the Skin.**—Three sets of glands develop in the skin—sweat glands and sebaceous glands, which are common to both sexes and are constantly active—and mammary glands, which are active in the female during the period of suckling.

A. Sweat Secretion—1. **Structure.**—The sweat glands are simple tubular glands coiled up in the subcutaneous tissue with ducts opening on the surface of the skin. The secreting epithelium somewhat resembles that of the convoluted tubules of the kidney. It has been calculated that a man possesses about two and a half million sweat glands, and that if spread out they would present a surface of very great extent.

2. **Functions.**—From these glands a considerable amount of sweat is poured out; but to form any estimate of the daily amount is no easy matter, since it varies so greatly under different conditions. Probably about 1000 c.cm. is an average amount. When poured out, sweat usually evaporates, and is then called *insensible perspiration*, but when large quantities are formed, or when, from coldness of the surface, or of the air, or from the large quantity of watery vapour already in the air, evaporation is prevented, it accumulates, and is called *sensible perspiration*.

A free secretion of sweat is usually accompanied by a dilatation of the blood vessels of the skin, but this may be absent, and it may occur without any sweat secretion—*e.g.* under the influence of atropine.

3. **Nervous Mechanism of Sweat Secretion.**—The sweat glands are under the control of the central nervous system. This may be very conveniently studied in the cat, in which animal the sweat glands are chiefly in the pads of the feet. If a cat be put in a hot chamber it sweats on the pads of all its feet. But if one sciatic nerve be cut the foot supplied remains dry. If the cat be placed in a warm place and the lower end of the cut sciatic stimulated, a secretion of sweat is produced. These sweat-secreting fibres all pass through the sympathetic ganglia, and back into the spinal nerves. Those to the hind leg come from the upper lumbar region, those for the forelimb from the lower cervical nerves, and those for the head in the sympathetic of the neck and partly in the fifth cranial nerve.

The centres presiding over these nerves are distributed down the medulla and cord. They are capable of (*a*) reflex stimulation, as when pepper is taken into the mouth; and (*b*) of direct stimulation by a venous condition of the blood, as in the impaired oxygenation of the blood which so frequently precedes death as the respirations fail.

But even after the nerves to the sweat glands are cut, the glands can be stimulated by certain drugs—*e.g.* pilocarpine. The action of heat seems also to be chiefly peripheral, setting up an unstable condition of the gland cells so that they respond more readily to stimulation.

4. **Chemistry of Sweat.**—Sweat from the horse is a sherry-coloured fluid, which, when pure, has a neutral or faintly alkaline reaction. Its specific gravity is about 1020 in the horse, and it contains about 5·5 per cent. of solids, of which 5 per cent. are inorganic and about 0·5 organic. Potassium is the most abundant base. Chlorides are present in small amounts. The chief organic substances present are proteins —some globulin and some albumin. Fat is also present, probably derived from the sebaceous secretions, and it combines with the potassium to form a soap.

B. Sebaceous Secretion.—The sebaceous glands are simple racemose glands which open into the hair follicles, and their function is to supply an oily material to lubricate the hairs. This secretion is produced by the shedding and breaking down of the cells formed in the follicles of the glands. Those lining the basement membrane are in a condition of active division, but the cells thrown off into the lumen of the follicle disintegrate and become converted into a semi-solid oily mass, which consists of free fatty acids and of neutral fats of glycerine and of cholesterin. These cholesterin fats are the *lanolins*, which differ from ordinary fats in being partly soluble in water. Free cholesterin is also present in the sebum.

C. Milk Secretion—1. Physiology.—Before pregnancy occurs the mammary glands are largely composed of fibrous tissue, with a large amount of fat, in which run the branching tubules of the glands as small solid blocks of cells.

As pregnancy advances these tubules grow outwards and increase, and the cells begin to divide, some remaining attached to the basement membrane, some coming to lie in the middle of the tubules. These latter undergo a fatty change and break down, and they are shed in the first milk which is secreted, the **colostrum**. The cells left upon the basement membrane elaborate the constituents of milk, and the presence of fat globules in their protoplasm is very manifest.

The milk, after being secreted, collects in the ducts of the glands and in the sinus below the nipple, and is expelled from these by the contraction of the muscular fibres in their walls, and by the suction of the young animal. The *excretion* of milk from the ducts is directly under the control of the nervous system, but the evidence as to the way in which the central nervous system influences the *secretion* of milk is by no means satisfactory. Clinical experience shows that it is profoundly modified by nervous changes, but so far stimulation of the nerves to the glands has not yielded definite results.

The chemistry of milk is considered upon p. 332, and the way in which fats and proteins are formed is dealt with on p. 385. The production of the disaccharid, lactose, and of the phospho-protein, caseinogen, implies a synthetic process in the protoplasm of the cells of the mammary glands.

The comparative composition of the milk of the cow, mare, and sheep is given below:—

	Cow.	Mare.	Sheep.
Water . . .	88	91 to 93	87
Protein . . .	3	1 to 2	4 to 5
Fats	3 to 4	1 to 1·5	4 to 5
Sugar. . . .	4 to 5	4 to 6	3 to 4
Salts	0·7	0·3	0·6

PART III

SECTION IX

REPRODUCTION

So far the animal has been studied simply as an individual. But it has also to be regarded as part of a species, as an entity which has not only to lead its own life, but to transmit that life to offspring.

The various problems of reproduction have been already studied by the student in connection with biology, and it is here sufficient to indicate some of the main points in the physiology of the process in mammals.

(*The structure of the organs of reproduction must be studied practically.*)

While the individual is actively growing, the reproductive organs are quiescent; but when *puberty* is reached, they begin to perform their functions—the testes to produce **spermatozoa**, the ovaries to produce mature **ova**.

The removal of the sexual organs in the young animal leads to arrest in the development of the special sexual characters, especially in the male, in which these characters are generally best marked. Simple ligature of the *vasa deferentia* has not this effect, although the tubules of the testes do not develop, and it therefore seems that the interstitial cells of the organs produce a hormone which causes the development of the sex characteristics.

The genital gland in both sexes is formed from a longitudinal thickening or ridge at the posterior part of the cœlom or peritoneal cavity. Over this ridge the endothelium thickens and becomes epithelial-like in structure. Groups of cells grow down into the tissue below.

In the **ovary** one of these cells in a group takes a central position and forms the ovum, while the other cells get arranged around it to form the zona granulosa, the whole group constituting a Graafian follicle.

In the **testis** the groups of cells form seminiferous tubules, in which the spermatozoa or male elements are developed.

Ovary.—In the adult the ovaries are oval structures covered by a columnar *germinal epithelium.* In the stroma are seen Graafian follicles in different stages of development. The central cell, the ovum, enlarges. The nucleus becomes prominent, and the nucleolus is also large. The protoplasm becomes encased in a transparent capsule—the *zona pellucida.* The cells of the *zona granulosa* multiply, and fluid, the *liquor folliculi*, appears among them, dividing them into a set attached to the capsule of the follicle and a set surrounding the ovum. When the follicle is ripe it projects on the surface of the ovary, and finally bursts, setting free the ovum into the peritoneal cavity. The ovum escapes into the peritoneal cavity and passes into the trumpet-shaped fimbriated upper end of the *Fallopian tube*, through which it reaches the uterus.

Testis.—In the adult this is enclosed in a dense fibrous capsule—the *tunica albuginea.* Posteriorly this is thickened, and forms the *corpus Highmori.* From this processes extend and form a supporting framework. In the spaces are situated the *seminiferous tubules*, which open into irregular spaces in the corpus Highmori—the *rete testis*, from which the efferent ducts, *vasa efferentia*, pass away and join together to form the *vas deferens.*

In the seminiferous tubules the spermatozoa are produced. Some of the lining cells divide into two, each forming a *supporting cell* and a *spermatogen.* The latter divides and subdivides till a group of cells lie on the top of the supporting cell. These are the *spermatoblasts.* In each spermatoblast the nucleus elongates and passes to the attached extremity, the protoplasm decreases in amount, and a long cilium develops from the free end, and the *spermatozoon* is thus produced.

Semen.—When the testes have become active, the glands of the prostate increase and produce a fluid which, with the spermatozoa, forms the semen.

The Œstrous Cycle.—In carnivora and herbivora alike, the adult female has cycles of sexual activity, the œstrous cycles, which are accompanied by changes in the genital organs. The cycle may be divided into three periods: (1) The *anœstrous* stage, during which the genital organs are at rest, the uterus and Fallopian tubes small, and the formation of Graafian follicles in the ovary quiescent; (2) the *proœstrous* stage, during which there is a rapid ripening of one or more Graafian follicles and a congestion and swelling of the Fallopian tubes and uterus, with sometimes hæmorrhages into the uterine mucous membrane; (3) the *œstrous* stage, during which coition is performed, and during which the Graafian follicle ruptures and sheds the ovum (ovulation). This in some animals—*e.g.* ferrets—occurs as the result of coition; in others—horse, cow, etc.—independently of it. Sometimes the ovum is not shed, and then it and the rest of the Graafian follicle atrophy.

Impregnation is effected by the transmission of spermatozoa into the genital tract of the female. For this purpose **erection** of the penis is brought about reflexly through a centre in the lumbar enlargement of the cord, the outgoing nerves being the nervi erigentes, which dilate the arterioles, and the internal pudics supplying the transversus perinei and bulbo-cavernous muscles by which the veins of the penis are constricted.

The semen is ejected by a rhythmic contraction of the bulbo-cavernous and other perineal muscles, an action which is also presided over by a centre in the lumbar region of the cord (p. 160).

The spermatozoon meets the ovum in the Fallopian tube or upper part of the uterus.

DEVELOPMENT

1. Early Stage

It is unnecessary here to describe the changes in the ovum before or immediately after its conjugation with the spermatozoon, since they are so fully dealt with in all works on biology.

The mammalian ovum is holoblastic, that is, undergoes complete segmentation, and forms a mulberry-like mass of cells (fig. 163, *A.*). The cells then get disposed in two sets, a layer of small surrounding cells and a set of large central cells (fig. 169, *B.*). The former constitute the Ectoderm and take part in forming the processes or primitive villi by which the ovum becomes attached to the maternal mucous membrane.

The latter spread out at one pole to form the *blastoderm* (fig. 170, *A*) and dispose themselves in three layers—the epiblast,

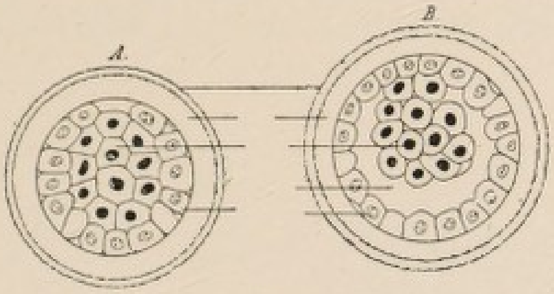


FIG. 169.—Ovum after segmentation, showing the formation of the Ectoderm (*a*) and Endoderm (*b*). From the cells of the latter the Blastoderm is formed. (ELLENBERGER.)

mesoblast, and hypoblast (fig. 170, *B* and *C*). From these layers the various parts of the body are derived as follows:—

I. *Epiblast.*—Nervous system, epidermis and appendages. Epithelium of the mouth, nose, naso-pharynx, and all cavities and glands opening into them, and the enamel of teeth.

II. *Hypoblast.*—Epithelia (*a*) of the alimentary canal from the back of the mouth to the anus and of all its glands; (*b*) of the Eustachian tube and tympanum; (*c*) of the trachea and lungs; (*d*) of the thyroid and thymus; and (*e*) of the urinary bladder and urethra.

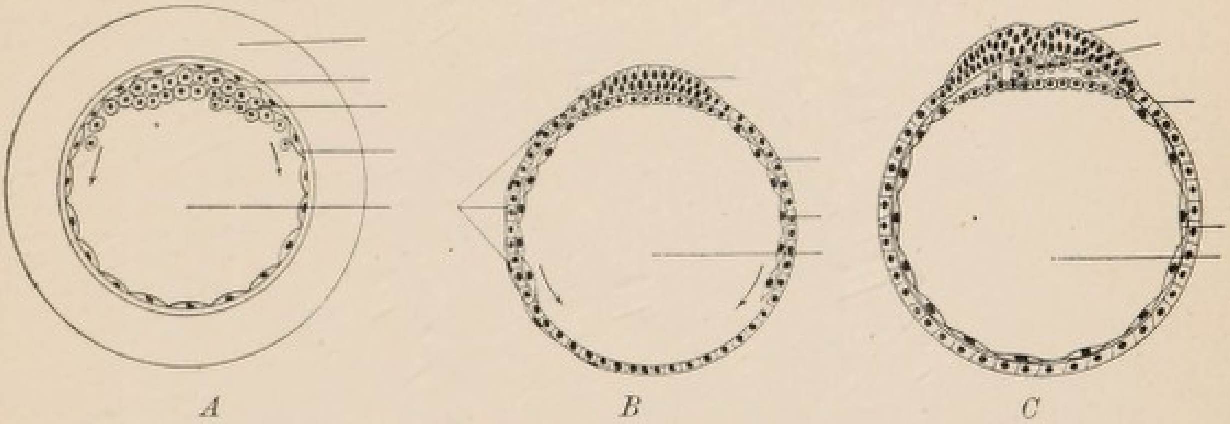


FIG. 170.—To show *A*, the spreading out of the Endoderm cells to form the Blastoderm; *B*, the formation of Epiblast and Hypoblast; and *C*, of Mesoblast. In *B* and *C* the ectoderm is not seen. (ELLENBERGER.)

III. *Mesoblast.*—All other structures.

By the formation of a vertical groove down the back of the blastoderm, a tube of epiblast cells (the neural canal) is enclosed, from which the nervous system develops by the conversion of some of the cells into neurons, and others into neuroglia cells (fig. 171).

The mesoblast on each side of this splits, and the outer part, with the epiblast, goes to form the body wall (Somatopleur), while the inner part with the hypoblast gets tucked in to produce the alimentary canal (Splanchnopleur) (fig. 171).

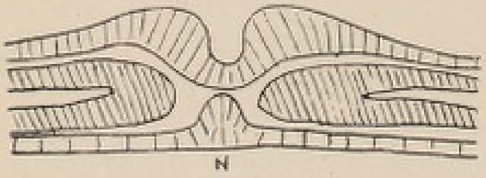


Fig. 171.—Transverse section of more advanced Blastoderm, to show Epiblast, Mesoblast, and Hypoblast, formation of Neural Groove and splitting of the Mesoblast.

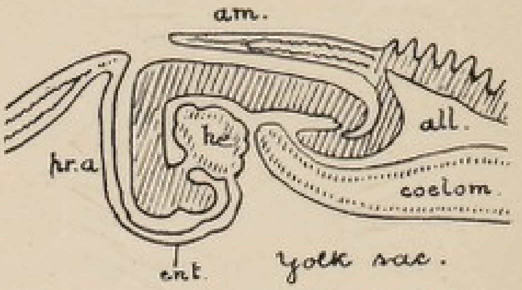


Fig. 172. — Longitudinal Section through Embryo to show it sinking down into ovum and the formation of the amnion, *am.* In the Mesoblast round, *all.*, the allantois, the blood vessels grow out to form the placenta.

The developing embryo sinks into the ovum, and, as a result of this, the somatopleur folds over it and, uniting above, encloses it in a sac—the **amniotic sac** (fig. 172, *am.*), which becomes distended with fluid—the **amniotic fluid**, in which the embryo floats during the later stages of its development, and which acts as a most efficient protection against external violence.

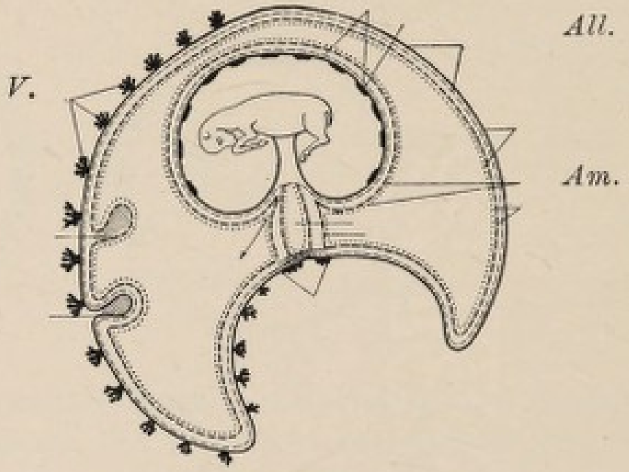


Fig. 173.—Schematic section through the pregnant uterus of the Mare to show the large allantoic sac, *All.*, filled with fluid surrounding the amniotic sac; *Am.*, the fluid in which the fœtus floats.

In the pig, horse and in ruminants, the connection of the fœtal blood vessels with the maternal structures is not very intimate, and when the young are born the fœtal part of the placenta separates from the maternal part, which is thus not shed. Hence such animals are called non-deciduata.

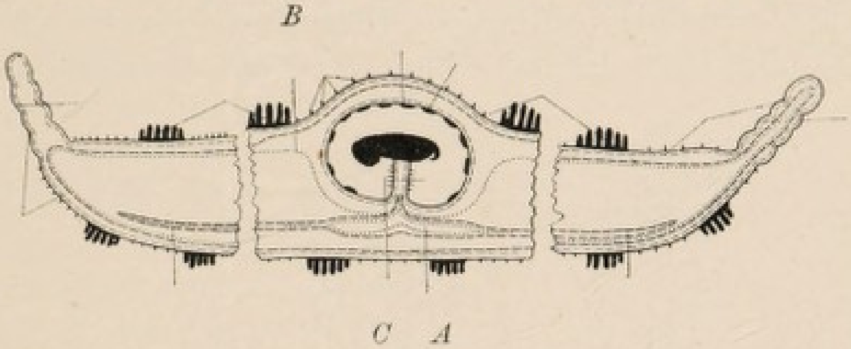


Fig. 174.—Schematic section of one cornu of the uterus of a ruminant at an early stage of gestation to show the elongated umbilical vesicle, *A*, and allantois, *B*, and the embryo in the amniotic sac, *C*.

In Rodents, Insectivora, Apes, Man and Carnivora, the association is so intimate that at birth the maternal part of the placenta is shed along with the fœtal. Hence these are called Deciduata.

2. Attachment to the Mother

The ovum gets enclosed in the uterine mucous membrane, which grows round it as the **decidua reflexa** (fig. 175, *D.R.*).

Almost as soon as the ovum is embedded in the maternal mucous membrane, it becomes surrounded by a nucleated mass of protoplasm—the **trophoblast**, formed of the cells of the ectoderm, and this probably transfers nourishment from the mother to the ovum. Very early the mesoblast of the embryo extends out in a number of finger-like processes into the trophoblast layer, and soon afterwards blood vessels shoot into these, and the **chorionic villi** are formed (fig. 176). The precise origin of the first blood vessels in these is not known, but ultimately they are derived from the **allantoic arteries** which pass out from near the posterior end of the hind gut. As the villi grow, the blood vessels in the maternal mucosa (fig. 175, *D.S.*) dilate, and the capillaries form large sinuses or blood spaces. Into these the chorionic villi pass, and thus the loops of fœtal vessels hang free in the maternal blood, and an exchange of material is possible between the mother and fœtus. This development goes on specially at one or more parts of the surface of the ovum, and the **Placenta** is thus formed. This acts as the fœtal lung, giving the embryo the necessary oxygen and getting rid of the waste carbon dioxide. It is the fœtal alimentary canal supplying the necessary material for growth and development; and it is the fœtal kidney through which the waste nitrogenous constituents are thrown off.

In the mesoblast, through which the allantoic arteries pass out, a vesicle filled with fluid, and at first communicating with the posterior gut, is developed (figs. 172, *all.*, 173 and 174). This is the **allantois**. In man it never attains any size, but in many of the lower animals it spreads all round and encloses the amnion.

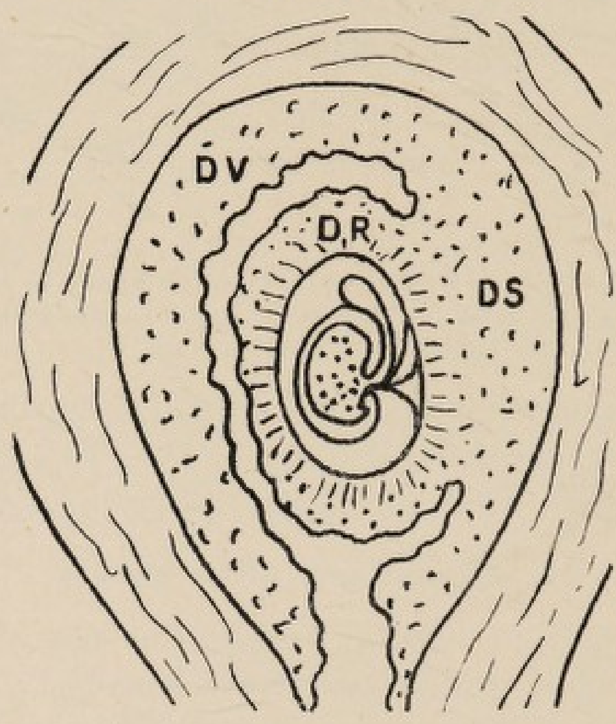


FIG. 175.—Longitudinal Section through the human uterus and ovum at the fifth week of pregnancy. *D.S.*, decidua serotina, which will become the placenta; *D.R.*, decidua reflexa; *D.V.*, the uterine mucous membrane called the decidua vera.

3. Fœtal Circulation

The performance of these functions by the placenta is associated with a course of circulation of the blood somewhat different to that in the post-natal state (fig. 177).

The blood coming from the placenta to the fœtus is collected into a single **umbilical vein**, *u.v.*, which passes to the liver, *l.* This divides into the **ductus venosus**, *d.v.*, passing straight through the organ, and into a series of capillaries among the cells. From these the blood flows away in the hepatic vein to the **inferior vena cava**, *p.v.c.*, which carries it to the right auricle. In this it is directed by a fold of endocardium, through the **foramen ovale**, *f.o.*, a hole in the septum between the auricles, and it thus passes to the left auricle, and thence to the left ventricle, *l.v.*, which drives it into the aorta, *a.a.*, and chiefly up to the head, *ant.a.* From the head the blood returns to the **superior vena cava**, *a.v.c.*, and, passing through the right auricle, enters the right ventricle, *r.v.*, which drives it into the pulmonary artery, *p.a.* Before birth this artery opens into the aorta by the **ductus arteriosus**, *d.a.*, while the branches to the lungs are still very small and unexpanded. In the aorta, this impure blood from the head mixes with the purer blood from the left ventricle, and the mixture is sent to the lower part of the body through the descending aorta, *po.a.* From each iliac artery, *i.a.*, an umbilical artery, *u.a.*, passes off, and these two vessels carry the blood in the umbilical cord, *u.c.*, to the placenta.

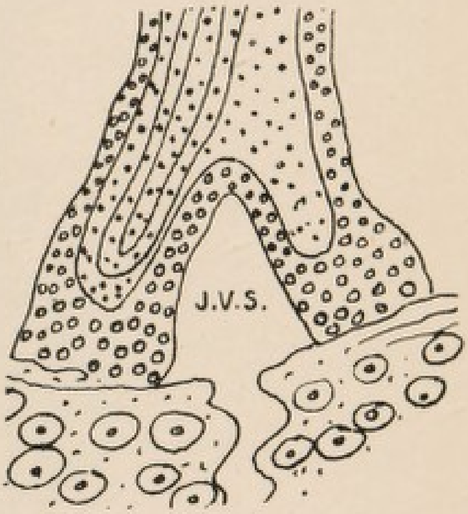


FIG. 176.—Longitudinal Section through the tip of a villus of the human placenta, covered by its trophoblast layer, and containing a loop of blood vessels, and projecting into a large blood sinus, *J.V.S.* in the maternal mucosa.

When the fœtus is born in the deciduata, the placenta is pressed upon by the contraction of the uterus, and the flow of blood between child and mother is arrested. As a result of this the respiratory centre is no longer supplied with pure blood and is stimulated to action. The lungs expand and the blood flows through them. In the non-deciduata the same result is brought about by the separation of the fœtal from the maternal placenta. In the **ductus venosus** a clot forms and the vessel becomes obliterated. The **ductus arteriosus** also closes up, and the **foramen ovale** is occluded. The circulation now takes the normal course in post-natal life.

Our knowledge of the differences between the physiological processes in intra-uterine and in extra-uterine life is still very imperfect, and the subject cannot be further discussed here.

4. Gestation and Delivery

The child remains in the uterus for nine months, and at the end of that period it is expelled during labour. **Labour** may be divided into three stages. In the first stage the uterus passes into contractions at intervals, and the lower part or cervix is dilated. In the second stage the contractions become stronger, and with the help of the contractions of the abdominal muscles, the young are expelled through the vagina either enclosed in

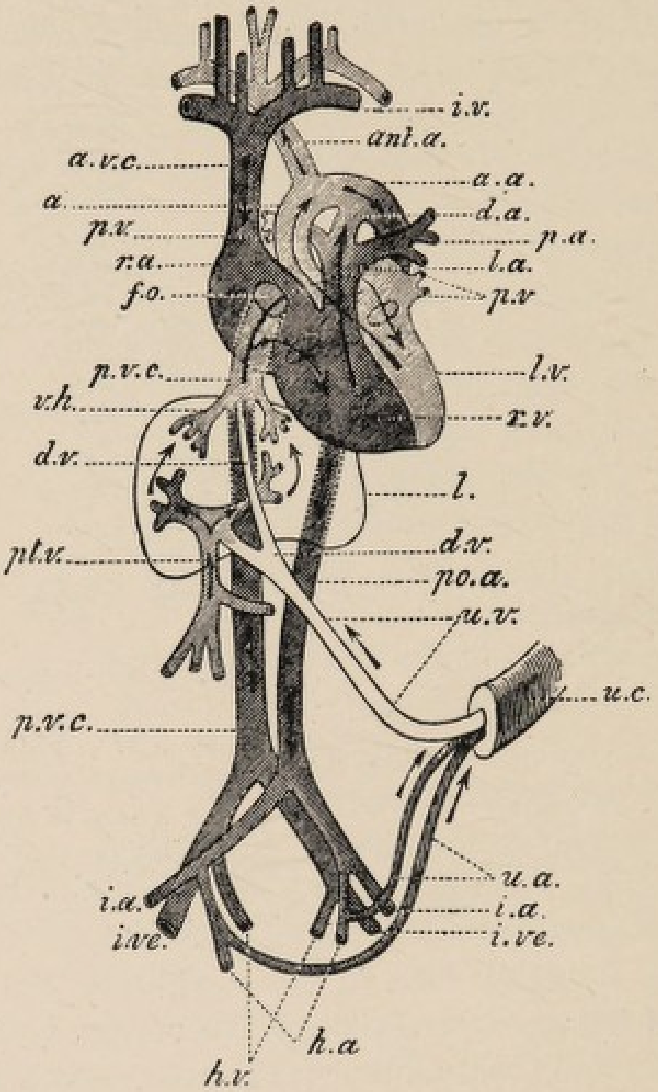


FIG. 177.—Scheme of Circulation in the Fœtus. *u.v.*, umbilical vein; *d.v.*, ductus venosus; *p.v.c.*, inferior vena cava pouring blood through the right auricle and through the foramen ovale, *f.o.*, into the left heart; *a.v.c.*, superior vena cava bringing blood from the head to pass through the right side of the heart, and through the ductus arteriosus, *d.a.*; *pt.v.*, portal vein. The degree of impurity of the blood is indicated by the depth of shading.

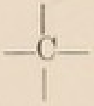
the membranes or in the deciduata free of the membranes. In the deciduata, the uterus is usually quiescent for a short time, and then contractions supervene, and the placenta and lining of the uterus are expelled as the *after-birth*. These uterine contractions are presided over by a nerve-centre in the lumbar enlargement of the cord, and in all probability the nervi erigentes play an important part in their production.

APPENDIX

SOME ELEMENTARY FACTS OF ORGANIC CHEMISTRY

THE following elementary facts may help the student who has neglected the study of the outlines of Organic Chemistry in understanding the chemical problems of physiology.

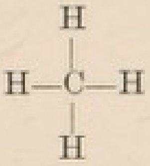
Organic compounds are built round the four-handed carbon atom



$$\begin{array}{c} | \\ -C- \\ | \end{array}$$

When each hand links to the one-handed hydrogen atom,

METHANE—

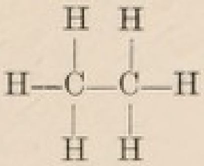


$$\begin{array}{c} H \\ | \\ H-C-H \\ | \\ H \end{array}$$

is formed.

By taking away a hydrogen atom from two Methane molecules and linking these molecules together

ETHANE—



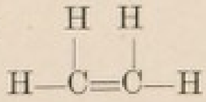
$$\begin{array}{c} H\ \ H \\ |\ \ \ | \\ H-C-C-H \\ |\ \ \ | \\ H\ \ H \end{array}$$

is produced.

By further linking more and more of these molecules together, similar molecules containing three, four, five or more carbon atoms are produced.

When each carbon has its due proportion of hydrogen atoms it is *saturated*, but if two hydrogen atoms are let go, the unoccupied hands of the carbon may join and form an *unsaturated* molecule, thus :—

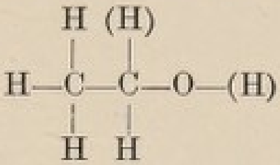
Ethane becomes Ethylene



$$\begin{array}{c} H\ \ H \\ |\ \ \ | \\ H-C=C-H \end{array}$$

When one hydrogen atom is taken away and the molecule has a hand ready to link with some other substance a *radical* is constituted, and these are known as METHYL, ETHYL, etc.

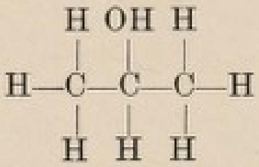
Alcohols.—When the two-handed oxygen atom,—O—linked to hydrogen H—and thus forming the hydroxyl molecule—OH is linked to the vacant hand of the radical, an alcohol is formed, *e.g.*—



$$\begin{array}{ccccccc} & & H & & (H) & & \\ & & | & & | & & \\ H & - & C & - & C & - & O-(H) \\ & & | & & | & & \\ & & H & & H & & \end{array}$$

Ethyl Alcohol.

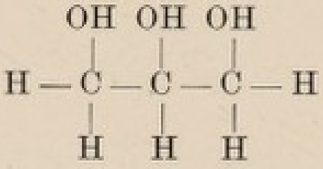
When the terminal carbon is thus oxidised a *Primary Alcohol* is formed—but if a middle carbon atom is oxidised, a *Secondary Alcohol* is produced—



$$\begin{array}{ccccccccc} & & H & & OH & & H & & \\ & & | & & | & & | & & \\ H & - & C & - & C & - & C & - & H \\ & & | & & | & & | & & \\ & & H & & H & & H & & \end{array}$$

Secondary Propyl Alcohol.

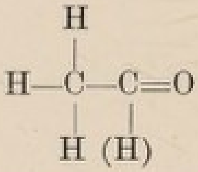
But the oxidation may involve more than one carbon atom and thus the *Polyvalent Alcohols* are produced—



$$\begin{array}{ccccccccc} & & OH & & OH & & OH & & \\ & & | & & | & & | & & \\ H & - & C & - & C & - & C & - & H \\ & & | & & | & & | & & \\ & & H & & H & & H & & \end{array}$$

Glycerin.

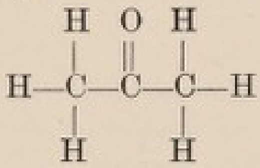
Aldehydes or **Aldoses.**—When, from a Primary Alcohol the two hydrogens marked above in brackets are removed, the vacant hand of the oxygen links to the vacant hand of the carbon to form an Aldehyde or Aldose—



$$\begin{array}{ccccccc} & & H & & & & \\ & & | & & & & \\ H & - & C & - & C & = & O \\ & & | & & | & & \\ & & H & & (H) & & \end{array}$$

Ethyl Aldehyde.

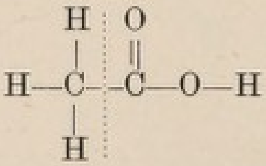
Ketones or **Ketoses.**—These are formed in the same way from the Secondary Alcohols, thus:—



$$\begin{array}{ccccccccc} & & H & & O & & H & & \\ & & | & & \| & & | & & \\ H & - & C & - & C & - & C & - & H \\ & & | & & & & | & & \\ & & H & & & & H & & \end{array}$$

Acetone, the Ketose of Secondary Propyl Alcohol.

Acids.—If the hydrogen of the Aldehyde marked in brackets is replaced by hydroxyl—OH, an acid is produced—

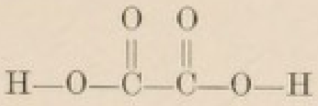


$$\begin{array}{cccccccc} & & H & \vdots & O & & & \\ & & | & \vdots & \| & & & \\ H & - & C & \vdots & C & - & O & -H \\ & & | & \vdots & & & & \\ & & H & \vdots & & & & \end{array}$$

Acetic acid.

The *carboxyl* group to the right of the dotted line is characteristic of the acids.

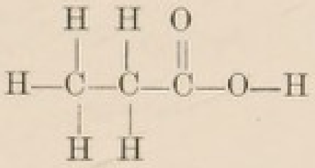
The oxidation may be carried on at each end of the line and the *divalent acids* are thus produced



$$H-O-\overset{\overset{O}{\|}}{C}-\overset{\overset{O}{\|}}{C}-O-H$$

Oxalic acid.

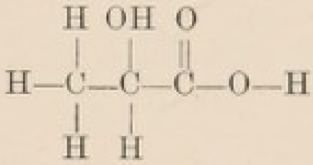
If in the radical of one of these acids a hydrogen is replaced by hydroxyl —OH, an *oxy-acid* is formed, thus :—



$$H-\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}-\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}-\overset{\overset{O}{\|}}{C}-O-H$$

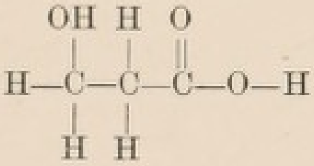
Propionic acid.

may be converted to the two Lactic acids called (α) and (β) oxy-propionic acid, according to the carbon which is oxidised



$$H-\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}-\underset{\underset{H}{|}}{\overset{\overset{OH}{|}}{C}}-\overset{\overset{O}{\|}}{C}-O-H$$

and

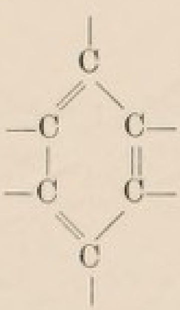


$$H-\underset{\underset{H}{|}}{\overset{\overset{OH}{|}}{C}}-\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}-\overset{\overset{O}{\|}}{C}-O-H$$

Similar oxy-acids are formed from the divalent acids.

CYCLIC COMPOUNDS

An important series of carbon compounds contain a ring of six carbons, each with an unsatisfied affinity, thus :—



When each hand holds a hydrogen, **Benzene** is formed.

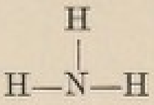
These hydrogens may be replaced by various molecules giving rise to a large series of different compounds.

If the ring contain less than six carbon atoms it is called heterocyclic. One of the most important of these is **Pyrrhol**—

which occurs linked to a benzene ring in certain important constituents of the protein molecule.

Nitrogen-containing Compounds

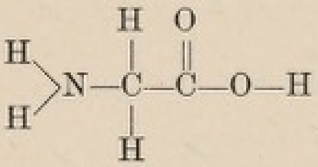
Ammonia.—The three-handed Nitrogen by linking with three hydrogens forms Ammonia,



$$\begin{array}{c} \mathrm{H} \\ | \\ \mathrm{H—N—H} \end{array}$$

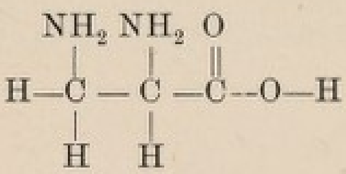
If one of these hydrogens is removed, Amidogen, which can link with other molecules, is produced.

Amino Acids.—If one of the hydrogen atoms in the radical of an acid is replaced by amidogen a *mon-amino acid* is formed, thus :—



Amino acetic acid.

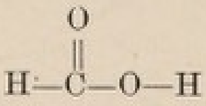
When two hydrogen atoms are thus replaced, a *di-amino acid* is produced—



$$\begin{array}{cccccccc} & \mathrm{NH_2} & & \mathrm{NH_2} & & \mathrm{O} & & \\ & | & & | & & \| & & \\ \mathrm{H}— & \mathrm{C} & — & \mathrm{C} & = & \mathrm{C} & \text{--}\mathrm{O}— & \mathrm{H} \\ & | & & | & & & & \\ & \mathrm{H} & & \mathrm{H} & & & & \end{array}$$

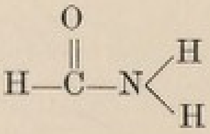
Di-amino propionic acid.

Amides.—If the amidogen molecule takes the place of the hydroxyl in the carboxyl of an acid an amide results, thus :—



$$\begin{array}{c} \mathrm{O} \\ \| \\ \mathrm{H—C—O—H} \end{array}$$

Formic acid.

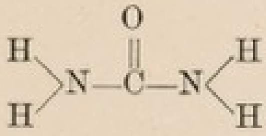


Formamide.

From the divalent carbonic acid—

$$H{-}O{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}O{-}H$$

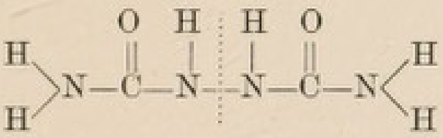
is formed—



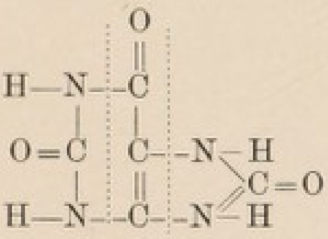
the important substance urea.

Urea molecules may link together—

(*a*) By dropping hydrogens, when Biuret is produced.



(*b*) By holding on to an intermediate radical of an acid, *e.g.* an unsaturated three carbon acid. These are Diureides, of which the most important is Uric Acid—



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ERRATA

Page 12, line 5, *for* "(p. 427)" *read* "(p. 416)."
,, ,, ,, 15, *for* "(p. 23)" *read* "(p. 210)."
,, 13, ,, 23, *for* "(p. 23)" *read* "(p. 24)."
,, 20, lines 11, 12, *for* "(fig. 176, p. 447)" *read* "(fig. 170, p. 435)."
,, 29, last line, *for* "(p. 393)" *read* "(p. 332)."
,, 40, line 10, *for* "p. 344" *read* "p. 330."
,, 58, ,, 12, *delete* from the word "opposing" to end of sentence, and *insert* "group, which fix the joint from which the movement is made."
,, 62, line 22, *for* "(p. 339)" *read* "(p. 327)."
,, ,, ,, 25, *for* "(p. 341)" *read* "(p. 328)."

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