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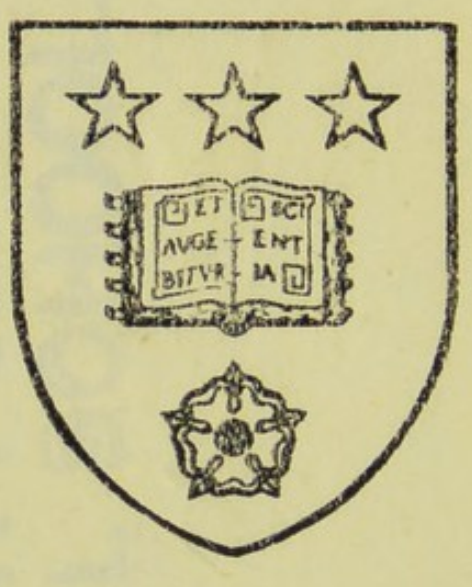
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Acid Chyme + Secretin = Secretion

↙

in blood stimulates the Pancreas
to give Trypsinogen with
succus Enterieus = Trypsin.

[illegible] Jones
[illegible]
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ELEMENTS OF HUMAN PHYSIOLOGY

ELEMENTS

OF

HUMAN PHYSIOLOGY

BY

ERNEST H. STARLING, M.D.Lond., F.R.C.P.

JOINT LECTURER ON PHYSIOLOGY AT GUY'S HOSPITAL

THIRD EDITION



LONDON

J. & A. CHURCHILL

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1897

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NOTE TO THIRD EDITION.

THE few changes that have been made in revising this book for a new edition will be found chiefly in the account of the Coagulation of the Blood, and in the section on the Central Nervous System. A number of additional illustrations have also been inserted.

ERNEST H. STARLING.

September, 1897.

PREFACE TO FIRST EDITION.

In this little book I have endeavoured to present as clearly and shortly as possible the main facts of Physiology that are of importance to students of medicine. The limits of space at my disposal would not allow me to include histology, nor do I regret its omission. This subject, which is properly a branch of Anatomy, is already adequately treated in the anatomical text-books, and the student should make use of one of these accounts or of Schäfer's admirable 'Essentials of Histology' at the same time that he is studying his physiology. A knowledge of the way in which the body is built up must go hand in hand with a knowledge of its functions.

In describing methods I have confined myself to the elucidation of the principles involved, since an intimate acquaintance with practical details can only be acquired in a laboratory course, without which all book teaching is in vain.

I have to express my indebtedness to my friend Mr. G. Bellingham Smith, who has drawn all the illustrations in this volume except those taken, with the kind permission of the authors, from well-known text-books.

ERNEST H. STARLING.

September, 1892.

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PHYSIOLOGY

CHAPTER I

INTRODUCTION

PHYSIOLOGY is the science of the phenomena of living organisms, and of the laws regulating those phenomena.

In its wider sense it will thus include the phenomena of all vegetable and animal life.

In this work, however, our immediate object is the physiology of man: but in physiology, as in all other sciences, the only sure foundation of knowledge is that gained by experiment; and since ethical considerations prevent our experimenting on our fellow-creatures, we find ourselves again and again forced to judge of the functions of men by analogy with those of lower animals on whom we can experiment. We can, however, learn many things from experiments which we may make on ourselves, and which do not necessitate any mutilation or involve any danger.

We find means, moreover, of checking the results of our experience in lower animals by studying the disorders of function caused in man by lesions of the various parts of the body, which we may observe in the wards and post-mortem room. Nature, however, rarely limits her experiments on our vile bodies to one function or organ, so that in most diseases we have such a complexity of disturbances that this method of investigation used by itself is apt to lead to many erroneous deductions.

The phenomena that we commonly associate with the possession of life are those of movement and, in the higher animals, of warmth.

Thus, in men, some part of the body is always in motion, and even in sleep the rhythmic respiratory movements still betoken to us the presence of life. If we see a frog on the ground, we instinctively poke it to see if it is alive, knowing that, if alive, it will respond to the stimulus and jump away.

This property of *reaction to stimulus*, or *irritability*, is fundamental and common to all living beings. We shall have to consider it more in detail later on.

Then, again, a living man is warm, and, in temperate climates, always warmer than the surrounding air. By means of the thermometer it is found that a healthy man's temperature is 98·4° F., and is maintained constantly at this point. The temperature of the surrounding medium being nearly always below this point, it is evident that the body must be continuously losing heat, and raising the temperature of surrounding bodies.

Thus we see that a living body is continuously losing energy, which may appear as work done on, or as heat imparted to, some external object.

Yet we know that an animal continues to perform work and to give off heat during the whole of its life, so that it must have some source from which to draw its energy. This source is the food.

Common experience teaches us that a man, to live, must eat, drink, and breathe. His food consists of certain bodies, which we call proteids, carbohydrates (including starches and sugars), and fats. Of these three classes, the proteids (which exist in large quantities in meat) are essential to the maintenance of life, though life is supported more advantageously if the other two classes are also made use of.

The proteids contain carbon, hydrogen, nitrogen, oxygen, and a small proportion of sulphur. Carbohydrates and fats contain carbon, hydrogen, and oxygen only.

All these foodstuffs are said to possess potential energy ; which simply means that they can combine with a further proportion of oxygen to form more stable compounds, and in so doing set free a certain amount of energy. This energy may appear in the form of heat, or we may use loaves or sugar or fat to feed an engine furnace with, and so convert the energy into work.

It is the oxidation of the foodstuffs, the burning of them to form CO_2 and water, that gives rise to the energy which appears in the animal body either as work or heat.

The oxygen necessary for this combustion is furnished by the atmosphere. With every breath we take in oxygen, with every breath we give out CO_2 and water.

Thus we may compare the animal body to a heat engine. The fuel, the source of energy, is represented by food. The inlet for the draught of air and the outlet for the waste gases, the products of combustion, are both combined in one organ, the lungs, which we use to take in oxygen and give out CO_2 and water ; and, just as the coal used in engines has some incombustible constituents which remain as ash and have to be raked out, so there are parts of our food which the body cannot make use of, and which leave the body as excrementitious matter or fæces, having passed though the alimentary canal without at any time having formed part of the tissues. There are still two constituents of foodstuffs which have to be got rid of after the elimination of CO_2 and H_2O by the lungs, namely, the nitrogen and sulphur contained in the proteids. This function is served by the kidneys. The nitrogen is combined in the body with carbon and oxygen to form a substance called urea, and in this form is excreted by the kidneys, together with salts and water, as urine. The sulphur is oxidised to a sulphate, and in this form also appears in the urine.

We must mention here that water and salts are indispensable and invariable components of the food. Neither of these possess any potential energy, but they are essential constituents of all living substances, and must be taken to

replace the loss of them from the lungs, skin, and kidneys, the water formed in the body by the oxidation of the hydrogen of the foodstuffs being far too small to compensate this loss.

The income and output of the body may be arranged in the form of an equation—

$$\text{Food} + \text{oxygen taken up} = \text{fæces} + {}_n CO_2 + {}_n H_2O + \text{urea } \left(CO\langle^{NH_2}_{NH_2}\right);$$

and in the same way we may make an equation of the income and output of energy—

Energy set free by burning of food to CO_2, H_2O, and urea = work done by body + heat given off.

The truth of these equations has been proved by many elaborate observations both on animals and men.

Thus from one point of view physiology may be regarded as the history of all the changes undergone by the food in its passage through the body, and the mechanisms by which its potential energy is transformed into the kinetic energy of the various vital manifestations.

But this analogy with the heat engine must not be pushed too far. In this the fuel, the source of energy, is always distinct from the machinery by which its energy is converted into work. In the body it is otherwise. The food that we take in is digested, assimilated, and built up to form part of the living framework of the body. This living stuff at the same time takes up oxygen, so that a molecule is formed containing all the elements necessary for evolution of energy. Under certain conditions the foodstuffs and the oxygen in the living molecule combine together, the unstable living molecule of high potential energy splitting up to form stable compounds with lower potential energy, a certain amount of energy being rendered kinetic or actual in the process in the form of heat or work. So the changes that the foodstuffs undergo in their passage through the body may be divided into two main stages :

(1) *Assimilative or anabolic changes.*—The food that is absorbed from the alimentary canal, and the oxygen that is taken in through the lungs, are built up into and become actual constituents of the living protoplasmic molecule. These processes, which are spoken of under the term *anabolism*, are associated with evolution of very little energy ; or it is possible that energy may become latent in the process, the building up being effected at the expense of some previously formed unstable compound.

(2) *Dissimilative or katabolic changes.*—These are the changes which are always associated with activity, that is, with the manifestation of some form of energy (heat, work, electrical change, &c.). The molecule of protoplasm breaks down, most of the atoms arranging themselves to form the stable compounds, CO_2, water, and perhaps urea, just as a molecule of nitro-glycerine when struck explodes with great evolution of heat, and with the formation of stable and more simple molecules. But in the living body the explosion is rarely (under physiological conditions) complete. There is always a remainder which does not undergo decomposition, and which we endow with the attribute of *living*, since it possesses the power of self-restitution, and can take up foodstuffs and oxygen, and so build itself up again into the same unstable molecule as before, ready to break down in part and give rise to kinetic energy.

These changes of breaking down of a highly complex living molecule, with the evolution of energy, are spoken of under the general heading of *katabolism.*

Before treating these processes any further, we must pause awhile to consider the manner in which the body is built up, and what are the essential morphological characters common to all forms of life. This unity in the structural basis of all living beings will be seen better after a study of one of the simplest forms ; and as a type of these we may take the well-worn example of the amœba.

This is a minute organism of variable size, found in stagnant water and in damp earth.

If we examine it under the microscope we find that it consists of a small lump of transparent material, which can be shown by chemical tests to belong to the proteid group of bodies, but which is distinguished from a mass of inert proteid by the facts that it is able to ingest and digest food and build it up into its own substance ; that it can move about from place to place, responds to stimulation by contracting up into a round ball, and has the power of reproduction by fission—that is, one amœba divides into two individuals exactly similar to the parent organism and to one another ; in short, this little lump is alive.

We find that there is some trace of differentiation even in this primitive organism. Thus towards the centre of the lump is a spherical or oval body (a nucleus), differing slightly in its chemical characters from the surrounding substance, which latter may also be differentiated into an inner granular or spongy portion, the *endosarc*, and a peripheral hyaline material, the *ectosarc*.

FIG. 1.

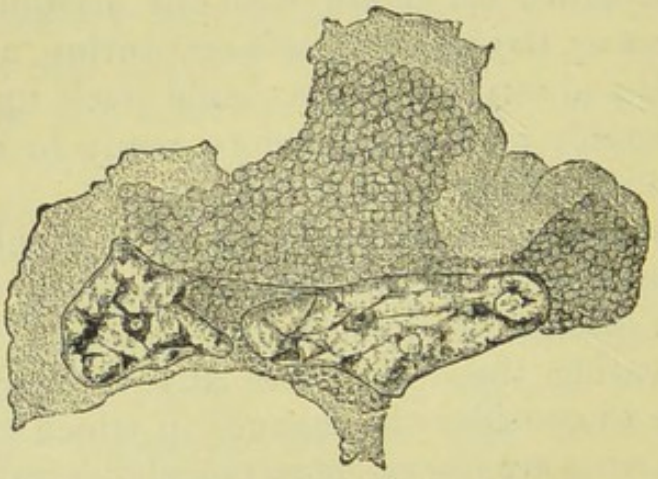


Figure of amœboid corpuscle, highly magnified, showing elongated nucleus, endosarc, and ectosarc (Schäfer).

The stuff composing the body of the amœba, and endowed with vital properties, is called *protoplasm*.

The term protoplasm has been used in two senses. By

histologists it is confined to a substance found in living bodies, or bodies that were once alive, and reacting in certain ways with certain stains and reagents. In this book, however, we shall use the term as a convenient expression for the substance forming the active living basis of all our tissues, although analysis may show considerable differences in its chemical composition in various organs. Protoplasm is, in fact, living stuff.

The little mass of protoplasm enclosing a nucleus is called a *cell*. Since, however, there are living organisms in which no trace of a nucleus is to be discovered by the most improved methods, we do not regard its presence as essential to our conception of a cell.

Now we find that all the higher animals, including ourselves, are made up of enormous aggregations of similar nucleated masses of protoplasm, and may be regarded as colonies of amœbæ. But, just as in a colony of men, with increasing growth of the community there is increasing differentiation of function, so in us some cells are eminently assimilative and digestive, others respiratory, others motile, while some are set apart for the purposes of reproduction.

Hand in hand with this physiological goes morphological differentiation—that is, the structure of each group of cells becomes modified to fit it for carrying on its own work, and its own work alone.

Thus the motor cells do all the external work required by the whole organism, both for purposes of defence and offence. Under this latter head we may class the work of getting food, since this must always be at the expense of some other living organism. In return for this they are supplied with food, water, and oxygen in an assimilable form by the activity of other groups of cells, just as a soldier—the community's instrument of offence and defence—is clothed, fed, and housed at the expense of the community for which he works.

A collection of cells, modified and built up together for some particular function, is called an organ when we are

considering its physiological import, or a tissue when we regard only its morphological aspect.

The Assimilation of Food

In some of the lowest forms of animal life, food can be taken in at any part of the surface of the body. In the amœba we can observe the whole process with the microscope, and we see how the particle of food that has been taken in undergoes partial solution—that is to say, part of it disappears and apparently becomes built up into the living stuff of the organism. The remnant that cannot be dissolved is again turned out of the body through any part of the surface.

The processes by which these minute animals assimilate food are very similar to those taking place in man and allied forms, only in the latter we find that there is a differentiation of function, a division of labour in which some cells of the body take up one part of the work of assimilation, while other cells are told off to carry on another part; and we are able to study the whole process much more fully since we can take it bit by bit. In man the work of taking up food is still performed by the surface of the body, but it is a special part of the surface, highly differentiated, and protected by its position and certain mechanisms from coming in contact with anything except food, so that it may devote its whole energies to this one function.

All the higher animals may be considered as built in the form of a tube, the external surface of which is differentiated for purposes of defence, and therefore forms also the organs by which the processes of the body act in harmony with changes in its environment.

The internal surface, on the other hand, is the special alimentary surface, and is called the alimentary canal.

Between these two surfaces the wall of the tube contains the supporting tissues of the body, the bones, &c., and also

the organs for the conversion of the potential energy of the food into motion and work, the muscles. In all the higher animals cavities are developed between the two surfaces in the substance of the middle layer—the body-cavities, represented in man by the pleural and peritoneal cavities; so that the alimentary canal for a considerable

FIG. 2.

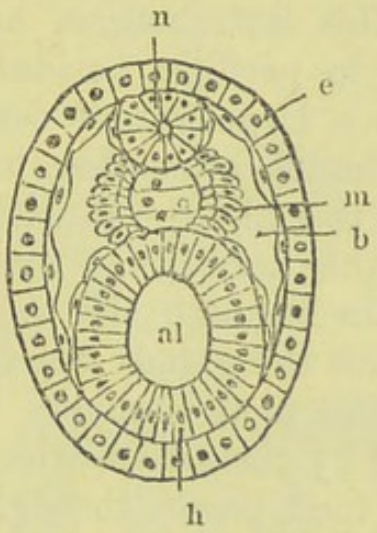


Diagram showing relations of embryonic layers. e. Epiblastic or outer layer. h. Hypoblastic or alimentary layer. m. Mesoblastic or middle layer. b. Body-cavity. n. Central nervous system. al. Alimentary canal.

part of its course is only connected with the body-wall by one side, and seems to hang down into the peritoneal cavity.

The tube of special alimentary cells forming the digestive canal is surrounded by motor cells derived from the middle layer. These serve to drive the food from one end to the other, and to expel the innutritious matter.

In order to get a greater number of working cells, there are recesses of the surface lined with cells, which are called glands, and protuberances into the lumen of the tube, which are called villi. Even among the cells of the alimentary surface there is differentiation of function. Thus the cells of the glands manufacture and pour out fluids,

varying in composition and action at different parts, which have the power of moistening and dissolving the constituents of the food, while the cells covering the villi seem more especially adapted for absorbing the food after it has been digested and rendered soluble. The glands may be simple tubular recesses in the mucous membrane, or may branch to such an extent as to form a bulky organ. The liver is a type of such an overgrown process of the alimentary epithelium. This latter organ, however, has other important functions to perform besides mere solution of foodstuffs. It is to a large extent concerned in further elaborating the foodstuffs after they have been absorbed into the body, so as to make the function of self-nutrition still easier for the other servants of the organism.

We may here run through the various parts of the alimentary canal, with the glands opening into it. From the mouth, where the food is chiefly broken up by the teeth and moistened by the saliva, which is secreted by the *salivary glands*, the food passes through the tubular œsophagus or gullet into the stomach. This is a saccular dilatation of the canal, situated in the upper part of the abdomen. In it the foodstuffs are acted upon by the gastric juice, secreted by small tubular glands, and the dissolved products are partly taken up or absorbed.

After the stomach the alimentary canal becomes narrowed again to form the small intestine. This is divided in man into three main divisions—the duodenum, about nine inches long; and the jejunum and ileum, about twenty feet long.

Into the upper part of the duodenum two glands, the liver and pancreas, pour their juices, while the whole internal surface is taken up with villi and tubular glands (crypts of Lieberkühn), so that digestion and absorption go on simultaneously. The ileum leads into the colon or large intestine. This is about twice as wide as the small intestine, from which it is separated by a valve, the ileo-colic valve. Its internal surface is entirely taken up with

cæcal

tubular glands, no villi being present. In this part of the canal absorption probably predominates over digestion. The lower part of the large intestine is the rectum, and

FIG. 3.

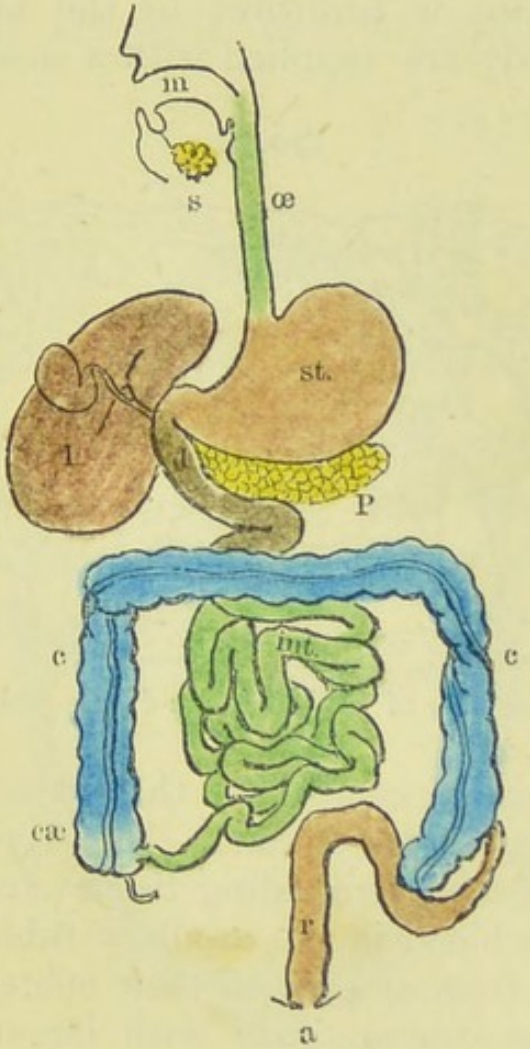


Diagram of alimentary canal. m. Mouth with salivary glands, s, opening into it. œ. Œsophagus. st. Stomach. d. Duodenum with pancreas, P, and liver, l, opening into it. int. Small intestine. cæ. Cæcum. c. Colon. r. Rectum. a. Anus.

opens by an aperture, the anus, on the surface of the body, by which the indigestible residue of the food, forming the fæces, is discharged.

Circulation of the Blood

In order that the foodstuffs taken up by the cells lining the alimentary canal should be distributed to all parts of the body, there must be some means of transporting the food. This means is furnished by the blood. All the tissues of the body are supplied with a close meshwork of

FIG. 4.

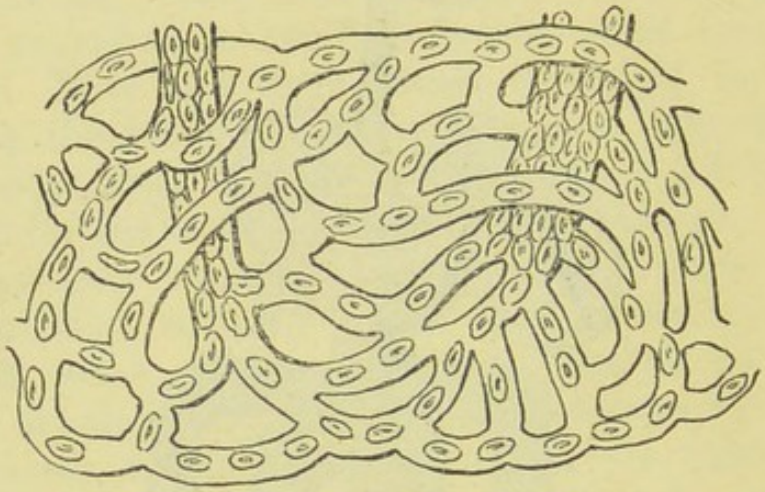


Diagram of capillaries in frog's web.

delicate tubes, called capillaries, the walls of which are formed by a single layer of cells. This layer is permeable to fluids, so that the surrounding tissues are practically in contact with the blood in the capillary tubes, and can take up nourishment from or give off their effete material to it. These capillaries communicate with larger tubes which have thicker walls, and these lead to and from a hollow organ with thick muscular walls—the heart.

The heart is divided into four cavities, two auricles and two ventricles, which are separated from one another by valves. These valves are so arranged that, when the heart contracts and diminishes its capacity, the blood can flow only in one direction. We may compare it to an enema syringe in which the compressing force is in the elastic wall instead of being supplied by the hand of the experimenter.

The tubes taking the blood from the heart to the tissues have thick elastic walls, and are called arteries; while those bringing the blood back from the tissues are called veins, and have thinner and more rigid walls.

Fig. 5 shows the course taken by the blood in its circulation through the body, as it is impelled by the contracting heart.

FIG. 5.

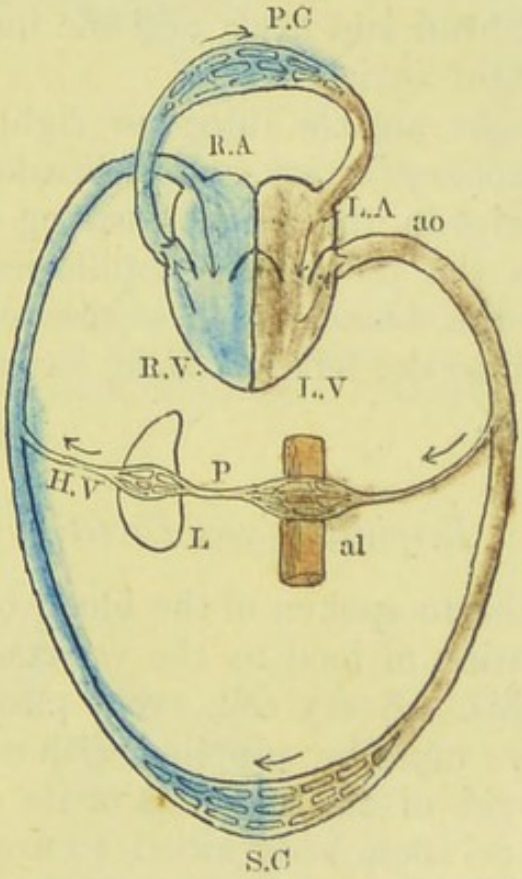


Diagram of circulation. L.V. Left ventricle. L.A. Left auricle. R.V. Right ventricle. R.A. Right auricle. ao. Aorta. S.C. Systemic capillaries. al. Alimentary canal. P. Portal vein. L. Liver. H.V. Hepatic vein. P.C. Capillaries of lungs.

Starting from the left ventricle, the blood is propelled through the aorta into the systemic arteries, and thence into the capillaries supplying the head, neck, body, limbs, and alimentary canal.

From the capillaries of the alimentary canal the blood

flows into a number of veins, which unite to form a large vessel, the portal vein. This then enters the substance of the liver and breaks up again into a number of capillaries, which ramify and anastomose round the hepatic cells.

The blood from these capillaries is again collected into a large vessel, the hepatic vein, which flows into the inferior vena cava. This latter vessel also conveys blood from the back, lower limbs, and kidneys.

The superior vena cava, with the blood from the upper extremities and head and neck, and the inferior vena cava open into the right auricle.

From the right auricle into the right ventricle, then along the pulmonary artery, which breaks up into innumerable capillaries in the lungs (forming the *lesser circulation*), then from the pulmonary capillaries along the pulmonary veins, the blood reaches the left auricle, from which it flows into the left ventricle, having completed its whole circulation.

Respiration and Excretion

We have hitherto spoken of the blood only as a medium for the distribution of food to the various tissues. But it is more than this. Every cell, every protoplasmic unit of the body, to live must be supplied with oxygen, and must be able to get rid of the products of its activity, namely, CO_2 and urea, or some body allied to urea. In all these functions the blood acts as the middleman between the cell hidden deep in the body and the cell on the surface of the body.

Thus, as the blood flows through the lungs, it is only separated from the air in the cavities (alveoli) of this organ by the thinnest possible layer of cells. Here we find that the blood changes its composition, giving up CO_2 and taking in oxygen.

When the blood reaches the tissues, a process the reverse of this takes place ('internal respiration'), the

FIG. 6.

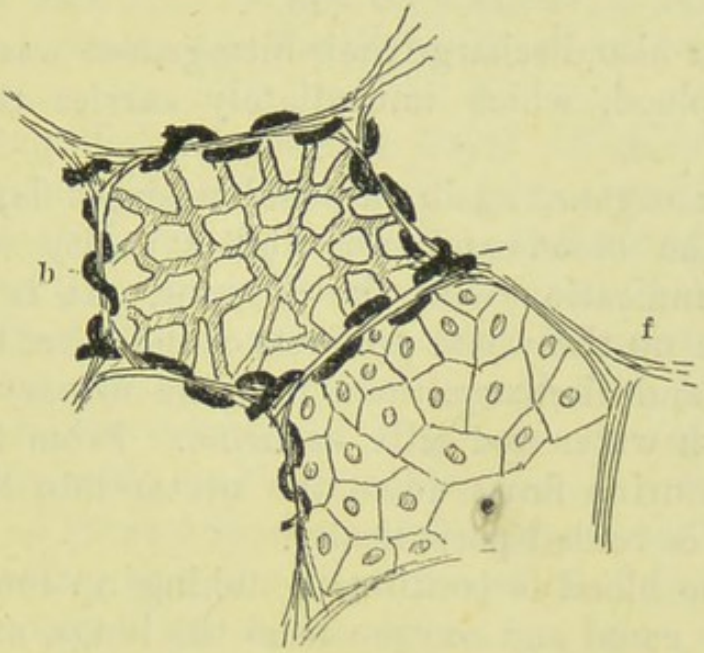


Diagram of lung tissue, showing—b. Capillary blood-vessels in walls of alveoli. e. Epithelium lining the alveoli. f. Cut edges of alveolar walls, consisting of connective-tissue fibres and elastic tissue.

FIG. 7.

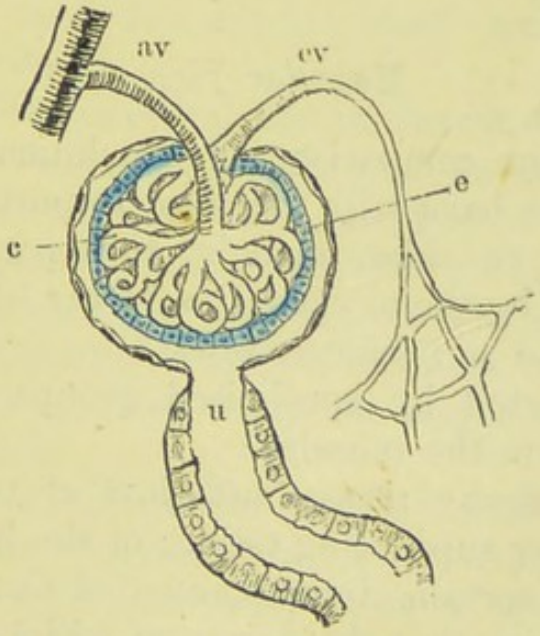


Diagram of kidney. av. Afferent blood-vessel. ev. Efferent blood-vessel. c. Loop of capillaries. e. Secreting epithelium. u. Urinary tubule leading to bladder and exterior.

cells of the tissues taking up oxygen and giving up CO_2 to the blood.

The cells also discharge their nitrogenous waste products into the blood, which immediately carries them to the kidneys.

In these organs, again, we find a single layer of cells between the blood-capillaries and a cavity which is in free communication with the exterior. It is these cells which take up the waste products of the other tissues from the blood and discharge them into the urinary tubule, together with water and salts, as urine. From the urinary tubule the urine flows down the ureter into the bladder, whence it is voided periodically.

Thus the blood is continually taking up food from the alimentary canal and oxygen from the lungs, and carrying them to the tissues. Here it parts with them and receives in exchange the products of tissue change (which are, indeed, only the products formed by the union of the oxygen with the food-stuffs), and, carrying these away, discharges them on the exterior of the body by means of the lungs and kidneys.

Muscular Tissues

Retaining our comparison of the human body with a heat engine, we have still the most important part of the mechanism to consider, namely, that part in which the heat produced by the oxygenation of the food is converted into motion and so performs work.

This is effected by specialised groups of cells united together to form the muscles.

These are fleshy masses attached at two ends to the bones and other supporting tissues of the body. They are capable under certain circumstances of shortening, that is to say, approximating the points to which their two ends are attached against resistance, so that they do work.

Thus the biceps muscle of the arm is attached above to

the shoulder-blade, and below to the radius, one of the bones of the forearm. When it contracts, it thickens and shortens, and draws up the forearm so as to bend the elbow-joint.

Thus it may do work in two ways. If the shoulder is fixed, contraction of the biceps will raise a weight held in the hand ; or the hand may be fixed, as in hanging on a horizontal bar, so that the effect of contraction of the muscles is to raise the shoulders and with them the whole body.

We also find muscular tissue, though less highly differentiated, in the interior of the body, surrounding the heart, blood-vessels, and alimentary canal. It is by the contraction of these hollow muscular tubes that the blood is set in motion, and the food propelled from one end of the alimentary canal to the other.

Co-ordination and Reaction

Here our analogy of the heat engine must cease. For an engine needs engineers and stokers to determine its work and keep it supplied with fuel. A man's body goes on seeking out food and feeding itself and working for sixty or seventy years.

According as the external circumstances vary, so a man must do more or less work, must take more or less food. Moreover, in such a complicated mechanism as the human body, there must be a delicate adjustment of the actions of the various organs to one another, so that the part which is doing most work should be best supplied with nutriment and oxygen, and no part waste its stored-up energies in doing useless work.

Thus there is an adaptation of the actions of the body as a whole to the requirements of its environment ('necessity'), and also mutual adaptation within the body of the actions of the various organs to one another. This harmonious working of the body and all its parts is effected by the governing and directive power of the central

nervous system, the brain and spinal cord of all the higher animals.

In comparing the human body to a tube, we alluded to the outer layer of cells as especially set apart for the purpose of protection, and for regulating the events of the body according to the changes in the environment. Very early in development, however, we find that a part of this surface becomes involuted to form a groove, the walls of which close over so as to form a canal—the primitive neural canal. The latter then becomes cut off for most of its extent from the external surface by an ingrowth of the middle layer or mesoblast.

The cells forming the walls of the canal grow and multiply, so that finally the canal is extremely minute in proportion to these walls.

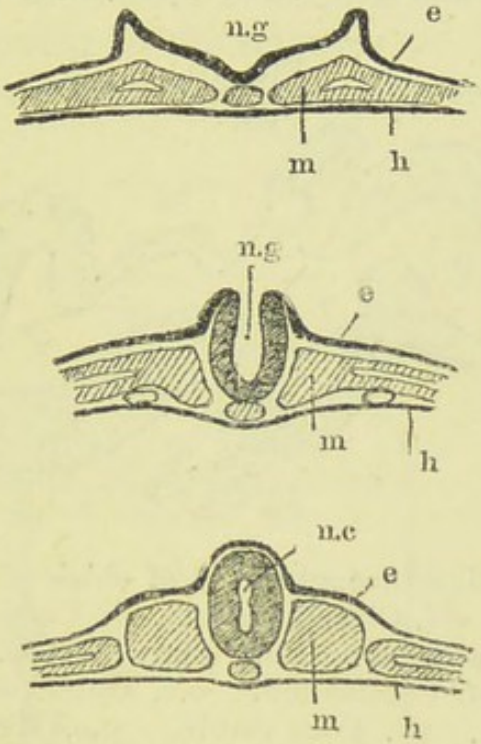
The spinal cord retains this primitive form of a canal with thick walls. At the anterior end of the body (head end) this canal becomes dilated, and sends out lateral and mesial prolongations. The walls of these also become thickened at some places and thinned at others, so that finally a bulky complicated organ is produced which we call the brain.

In Figs. 8, 9, and 10 the different parts of the central nervous system are shown diagrammatically, and from these the origin of the whole brain and spinal cord from a simple canal pinched off from the epiblast will be evident.

But this tube of specially 'reactive' or, as we shall always call them, *nervous* cells, still remains connected with the periphery by strands of protoplasm which we call nerves. These strands, in many cases, end close under the surface of the skin in various forms of cells, specially differentiated for feeling different kinds of stimuli.

By this means the central system may become aware of all the changes occurring at the periphery of the body. But it is necessary that the organism should be able to *react* to changes in its surroundings, and we find that, very early in the development of the body, certain cells in the

FIG. 8.



Diagrams showing formation of the nervous centre (brain and spinal cord) by a tucking-in of the outer or epiblastic layer. e. Epiblast. m. Mesoblast. h. Hypoblast. n.c. Neural canal. n.g. Neural groove.

FIG. 9.

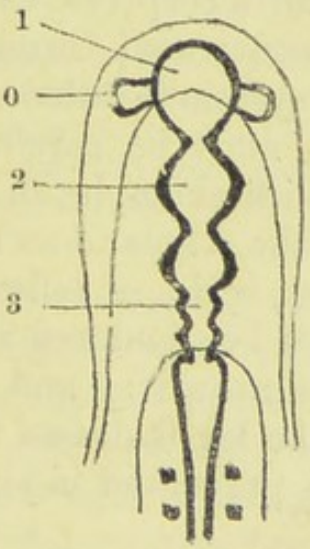
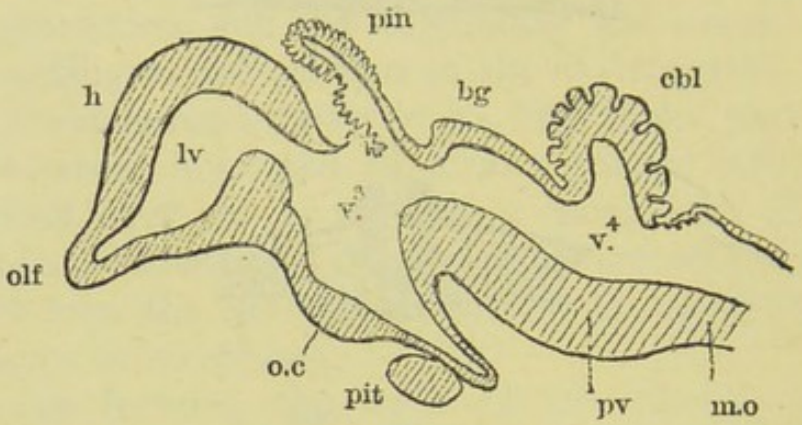


Diagram of the cerebral vesicles of the brain of a chick at the second day (Cadiat). 1, 2, 3. Cerebral vesicles. 0. Optic vesicles.

wall of the tube send out long protoplasmic processes which become connected with the muscles, glands, heart,

FIG. 10.



Longitudinal section through brain of chick of ten days (after Mihalkovicz). olf. Olfactory lobes. h. Cerebral hemisphere. lv. Lateral ventricle. pin. Pineal gland. bg. Corpora bigemina. cbl. Cerebellum. o.c. Optic commissure. pit. Pituitary body. pv. Pons varolii. m.o. Medulla oblongata. v^3, v^4. Third and fourth ventricles.

and blood-vessels. Through these processes impulses descend from the brain or spinal cord in response to stimuli which have proceeded up the sensory nerves from the periphery.

This change in the intra-corporeal events determined by a change in the extra-corporeal through the intervention of the central nervous system is called a *reflex action*. The meaning of this term must be carefully borne in mind, since we shall meet with examples of it in every stage of our subject. In fact, the whole of an animal's life may be looked upon as one long series of reflex actions.

Perhaps the idea will be rendered more concrete by an example. If we decapitate a frog and then dip one of his toes into dilute acid, the leg is drawn up.

This *reaction* may be prevented in either of the following ways:

1. Section of the sensory (afferent) nerves from the toes to the spinal cord.

2. Destruction of the spinal cord.

3. Section of the motor (efferent) nerves coming from the cord and running to the muscles.

4. Destruction of the muscles of the leg.

Fig. 11.

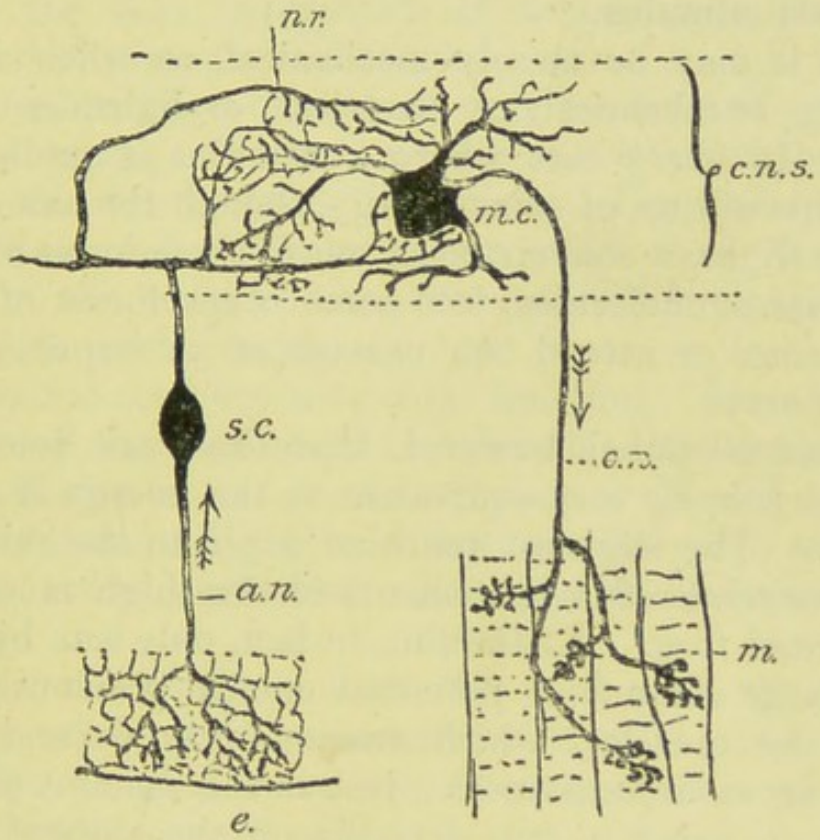


Diagram of reflex action. *e.* Sensory epithelium. *a.n.* Afferent nerve-fibre. *s c.* Sensory cell. *c.n.s.* Central nervous system. *n.r.* Branch of sensory cell in close contact with processes of *m.c.*, motor cell. *e.n.* Efferent nerve-fibre, terminating in end-plates on the muscle, *m.*

Thus the elements composing a reflex arc are—

(1) A sentient surface (such as the skin) connected by—

(2) A sensory or afferent nerve

(3) To a cell or group of cells, or of nerve-tracts in the central cerebro-spinal axis. This again is connected by—

(4) A motor or efferent nerve to

(5) A muscle or group of muscles.

For muscle in (5) we may substitute gland-cell or any

other cell in the body capable of responding by some change in its condition to a stimulus reaching it from the central nervous system.

To fire off a reflex arc, all that is necessary is an appropriate stimulus applied to the sentient surface. Now we find that in all animals almost any form of energy may serve as a stimulus.

Thus it may be merely mechanical, as when we poke the frog, or chemical, or electrical, or light, or heat, or sound. In every case where a stimulus is applied there is an expenditure of some energy, though the amount may be very slight, a conversion of one of these forms of motion (of masses or molecules) into some other forms of motion which cause or attend the passage of an impulse up the afferent nerve.

It must be noted, however, that the work done by the stimulus is in no way equivalent to the energy it sets free reflexly. The slightest touch of a pin to the skin causes most powerful reflex movements of the thigh muscles of a decapitated frog. A stimulus, in fact, only acts by setting free a large amount of potential energy previously stored up in the muscles, which amount may depend on the most diverse circumstances ; just as the amount of energy set free in firing a gun depends on the amount of gunpowder in the charge, and not on the size of the fulminating cap used to fire it. This simile, however, must not be taken too literally. Under normal circumstances a stronger stimulus, within certain limits, will give rise to a stronger evolution of energy (contraction of a muscle, &c.) ; but in every case the work done by the muscle far transcends in amount the work done in stimulating the muscle.

In all higher animals it is not the whole sensory surface that will respond to all forms of stimuli. Here again there is a division of labour among the sensory cells, some taking on the function of converting light, others heat, others sound, and so on, into a nervous impulse, which

may ascend to the central nervous system, and there give rise to some form of response as a reflex action.

Thus we have the formation of organs of special sense, containing sensory cells which under normal circumstances react to one form of stimulus, and only one. The eye receives impressions of light, the ear of sound, special cells in the skin impressions of temperature (heat and cold), and of pressure and touch.

The higher sense-organs, as they are termed—the eye, olfactory organ, and ear—are connected with the upper part of the neural tube, the brain. The end-organs of temperature and touch are distributed over the whole surface of the body, and are connected to the neural tube through its whole length.

The spinal cord has a twofold function. It serves as a conductor of impulses started by stimuli at the surface of the body to the brain, and as a conductor of efferent impulses from the brain. It may also be regarded as a collection of reflex *centres* regulating all kinds of movements and functions.

The nerves, which connect the cord with all parts of the body, are arranged symmetrically on the two sides of the body, so that there are thirty-one pairs of nerves arising from the spinal cord.

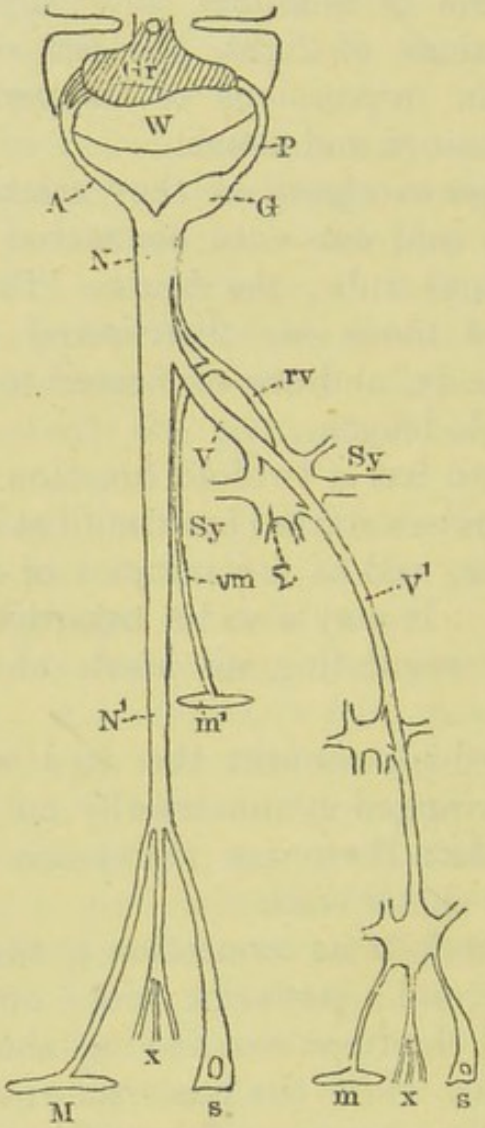
Each nerve-trunk at its connection to the cord is divided into an anterior and a posterior root; and we shall show later on that all the impulses leaving the cord pass along the anterior roots, while the posterior roots are composed exclusively of fibres bearing afferent impulses.

A short distance from the cord these two roots join, and the mixed nerve-trunk thus formed divides again and again, supplying the sensory end-organs and muscles of a definite segment of the body.

An important branch of the mixed nerve-trunk (though small anatomically) is the ramus communicans of the sympathetic. The fibres forming this little nerve pass into a chain of ganglia (*i. e.* collections of nerve-cells) situated

along the back of the body-cavity, in front of the spinal column, and sending a prolongation up into the neck.

FIG. 12.



Scheme of the nerves of a segment of the spinal cord (Foster). Gr. Grey; W, white matter of the cord. A. Anterior; P, posterior root. G. Ganglion on posterior root. N. Whole nerve giving off (N^1) somatic nerve to muscle (M), or sensory cell S, and visceral branch V, which passes through various ganglia of the sympathetic system before reaching the visceral muscle m, or sensory cells. rv is the grey ramus communicans which runs back from the ganglion Σ to the spinal cord, and gives off a branch vm, which runs in connection with the spinal nerve to the blood-vessels of the limbs. Sy. The sympathetic chain uniting the ganglia at the series Σ.

Some of the fibres become connected with these ganglion-cells, while others simply pass through the ganglion. All the fibres, however, before passing to their destination, probably become connected with nerve-cells situated more peripherally. This destination is all the organs of vegetative life, alimentary canal, heart, blood-vessels, glands, &c.

The whole system of visceral nerves, formed from the nerve-fibres of the rami communicantes, is called the sympathetic system.

The accompanying diagram will serve to illustrate the general plan of distribution of a single spinal nerve, and its connections with the sympathetic system.

An unending series of reflex actions is going on in our body, and of many of these we may be quite unaware. But in very many cases we learn that something is going on when a stimulus affects our afferent nerves by having what we call a *feeling* or *sensation*. In order to experience a sensation we must be conscious, and therefore sensations are classed with emotions, ideas, volitions, as states of consciousness.

A pure investigation of states of consciousness, however, belongs to the province of the psychologist. We have only to deal with them so far as the function of afferent nerves is concerned, since it is difficult to obtain an objective sign of their activity (though, as we shall see later, such signs are present).

We have evidence that in man and the higher animals consciousness is intimately bound up with the outgrowths from the front of the neural tube, which we call the cerebral hemispheres. On the integrity of these, too, depends the carrying out of the so-called spontaneous or voluntary movements,—that is to say, movements which are not, so far as we can tell, called forth by any directly preceding stimulus or change in the environment of the animal.

The parts of the brain below the hemispheres seem built up on much the same plan as the spinal cord, and like this

contain a collection of reflex centres and nerve-paths. These reflex mechanisms, however, are very important, since their afferent channels are the important nerves subserving the functions of seeing, hearing, smelling, tasting, &c.

The importance of the cerebral hemispheres in the normal life of the animal can be well shown in the frog. If in this animal we remove the cerebral hemispheres, we find that it still acts in all respects as a normal frog, except that it is incapable of interpreting its sensations or of initiating voluntary acts. If we put it in water, it swims about till it comes to the edge of the basin, when it crawls up and sits on the edge. Stroke its back and it croaks. Put it on a horizontal board, it remains perfectly still. Incline the board, the frog climbs up it. All these complicated movements are brought about immediately by changes in the environment. They are examples of reflex action.

But if we leave the brainless frog to itself, and protected from disturbing influences, it sits there till it becomes a lifeless mummy. Having lost the greater part of its consciousness, it can no longer *feel* hungry, it does not *know* its food when it sees it, and therefore does not *will* to move in order to get it.

Reproduction and Heredity.

The production of new individuals, the crowning point of an animal's existence, is carried out by means of certain special cells, the spermatozoa in the male and the ova in the female, which represent potentially all the peculiarities of the parent organism. By the union and fusion of parts of a spermatozoon and ovum a single cell is produced, the fertilised ovum, as it is termed ; and from this cell by division and differentiation is formed the new individual, endowed with structures and properties similar to and derived from both parents. The rest of the cells of the body afterwards die, having served their function when they have reared the new family of individuals.

Thus from a broad standpoint all the complicated processes that we study in physiology, all the toil and turmoil of human existence, are nothing but "the by-play of ovum-bearing organisms." The biological destiny of man is accomplished with the production and rearing of a new individual.

Now we have shown above that in many respects the body may be regarded as a mechanism, controlled by external circumstances, and converting the potential energy of food into the kinetic energy of warmth and movement.

This comparison is further justified when we find that in all processes of the body there is no creation of energy. All energy possessed by the body is derived from the potential energy contained in the food, which in its turn represents the stored-up energy of the sun's rays.

On these accounts many have thought that no other factors were at work in living bodies than the intermolecular relations which comprise the laws of physics and chemistry, and that even the supreme facts of consciousness might be explained in this manner. But past experience warns us to be very careful before accepting purely physico-chemical conceptions of any vital phenomena. Again and again, as we shall see when discussing the processes of absorption, secretion, respiration, &c., have purely physical explanations been put forward, only to be overthrown by further investigations.

In fact, every cell in the body, like a conscious being, seems to have a power of selection, a power to eschew the evil and choose the good, the good being that which is necessary to its preservation as a unit of the cell community. A layer of living protoplasm, one twenty-thousandth of an inch in thickness, is able to take up materials on one side and discharge them on the other, in direct opposition to all known physical laws of diffusion or osmosis.

We may discover the functions of a living cell and the conditions of its activity, and, in general terms, the source from which it derives its energy ; but beyond this we have

been foiled in all attempts to find out how the cell uses the energy of the food for its own aims. It does not at present seem likely that any physico-chemical hypothesis will ever explain how all the physical and intellectual peculiarities may be transmitted from father to son through one single minute cell, a spermatozoon, five hundred millions of which would hardly occupy one cubic millimetre.

We shall, therefore, in the following pages discuss the functions of the various organs, the conditions of their activity, and the physical and chemical changes which can be demonstrated to occur in the organs concomitantly with their activity.

These objects of physiology are still very imperfectly known, and probably need yet many years of laborious research for their elucidation. But when we are fully acquainted with the laws and conditions of the activities of normal living structures, we shall be able to attack the problems of disease with a sure hope of success; for, knowing how the organism will react to all manner of circumstances, we shall be able to put it into an artificial environment which will counteract the effects of the previous abnormal environment, and so restore the organism to a healthy condition.

CHAPTER II

THE CHEMICAL CONSTITUENTS OF THE BODY

THE results of ultimate analysis teach us that twelve chemical elements enter into the composition of all living organisms. These are carbon, hydrogen, oxygen, nitrogen, sulphur, phosphorus, chlorine, potassium, sodium, calcium, magnesium, and iron. They are essential to the life of the animal. Other elements, such as silicon, fluorine, manganese, are found occasionally, but it is not known whether the minute quantities of these substances which are found are merely accidental, or necessary to life.

If the body of an animal be heated, with free access of oxygen, the carbon and oxygen are burnt up and escape as carbon dioxide and water; the nitrogen escapes as an oxide, and the rest of the elements remain as the ash.

One hundred parts of the ash of a young dog contain—

K_2O	8·5
Na_2O	8·2
CaO	35·8
MgO	1·6
Fe_2O_3	0·34
P_2O_5	39·8
Cl	7·3

Most of these constituents of the ash exist in the tissues as salts, either free or in a very loose state of combination with other substances.

Nearly all the iron, phosphorus, and sulphur, however, are found in the body, not as salts, but as complicated organic compounds with proteids and allied bodies.

Chemical analysis need not go so far as the production of the ultimate principles. In the dead body a large number of proximate principles have been discovered, many of which can only be produced in the laboratory of a living cell.

Of these proximate principles, the most important class is that of proteids, which we shall therefore consider first.

Proteids.—These bodies are found in all protoplasm, and are more abundant in those tissues where growth is actively going on. They are, in the condition we generally come across them, amorphous, indiffusible, and varying in their solubilities. This last property is used as the basis for their classification. They all contain oxygen, hydrogen, nitrogen, carbon, and sulphur; and their composition varies round the following numbers :

Oxygen	22 per cent.
Hydrogen	7 „
Nitrogen	16 „
Carbon	53 „
Sulphur	2 „

They cannot be built up in the animal's body from simpler compounds, and must therefore always be supplied to it in the food. This fact furnishes one of the most striking differences between animals and plants, which can form proteids out of salts of nitrogen and ammonia, together with carbon and water, that they derive from the atmosphere. All proteids that enter the body are sooner or later broken down and oxidised to form CO_2, water, and urea. The urea, when it leaves the body, is converted by ferment action into ammonium carbonate; and from these three products of animal metabolism, CO_2, water, and ammonia, the plant recommences the laborious task of building up the proteid again.

When proteids are heated with baryta water, they are broken up, with the formation of various amido-acids, belonging to both fatty and aromatic series; so that a

proteid may be roughly regarded as a combination of fatty and aromatic radicals, the nitrogenous amido-radical (NH_2) being interpolated in many of its constituent molecules. Thus when a proteid is broken up in the human body or by the action of any living organisms (*e. g.* organised ferments), it may give rise to a fatty moiety and to a nitrogenous moiety (urea), or to a fatty half and an aromatic half. An example of this last change is furnished by the action of the pancreatic juice on proteids.

Beyond these very general conceptions, we know very little about the constitution of these bodies. Research into their constitution has been aided by the discovery that it is possible to obtain them in a crystalline state.

Analyses of proteids in as pure condition as possible give the following empirical formulæ. It must be remembered, however, that the real formulæ may be many times the formulæ given here, which are the smallest possible, in order that a whole number of atoms may be contained.

Egg albumen. $C_{204}H_{322}N_{52}O_{66}S_2$.
Proteid in hæmoglobin (from horse). $C_{680}H_{1098}N_{210}O_{241}S_2$.
Proteid in hæmoglobin (from dog). $C_{725}H_{1171}N_{194}O_{214}S_3$.
Crystallised globulin (from pumpkin seeds). $C_{292}H_{481}N_{90}O_{83}S_2$.*

General Tests for Proteids

1. On boiling proteids in a very slightly acid solution, they are coagulated and form an insoluble white precipitate.

2. On pouring a solution of proteid carefully down the side of a test-tube containing strong nitric acid, so as to form a layer on the top, a white layer of coagulated proteid is produced at the junction of the two fluids.

3. On adding strong nitric acid to a proteid solution and boiling, a yellow colour is produced, which turns to deep orange when ammonia is added (xanthoproteic reaction).

* Bunge, 'Physiological Chemistry.'

4. Millon's reagent. An acid solution of nitrate of mercury gives a white precipitate, which turns a brick-red on boiling.

5. Acetic acid and potassium ferrocyanide give a white precipitate.

Biuret Test :— 6. Excess of caustic potash or soda, with a drop of dilute copper sulphate, gives a violet colour.

7. Saturation of proteid solutions with ammonium sulphate causes complete precipitation of all proteids present.

8. All coagulable proteids are completely precipitated by adding to their solutions an equal bulk of 10 per cent. trichloracetic acid.

Classification of Proteids

1. Native Albumens.—These are soluble in pure water, and are precipitated by saturation with sodio-magnesium sulphate or with ammonium sulphate.

Egg albumen forms the greater part of the white of egg. It gives the ordinary proteid tests, and is precipitated if shaken up with a drop of dilute sulphuric acid and excess of ether. It rotates the plane of polarised light to the left 35·5°. If injected into the circulation it is excreted by the kidneys, and gives rise to albuminuria.

Serum albumen occurs in large quantities in the blood-plasma and serum, and in small quantities in most tissues of the body. It coagulates at 75° C., and is distinguished from egg albumen by its greater specific rotary power (56°), and by the fact that it is not precipitated by ether and sulphuric acid, and if injected into the circulation does not reappear in the urine.

2. Globulins.—These bodies are insoluble in pure water, and require a certain amount of neutral salt present to dissolve them. They are the most interesting of all proteid groups, playing an important part in nearly all vital processes. But it must be remembered that we are not justified in speaking of the globulins which we extract

from the tissues and treat by precipitation and washing till they are no longer altered by these processes, as the active agents in the complex proteid interactions which make up the sum of vital phenomena. Our purified proteid is a wreck, and represents merely the framework on which the living protoplasmic molecule was built up.

All the globulins are precipitated from their solutions by saturation with magnesium sulphate, and partially by saturation with sodium chloride. The chief members of this class are—

Crystallin, obtained from the crystalline lens by passing a stream of CO_2 through an aqueous extract of this body.

Paraglobulin.

Fibrinogen.

Myosin.

These three bodies will be considered in the chapters on blood and muscle.

3. Derived Albumens.—These may be regarded as compounds of proteids with acids or alkalies.

Acid albumen. is formed by the action of warm dilute acids or of strong acids in the cold on any of the preceding bodies. If an alkaline solution be added so as to nearly neutralise the solution of acid albumen, this latter is precipitated. If the precipitate be suspended in water and heated, it is coagulated and becomes insoluble in dilute acids or alkalies.

Alkali albumen is formed by the action of strong caustic potash on white of egg or on any other proteid; or by adding alkali in excess to a solution of acid albumen. It is precipitated on neutralisation of its solution.

The *caseinogen* of milk is often included in this group, although it presents important differences from ordinary alkali albumen, and is more nearly allied to the nucleo-albumens. It is only precipitated by acetic acid in considerable excess, and is not easily converted into acid albumen. With rennet ferment it undergoes coagulation, and forms casein or cheese (*vide* Chap. VII).

4. Fibrin.—A stringy proteid formed in the clotting of the blood, and giving solidity to the clot. It is insoluble in water and salt solutions. In dilute hydrochloric acid it swells up, and if kept at 60° C. it dissolves with the formation of acid albumen. If suspended in water and heated it is coagulated, and is no longer capable of swelling up in dilute hydrochloric acid.

5. Coagulated Proteids.—Any member of the preceding classes, when heated in a neutral or slightly acid solution, is converted into coagulated proteid. In this condition it is insoluble in water, saline solutions, or weak acids. It is dissolved by strong acids or alkalies or by the digestive ferments, such as the gastric and pancreatic juices.

HYDRATED PROTEIDS.—When proteids are subjected to the action of superheated water or steam, or are heated with acids, or acted on at the body temperature by certain ferments (pepsin or trypsin), they undergo a change which is supposed to be attended with the addition of one or more molecules of water to the proteid molecule (hydrolysis). The final result of this action is peptone. As intermediate products between peptones and proteids we find a group of bodies known as proteoses or albumoses.

1. Albumoses.—These are all precipitated from their solutions by saturation with ammonium sulphate. On addition of nitric acid they give a precipitate in the cold, which is dissolved on heating, but reappears on cooling. On adding an excess of caustic potash and a drop of *very dilute* copper sulphate to a solution of albumoses, a pink colour is produced (biuret reaction). If more copper sulphate be added, the pink colour is changed to violet, similar to that produced in a solution of proteids.

According to their solubilities three varieties of albumoses may be distinguished :

a. Proto-albumose.—Soluble in pure water. Precipitated by saturation with sodium chloride or ammonium sulphate. With acetic acid and potassium ferrocyanide it gives a white precipitate.

b. Hetero-albumose.—Insoluble in pure water. Soluble in weak saline solutions or dilute acids. Precipitated by saturation with salt, or by acetic acid and potassium ferrocyanide.

c. Deutero-albumose.—Soluble in pure water. Not precipitated by saturation with common salt, except after addition of a little strong acetic acid. Entirely precipitated by saturation with ammonium sulphate. It gives no precipitate with acetic acid and potassium ferrocyanide.

2. Peptones.—Soluble in pure water; diffusible through animal membranes; with caustic potash and copper sulphate they give the same reaction as albumoses. From the latter class peptones are distinguished by the fact that they are not precipitated at all by saturation with ammonium sulphate or with any neutral salt.

Albumoses and peptones give the xantho-proteic and Millon's reactions common to all proteids; and like these are precipitated by tannic acid, mercuric chloride, and potassio-mercuric iodide.

Conjugated Proteids.—This name may be applied to various complicated bodies, which resemble one another only in the fact that in each of them a proteid radical is combined with some other body.

1. *Hæmoglobin*, the red colouring matter of the blood, is readily crystallisable. On boiling an aqueous solution it splits up into coagulated proteid (globin) and an iron-containing body named hæmatin ($C_{32}H_{32}N_4O_4Fe$). Its properties will be described in the chapters on blood and respiration.

2. *Nucleo-albumens.*—These are a group of bodies occurring in large quantities in cell-nuclei, in protoplasm, in the chyle, in lymph, and in blood-plasma. They consist of proteid combined with a nitrogenous body rich in phosphorus, called nuclein. They are in most cases soluble in water or in salt solutions. When subjected to gastric digestion, they are split up, the proteid half being converted into albumoses and peptones, while the nuclein is

precipitated. The nuclein thus obtained is a white amorphous powder, insoluble in water, salt solutions, or acids, but soluble in strong alkalies. It consists of a combination of proteid with a complex body containing nitrogen and phosphorus, known as nucleic acid. When the latter is heated with strong acids, it breaks up into phosphoric acid and a number of other substances, amongst which the most important are bases, allied to uric acid, belonging to the xanthin series (xanthin, hypoxanthin, adenin).

3. *The tissue-fibrinogens* of Wooldridge may probably be included in this class. These are bodies which may be extracted from any organ rich in cells, by mincing and then treating with water or dilute salt solution. From the solutions so obtained they are precipitated by acidifying with dilute acetic or sulphuric acid. They are soluble in excess of acid, and are easily soluble in alkalies. They are highly unstable bodies, and undergo changes in the mere act of precipitation and re-solution. Like the other nucleo-albumens they yield a precipitate rich in phosphorus on gastric digestion. When injected into the blood in sufficient quantities, they cause intravascular clotting. In many cases lecithin occurs in intimate association with these bodies, but it is not known how far this substance forms an integral part of their molecule.

4. *Mucin.*—This is a glucoside, being composed of a proteid (globulin) combined with animal gum, which by treatment with dilute sulphuric acid can be hydrated into a reducing but non-fermentable sugar. It swells up in water, forming a viscid, slimy mass. It is precipitated by acetic acid, and is insoluble in excess of this reagent. It is soluble in dilute alkalies.

The whole class of conjugated proteids gives the xantho-proteic and Millon's tests.

Bodies allied to Proteids, or Albuminoids.—Under this heading we may group a number of diverse bodies.

1. *Gelatin*, which may be extracted from all connective tissues, especially bone and white fibrous tissue, by pro-

longed boiling with water. It forms a solution in water, which is liquid at high temperatures, but sets into a jelly when cold. It is precipitated by tannic acid, but not by acetic acid. No tyrosin can be formed from it by boiling with dilute sulphuric acid, showing that no aromatic moiety is present in this body, and on this account gelatin does not give a red colour when boiled with Millon's reagent. Gelatin is not present as such in the tissues, but is formed from a precursor (collagen) by prolonged boiling with water.

2. *Chondrin* may be extracted by boiling cartilage. Its solutions are precipitated by acetic acid, and form a jelly when cold. On boiling with dilute acids it is split up, with the formation of a body possessing the power of reducing Fehling's solution. It has been shown that chondrin is a compound of gelatin with a sulpho-acid (chondroitin-sulphuric acid). Chondroitin is decomposed by boiling with acids, and forms a body, chondrosin, which reduces Fehling's solution, and is a derivative of glucose, being a compound of glycuronic acid ($C_6H_{10}O_7$) and glucosamin ($C_6H_{11}O_5.NH_2$).

3. *Elastin*, the substance of which the yellow fibres of connective tissue are composed, is insoluble in water and dilute acids or alkalies. It is very slowly dissolved by gastric juice.

4. *Keratin* forms the main part of the horny layer of the skin, nails, hair, hoofs, &c. It is very insoluble. It presents the same elementary composition as the proteids, but is distinguished from them by the very large quantity of sulphur present, which may amount to 5 per cent. A very similar substance, *neuro-keratin*, can be obtained from the supporting framework (neuroglia) of nervous tissues.

5. *Lardacein*, or amyloid substance, is a body allied to the proteids, which is found in the middle coats of the blood-vessels, in the liver and other organs under certain pathological conditions. It is insoluble in water, alkalies, acids, or gastric juice. It gives a red-brown colour with

iodine, which on the addition of strong sulphuric acid turns to a dirty blue colour.

FATS.—These bodies consist of the elements carbon, hydrogen, and oxygen. They occur to some extent in most tissues, and form the greater part of adipose tissue.

The fat of adipose tissue consists of a mixture—olein, palmitin, and stearin, the first being liquid and the two latter solid at ordinary temperatures.

Fats may be considered as compounds of the triatomic alcohol, glycerin ($C_3H_5(OH)_3$), with oleic, stearic, or palmitic acid, water being eliminated in the act of combination. Thus:

$$\underset{\text{Glycerin.}}{C_3H_5(OH)_3} + 3\underset{\text{Oleic acid.}}{(C_{18}H_{33}O.OH)} =$$

$$\underset{\text{Olein.}}{C_3H_5(O.C_{18}H_{33}O)_3} + \underset{\text{Water.}}{3H_2O}.$$

Fats are insoluble in water, but soluble in ether and alcohol. When boiled with alkaline solutions they are split up with the formation of glycerin, and a compound of the fatty acid with the alkali, which is called a *soap*. The alkaline soaps are soluble in water.

In the fats of milk (butter) we find lower acids of the fatty series, such as *butyric*, *caprylic*, and *caproic* acids, combined with glycerin. *Acetic acid* is also a member of the fatty acid series. It occurs in the body as an amido-acid, *glycin*.

Lecithin.—This substance is a wax-like body which is universally distributed in the organism, and is found in especially large quantities in the white matter of nerves and of the spinal cord. It may be regarded as a compound of a molecule of glycerin with two of stearic acid, one of phosphoric acid, and a molecule of a nitrogenous base, cholin. Its composition is represented by the following formula:

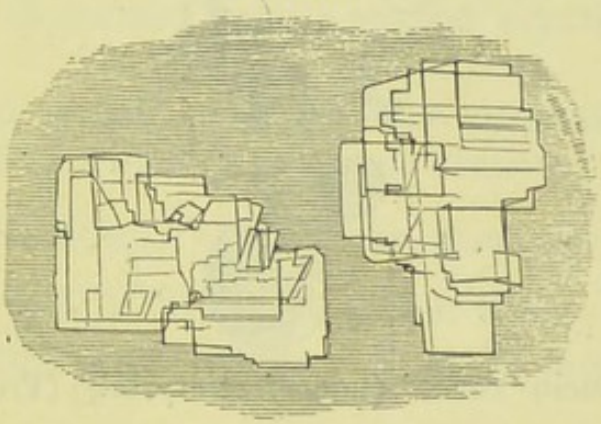
$$C_3H_5\begin{cases}(C_{18}H_{35}O_2)_2\\ O-PO\begin{cases}OH\\ O-C_2H_4-N(CH_3)_3OH.\end{cases}\end{cases}$$

Lecithin is miscible in all proportions in ether, alcohol,

and fats. It swells up in water, of which it can imbibe a large quantity.

Cholesterin may be considered here, although it does not belong to the group of fats. Like lecithin, it is found wherever protoplasm is present, and seems to be an essential constituent of every living cell. It is a monatomic alcohol ($C_{26}H_{43}.OH$). It is easily soluble in ether or hot

FIG. 13.



Cholesterin crystals (Bowman).

alcohol. From the latter it is deposited, on cooling, in typical plate-like crystals, each of which has a corner knocked out. It is insoluble in water, but slightly soluble in a solution of bile-salts. Its history and use in the body are absolutely unknown.

NITROGENOUS DERIVATIVES OF THE PROTEIDS.—Most of these bodies fall into the group of amido-acids. These are organic acids, belonging chiefly, though not exclusively, to the fatty acid series, in which a molecule of hydrogen is replaced by the radical amidogen. Thus glycin or amido-acetic acid is formed from acetic acid $\begin{matrix} CH_3 \\ | \\ COOH \end{matrix}$ by the replacement of a molecule of H by the radical NH_2, forming the body $\begin{matrix} CH_2.NH_2 \\ | \\ CO.OH \end{matrix}$. It occurs in the body in the bile, conjugated with cholalic acid to form glycocholic acid.

Taurin, or amido-isethionic acid, $SO_2\begin{cases} OH \\ C_2H_4.NH_2 \end{cases}$ is found in the bile as taurocholic acid.

FIG. 14.

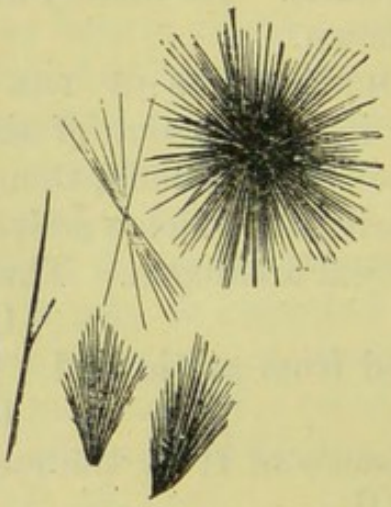


Leucin 'cones' (imperfect crystals) (Frey).

Leucin, or amido-caproic acid, is formed in the pancreatic digestion of proteids.

Tyrosin, which is formed in the same way or by boiling

FIG. 15.



Tyrosin crystals (Frey).

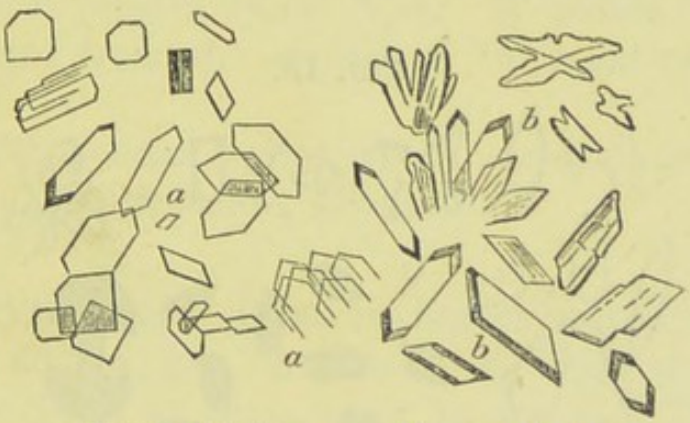
proteids with dilute sulphuric acid, is a compound of amido-propionic acid with an aromatic radical. It may be pre-

pared by evaporating down a solution of proteids which have been acted on for twenty-four hours with pancreatic juice. When the liquid is allowed to cool, crystals of tyrosin separate out. These crystals form slender needles arranged in sheaves or radiating from a centre. The mother-liquor is evaporated to a syrupy consistence, extracted with alcohol, and the extract allowed to stand. As the alcohol evaporates, yellowish-brown spheres, consisting of masses of ill-formed needle-shaped crystals of leucin, separate out.

A solution of tyrosin with Millon's reagent gives a red colour, the tint of which deepens on heating.

Urea, or carbamide, $CO\begin{cases}NH_2\\NH_2\end{cases}$, is isomeric with ammonium cyanate, $(NH_4)CNO$, from which it may be prepared by simply heating with water. It is the most important

Fig. 16. Fig. 17.



Urea nitrate. Urea oxalate.

of all the nitrogenous extractives that we have to deal with, since the greater bulk of the nitrogen produced by the disintegration of proteids leaves the body in the form of urea.

It may be prepared from urine in the following way:—The urine is evaporated to a small bulk ($\frac{1}{6}$), and strong pure nitric acid is added in excess, keeping the mixture cool. Crystals of urea nitrate are

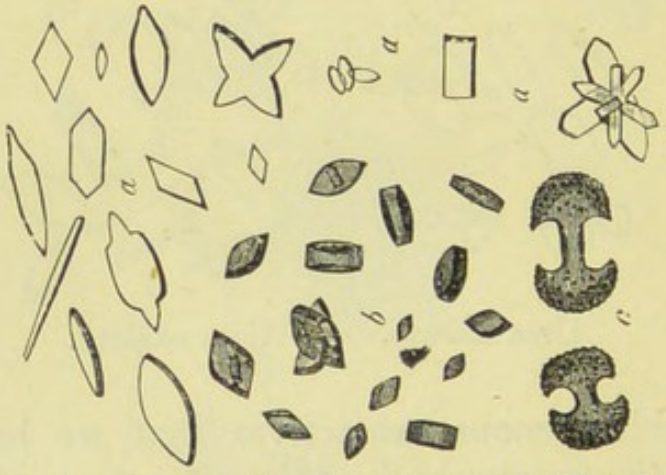
deposited. These are collected and dried between filter-paper, and made into a paste with a large quantity of barium carbonate and spirit. The paste is dried in a water-bath and extracted with alcohol. The alcoholic extract is filtered off and allowed to evaporate, when crystals of urea separate out. These may be redissolved, decolourised by animal charcoal, and allowed to crystallise out once more.

Urea crystallises in four-sided prisms. It is odourless and colourless, readily soluble in alcohol and water. With nitric acid it forms nitrate of urea, which crystallises in octahedra.

Uric acid.—A small amount of nitrogen is constantly excreted in man in the form of uric acid ($C_5H_4N_4O_3$). In birds and reptiles, however, it takes the place of urea, and is the medium for the excretion of the greater part of the nitrogen.

It may be prepared from urine by adding 5 c.c. of hydrochloric acid to 200 c.c. of urine, and allowing the mixture to stand for twenty-four hours. Crystals of uric

FIG. 18.



Various forms of uric acid crystals (Frey).

acid then separate out, which are generally coloured dark red by the urinary pigment. It crystallises in rhombic prisms. It is extremely insoluble in water and acids, but easily soluble in alkalies, with the formation of alkaline

urates. It may be prepared synthetically by heating glycin and urea together, so that it is probably allied in structure to the latter body.

Test for uric acid :—If a little nitric acid be added to some uric acid in a porcelain capsule, and the mixture evaporated to dryness, a yellow residue is obtained, which turns a brilliant purple on the addition of ammonia (*murexide* test).

Creatin is found in fairly large quantities in muscles, and can therefore be easily obtained from Liebig's extract of meat. When boiled with baryta water, it takes up water and gives rise to sarcosin (methyl-glycin) and urea :

$$\underset{\text{Creatin.}}{C_4H_9N_3O_2} + H_2O = \underset{\text{Methyl-glycin.}}{\begin{vmatrix} CH\begin{cases} NH_2 \\ CH_3 \end{cases} \\ CO.OH \end{vmatrix}} + \underset{\text{Urea.}}{CO\begin{cases} NH_2 \\ NH_2 \end{cases}}$$

Creatinin is creatin *minus* H_2O. It occurs in the urine, being formed from the creatin of the meat taken in with the food.

Other nitrogenous bodies which we need only mention, are xanthin, hypoxanthin, allantoin.

CARBOHYDRATES.—These are bodies consisting of carbon, hydrogen, and oxygen, the latter two being present in the same proportions as they exist in water. Their general formula is therefore $C_xH_{2n}O_n$. They may be divided into the following classes.

1. Amyloses.—$(C_6H_{10}O_5)_n$

Starch does not occur in the living body, but constitutes an important foodstuff, being present in large quantities in nearly all vegetable food. It is a white powder consisting of microscopic grains with concentric rings. It is insoluble in cold water. When boiled with water it swells up to

form an opalescent semi-solution. This solution gives an intense blue colour with iodine. On boiling with dilute acids, starch is converted first into dextrin and then into dextrose. With various ferments, such as diastase (malt ferment), salivary or pancreatic ferment, it undergoes hydrolysis, and is converted into dextrin and maltose. The change that occurs on boiling with acids may be thus represented :

$$\underset{\text{Starch.}}{C_6H_{10}O_5} + \underset{\text{Water.}}{H_2O} = \underset{\text{Dextrose.}}{C_6H_{12}O_6}.$$

Glycogen, or animal starch, is found in the liver, muscles, and other tissues of the body, and occurs in especially large quantities in all fœtal tissues. It is a white powder, soluble in cold water, forming an opalescent solution. With iodine it gives a mahogany-red colour. It is affected by acids and ferments in the same way as starch. It is precipitated from its solution on the addition of alcohol to 60 per cent.

Dextrin.—Two varieties of this body may be distinguished according to their reaction with iodine—erythrodextrin, which gives a red colour with iodine ; and achroodextrin, which gives no colour.

It is said to occur in small quantities in blood, muscle, and liver, but it is chiefly of importance as being an intermediate product in the digestion of starch. It is gummy and amorphous, readily soluble in water, but insoluble in alcohol and ether. On boiling with acids it is converted into dextrose.

Cellulose is the colourless material which composes the cell-walls and woody fibre of plants, and so occurs to a large extent in our food. In man, however, it does not undergo digestion, and therefore need not be further considered here.

2. Sucroses or Saccharoses.—$C_{12}H_{22}O_{11}$

The most important member of this group is *cane-sugar* which takes a prominent place in our dietary. It is crys-

talline, and easily soluble in water. On boiling with dilute mineral acids, or under the action of certain ferments, it undergoes inversion, taking up one molecule of water, and splitting into dextrose and lævulose.

$$\underset{\text{Cane-sugar.}}{C_{12}H_{22}O_{11}} + H_2O = \underset{\text{Dextrose.}}{C_6H_{12}O_6} + \underset{\text{Lævulose.}}{C_6H_{12}O_6}.$$

Under the action of the yeast fungus, cane-sugar is first inverted, and the invert-sugar is then converted into alcohol with the ebullition of CO_2.

$$C_6H_{12}O_6 = \underset{\text{Alcohol.}}{2C_2H_6O} + 2CO_2.$$

Cane-sugar does not reduce alkaline solutions of cupric hydrate, such as Fehling's solution.* When warmed with sulphuric acid it turns black.

Lactose or *milk-sugar* occurs in milk. It is much less soluble in water than cane-sugar, and is only faintly sweet. It reduces Fehling's solution. On boiling with dilute acids it takes up water, and is converted into dextrose and an isomeric sugar known as galactose.

$$\underset{\text{Lactose.}}{C_{12}H_{22}O_{11}} + H_2O = \underset{\text{Galactose.}}{C_6H_{12}O_6} + \underset{\text{Dextrose.}}{C_6H_{12}O_6}.$$

With the lactic acid organism it is converted into lactic acid. To this conversion of lactose into lactic acid is due the souring of milk.

$$\underset{\text{Lactose.}}{C_{12}H_{22}O_{11}} + H_2O = \underset{\text{Lactic acid.}}{4C_3H_6O_3}.$$

Maltose is the end-product of the action of diastase, sali-

* Fehling's solution is made by dissolving copper sulphate in water, and adding to it a mixture of solutions of sodio-potassium tartrate and caustic soda. The presence of the tartrate prevents the cupric oxide from being precipitated. The proportion of the ingredients is so arranged that 10 c.c. of the solution are totally reduced by ·05 grm. of dextrose.

vary or pancreatic ferment on starch. It reduces Fehling's solution, and is converted on boiling with dilute mineral acids into dextrose.

3. Glucoses.—$C_6H_{12}O_6$

Dextrose or *grape-sugar* is found in small quantities in the blood and numerous tissues of the body, and is the form to which all carbohydrates are converted before they reach the circulation. It is easily soluble in water and alcohol, reduces Fehling's solution, and gives a brown colour when heated with strong caustic potash. It rotates the plane of polarised light to the right.

Lævulose is a constituent of fruit-sugar and invert-sugar. It gives the same tests as dextrose, except that it rotates the plane of polarised light to the left.

Galactose we have already mentioned as being produced by the action of hydrating agents on lactose. It reduces Fehling's solution.

Inosit or *muscle-sugar* is found in minute quantities in muscles and other organs of the body. Its solutions have no action on polarised light, and do not reduce Fehling's solution.

Although inosit has the same elementary formula as grape-sugar, and is therefore considered here, it is not a member of the carbohydrate group at all, but belongs to the aromatic series.

All the sugars, like all aldehydes and ketones, when boiled with phenylhydrazine ($C_6H_5NH.NH_2$) and acetic acid, give rise to more or less insoluble crystalline compounds known as osazones. The form and melting-point of these crystals afford an important means of isolating or recognising the variety of sugar present in a solution.

CHAPTER III

BLOOD AND LYMPH

We have seen that the blood, which circulates through all parts of the living body, coming into close relationship with all the tissues, acts as a medium of communication between the cells in the interior of the body and those on the surface, carrying the absorbed foodstuffs which have been taken up by the cells lining the alimentary canal to all the other cells of the body, and from these receiving in exchange their waste products, CO_2 and urea, or some precursor of these substances, to discharge them through the intermediation of excretory cells on the surface or lining involutions of the outer surface of the body, such as the skin, kidney, and lungs.

It is evident that the composition of the blood must be always varying, according to the nature of the tissues it has just traversed, and these variations will be more fitly considered when we come to the discussion of the activities of the various tissues. But we find that the blood has a certain power of regulating its composition, or perhaps this function must be ascribed to the various tissues through which the blood passes. However this may be, the fact remains that the blood has an average composition which it is our duty in this chapter to describe, and round which its composition only varies to a certain (definite) extent.

The blood of man and most vertebrates is a red liquid, rather viscous, and to the naked eye homogeneous. Arterial blood, *i. e.* the blood in the pulmonary veins, left side of the heart, and the arteries generally, is bright scarlet; while venous blood, *i. e.* blood in the systemic

veins, right heart, and pulmonary artery, is of a brownish-red hue.

Shaking up venous blood with air or oxygen changes it to arterial blood, and we shall see later that the bright colour is due to the formation of a loose combination of one of the constituents of the blood, hæmoglobin, with oxygen. This combination is normally formed in the lungs, and is robbed of its oxygen in the tissues.

On microscopic examination the blood is found to consist of a nearly colourless fluid, the *liquor sanguinis* or blood *plasma*, holding in suspension an enormous number of solid bodies, the *red* and *white blood-corpuscles*.

The colour of the blood is entirely due to the red corpuscles. These are, in man, non-nucleated biconcave discs about $\frac{1}{3200}$ of an inch in diameter, and a third of this in thickness. The colour of a single corpuscle is yellow, the red colour being only apparent when large numbers of them are seen together.

They are soft, flexible, and elastic, so that they can readily squeeze through apertures and canals narrower than themselves without being permanently distorted. Each red corpuscle consists of a framework or *stroma* composed chiefly of proteid material, containing in its meshes, or in a state of loose chemical combination with it, a red colouring matter, hæmoglobin, to which is due the colour of the corpuscles and of the blood itself.

By treating the blood with weak solutions of tannic or boracic acid, a separation occurs between the hæmoglobin and the stroma, the former appearing as a small ball near the centre of a colourless blood-disc, or the hæmoglobin may be extruded and lie just outside the stroma. If the plasma be made denser by evaporation, or by addition of salts to it, water diffuses from the corpuscle into the plasma, and the corpuscle shrinks and becomes wrinkled or *crenated*. If, on the other hand, the plasma be diluted, water diffuses from the surrounding medium into the corpuscle, which swells up and becomes spherical.

There are about five million red corpuscles in a cubic millimetre of blood.

In birds, amphibia, and fishes, the red corpuscles differ from those of mammals in being nucleated. Those of the frog, for instance, are oval structures, each containing an oval nucleus with a well-marked nuclear network. The hæmoglobin is diffused through the protoplasm of the cell-body, and does not extend to the nucleus. Mammals during the early part of their fœtal life also possess nucleated red corpuscles. These, however, soon disappear entirely, to make way for the ordinary non-nucleated red discs. In the camel the red corpuscles are oval in shape like those of the frog, but possess no nucleus. They are also much smaller than those of the frog.

The colourless corpuscles, or *leucocytes*, are rather larger than the red ($\frac{1}{2500}$ inch in diameter), and much fewer in number, there being only one white corpuscle to about 300 to 600 red.

They are colourless nucleated masses of protoplasm very similar to the simple organism described in the Introduction as the amœba. Like this, they have the power of moving from place to place, of taking up food particles, and probably of reproduction by fission.

Several varieties of leucocytes exist in the blood. The most numerous variety presents a nucleus which is lobed or composed of several parts united by fine threads. The protoplasm contains some very fine granules which have only a faint affinity for acid dyes such as eosin.

More sparse are the leucocytes known as 'hyaline.' These possess only a single round or oval nucleus, and their protoplasm is free from granules.

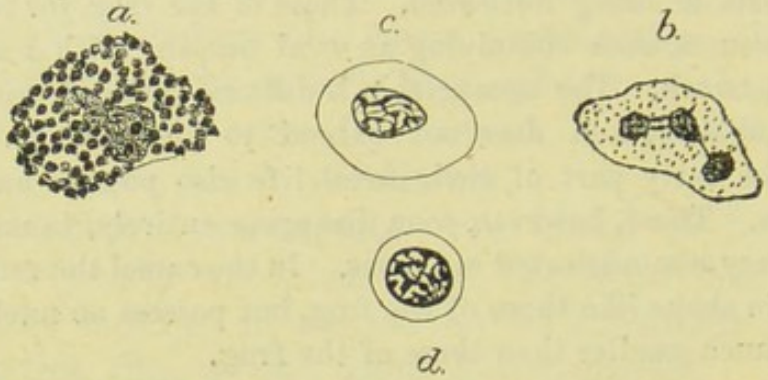
About 10 per cent. of the leucocytes present a mass of coarse highly refracting granules in their protoplasm. These granules stain intensely with eosin and other acid dyes, and are therefore designated eosinophile. The nucleus is lobed or reniform.

The fourth variety represented in the figure is the *lymphocyte*. This consists of a large round nucleus surrounded by a thin layer of hyaline protoplasm. It is derived



from the lymphatic glands, and probably represents an immature form of the hyaline leucocyte.

Fig. 19.



Various forms of leucocytes. *a*. Eosinophile corpuscle. *b*. Ordinary polynuclear leucocyte ('neutrophile'). *c*. Hyaline corpuscle. *d*. Lymphocyte.

Very rarely we find a fifth form of corpuscle containing granules which stain deeply with basic dyes, such as hæmatoxylin or methylene blue, and are therefore called *basophile*.

Besides the red and white corpuscles, a third formed element has been described under the name of blood-platelets. These are small bodies, disc-shaped or irregular, about one quarter the diameter of a red corpuscle, and are always to be observed on examining blood immediately after it has left the body. They have also been called hæmatoblasts, on the assumption that they were precursors of the red blood-corpuscles. It is still doubtful, however, whether these platelets exist as such in normal circulating blood, or whether they are not really a precipitate produced in the plasma as it commences to die or to cool down.

Chemistry of the Red Blood-corpuscles

We have already mentioned that these can be regarded as consisting of two parts, the hæmoglobin and the stroma, probably in a state of loose chemical combination.

By various means it is possible to destroy this combina-

tion and to dissolve out the hæmoglobin, leaving the colourless, swollen-up stroma floating in the plasma. The effect of this is to make the blood darker but more transparent. In this condition it is spoken of as 'laky blood.'

Blood may be made laky by the following means :

(*a*) Addition of a small amount of ether.

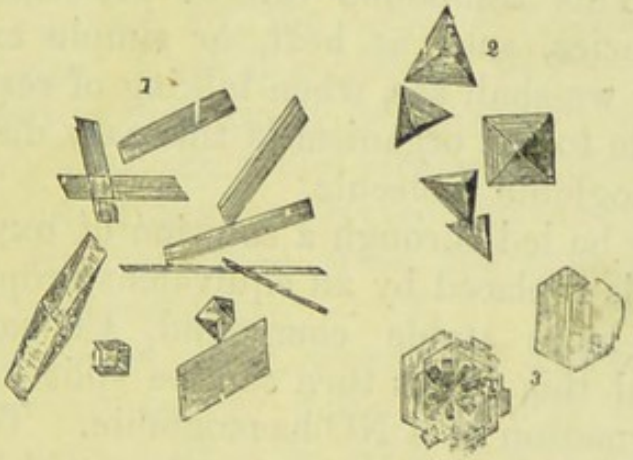
(*b*) Free dilution with water.

(*c*) Alternate freezing and thawing of the blood.

(*d*) Addition of bile salts ; and various other ways.

If this blood be allowed to stand in a cool place for an hour or two, a mass of crystals is deposited, which consist of oxyhæmoglobin. This crystallisation occurs very readily in the blood of some animals, such as the rat and guinea-pig ; much less so in that of others, such as man, rabbit, and sheep.

FIG. 20.



Crystals of oxyhæmoglobin. 1. From rat. 2. From guinea-pig. 3. From squirrel.

Oxyhæmoglobin thus obtained and purified by recrystallisation forms rhombic prisms or tablets of a dark red colour (Fig. 20). It is a compound of a proteid with an iron-containing residue (hæmatin), and is distinguished from all other proteids by the ease with which it crystallises. Its percentage composition probably varies slightly in different animals.

Elementary analysis of hæmoglobin crystals from the blood of the horse gave the following results :

Carbon	51·15
Hydrogen	6·76
Nitrogen	17·94
Sulphur	0·389
Iron	0·336
Oxygen	23·425

The empirical formula for hæmoglobin calculated from this would be—

$$C_{712}H_{1130}N_{214}O_{245}FeS_2.$$

The most important property of hæmoglobin is its power of uniting with a definite proportion of oxygen to form an easily dissociable compound, oxyhæmoglobin. One gram of hæmoglobin will combine with from 1·6 to 1·8 c.c. of oxygen (measured at 0° C. and 760 mm. pressure). This compound can be dissociated again by various agencies, such as heat, or simple exposure to a vacuum, and we shall see, when talking of respiration, how very valuable to the organism is this easy dissociability of the oxyhæmoglobin molecule.

If CO gas be led through a solution of oxyhæmoglobin, the oxygen is replaced by an equivalent proportion of CO, so that a more stable compound, CO-hæmoglobin, is formed; and this in its turn can be split up by NO gas with the formation of a NO-hæmoglobin. Thus the order of stability of these three compounds would be—

NO-hæmoglobin.
CO-hæmoglobin.
O_2 hæmoglobin.

The poisonous properties of CO gas are due to this power it has of turning out the oxygen from the hæmoglobin, thus depriving the tissues of the oxygen which is normally carried to them by the red corpuscles.

Oxyhæmoglobin is a brighter red and slightly less soluble than hæmoglobin. Solutions of the latter are

dichroic, appearing green by reflected and bluish red by transmitted light.

The reduction of oxyhæmoglobin to hæmoglobin is easily effected by various reducing agents, such as ammonium sulphide or Stokes' fluid (an alkaline solution of ferrous tartrate). This change in the colour of the compound is accompanied by a very evident change in its absorption spectrum.

Dilute solutions of oxyhæmoglobin placed in front of the slit of a spectroscope give a very pronounced absorption spectrum, showing two black bands between Frauenhofer's lines D and E.

On adding a few drops of Stokes' fluid to the solution and warming gently, these two bands disappear, and are replaced by a single band, rather fainter and broader than the O_2Hb bands, and situated between them. On shaking the solution up with air, the bands of O_2Hb return, only to disappear again when it is allowed to stand.

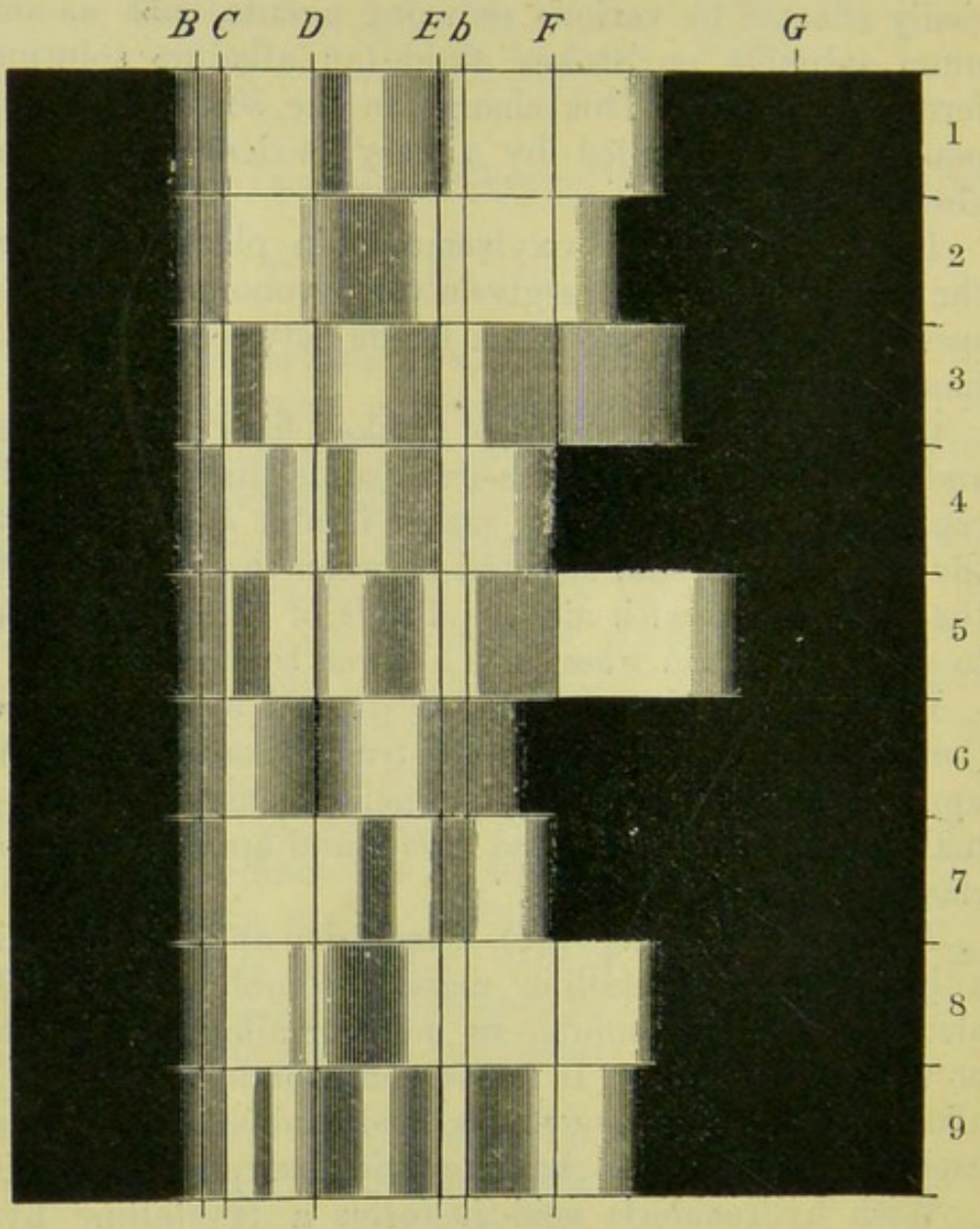
Hæmoglobin is very easily destroyed by various means (heat, alcohol, weak acids, and strong alkalies), being split up into an iron-containing pigment, hæmatin, and a proteid residue, which is called *globin*, and apparently is to be classed with the globulins.

Hæmatin ($C_{32}H_{32}N_4O_4Fe$), when dried and purified, forms a bluish-black crystalline mass, insoluble in water and alcohol, but easily soluble in acids or alkalies in alcoholic or watery solutions. It forms compounds with acids and alkalies, which are known as acid and alkaline hæmatin, each of which gives a characteristic absorption spectrum.

With hydrochloric acid it forms a crystalline hydrochlorate known as *hæmin*. This compound is prepared with extreme ease, and this fact, combined with the very definite appearance of its crystals, renders it a very delicate test for blood.

To prepare hæmin crystals a little dried blood, hæmoglobin, or hæmatin is heated with a minute crystal of common salt and glacial acetic acid, and then allowed to

FIG. 21.



Absorption spectra of hæmoglobin and its derivatives. 1. Oxyhæmoglobin. 2. Reduced hæmoglobin. 3. Methæmoglobin. 4. Alkaline methæmoglobin. 5. Acid hæmatin in ether. 6. Alkaline hæmatin in rectified spirit. 7. Reduced hæmatin. 8. Acid hæmatoporphyrin. 9. Alkaline hæmatoporphyrin. (From MacMunn.)

cool. Hæmin crystallises out, and can be recognised on examination under the microscope. The crystals are dark brown, sometimes nearly black, and present the form of rhombic plates, sometimes arranged in radiating bundles.

Fig. 22.



Hæmin crystals.

Alkaline hæmatin is interesting from the fact that it may be reduced by ammonium sulphide, and reoxidised on shaking with air, just like a solution of O_2Hb. The spectrum of oxyalkaline hæmatin shows one absorption band close to D. Reduced alkaline hæmatin gives two sharp absorption bands, similar to those of oxyhæmoglobin but rather nearer the blue end of the spectrum (Fig. 21).

A body similar to, if not identical with, reduced alkaline hæmatin, *hæmochromogen*, is formed when hæmoglobin is warmed with caustic potash in a vessel from which all air has been driven out by the passage of a stream of hydrogen or other neutral gas.

Other derivatives of hæmoglobin are—

a. Methæmoglobin.—If blood or a solution of oxyhæmoglobin be treated with amyl nitrite or potassium permanganate, it assumes a chocolate-brown colour, and on examination with the spectroscope is found to present a distinct band in the red, between C and D, due to the presence of methæmoglobin. If it is now treated with a few drops of ammonium sulphide, the methæmoglobin is converted into reduced hæmoglobin, apparently passing through a stage of oxyhæmoglobin, in which the two bands of this sub-

stance may be made out with the spectroscope. Methæmoglobin is therefore probably a peroxyhæmoglobin, in which the oxygen is more closely bound to the hæmoglobin molecule than in O_2Hb.

b. Hæmatoporphyrin ($C_{16}H_{18}N_2O_3$), or iron-free hæmatin, is easily prepared by the action of strong sulphuric acid on blood, hæmoglobin, or hæmatin. It forms a deep purple solution with characteristic spectrum in the acid, from which it is precipitated as a black powder on free dilution with distilled water. It is isomeric with bilirubin.

c. Hydrobilirubin ($C_{32}H_{40}N_4O_7$) is produced by the action of tin and sulphuric acid on an alcoholic solution of hæmatin.

d. Hæmatoidin (probably identical with bilirubin) occurs as orange-red rhombic tables in old blood-clots in the body.

The STROMA may be obtained from laky blood by the addition of dilute sulphuric acid or acid sodium sulphate, by which the swollen-up stromata are shrivelled up; they may be collected by allowing the liquid to stand, or by means of the centrifuge. On chemical analysis they are found to consist chiefly of globulins, with small quantities of fats, lecithin, and cholesterin.

Important constituents of the red corpuscles are the salts and water. The salts are chiefly potassium and phosphoric acid compounds, there being very little chlorides present, and little or no sodium (cf. the serum).

The corpuscles contain about two thirds of their total weight of water.

Life-history of a Red Blood-corpuscle

There can be no doubt that a continual destruction of red blood-corpuscles is going on in the body. Thus an animal secretes every day by the agency of the liver a considerable amount of bile, containing a pigment, bilirubin. Now this pigment can be shown to be derived from the hæmoglobin of the red blood-corpuscles. In cases

where an effusion of blood has taken place into the brain or the connective tissues, we often find, some months after the lesion, that the corpuscles and red pigment have disappeared, and that the connective tissue in the vicinity contains a number of yellowish-brown crystals, known as hæmatoidin crystals. These crystals are identical in form, composition, and reactions with bilirubin, the colouring matter of the bile.

Under normal circumstances, however, the conversion of hæmoglobin into bile-pigment, as we shall see later on, takes place exclusively in the liver. It is found that if by the injection of poisons a number of red corpuscles are broken up and destroyed, setting free hæmoglobin in the blood-plasma, there is marked increase in the amount of bile-pigment formed by the liver; and a similar increase may be brought about by the injection of solutions of pure hæmoglobin into the blood. What is the chemical change involved in this conversion?

From a comparison of the formula of hæmatin ($C_{32}H_{32}N_4O_4Fe$) with that of bilirubin ($C_{16}H_{18}N_2O_3$), we see that the change is associated with a loss of iron; and we find, as a matter of fact, that in all cases in which there is an increased *hæmatolysis* (destruction of red corpuscles), there is at the same time an accumulation of iron in the liver. This accumulation is especially well marked in cases of pernicious anæmia. It seems probable that, under normal circumstances, the hæmoglobin is broken up in the liver, part of the hæmatin molecule being transformed into bilirubin and turned out of the body with the fæces, while the iron is stored up in the liver to assist in the formation of fresh hæmoglobin or new red blood-corpuscles.

We have not yet been able in the laboratory to convert hæmatin directly into bilirubin. Iron-free hæmatin, or hæmatoporphyrin, is however very nearly allied to bilirubin, the formulæ of these two bodies being almost identical. We can moreover, by the action of reducing agents, obtain identical products from hæmatin and bilirubin. Thus, by

treating hæmatin with tin and hydrochloric acid, or by acting on bilirubin with sodium amalgam, a body, hydrobilirubin, is produced, which is apparently identical with urobilin, the chief pigment of the urine.

It is evident then that the pigments excreted from the body in the urine and fæces are derived from hæmatin, and therefore that a disintegration of the red blood-corpuscles must be continually taking place.

Since, in a healthy animal, the amount of corpuscles in the blood remains approximately constant, a continual production of new corpuscles must go on to take the place of those destroyed and discharged to form bile and urinary pigments. This new formation is supposed to take place chiefly in the red marrow of the bones. Here we find nucleated cells, the protoplasm of which is coloured with hæmoglobin. The red blood-discs seem to be formed from these cells, either by a budding off of portions of the protoplasm, or, according to some authors, the cells themselves, after division, become converted into red blood-discs by the disappearance of the nucleus.

Similar cells have been observed in the spleen after great loss of blood, and on this account a hæmopoietic function has also been ascribed to this organ. According to others, the red blood-discs are produced in the plasma, the blood-platelets being looked upon as their precursors.

Thus, although we are certain about the fact that blood-corpuscles are being continually destroyed and regenerated, there is considerable doubt as to the exact mode and place in which this regeneration occurs.

In the embryo and new-born animal the steps of the process are known much more definitely.

As I have already mentioned, the red corpuscles at an early stage of fœtal life are nucleated, like those of the frog or bird. In the vascular area of the chick, nests of nuclei are found embedded in colourless masses of non-differentiated protoplasm. A little later it is seen that these nuclei are all surrounded with a differentiated

portion of the protoplasm, which now contains hæmoglobin, the intervening undifferentiated portions having become more fluid, and representing the future blood-plasma. Very soon the masses of protoplasm become channelled and connected with one another and with the large vessels coming from the heart, and the fully formed blood moves on into the general circulation in response to the heart-beat.

Towards the end of fœtal life we find similar branched masses of protoplasm containing nuclei. These nuclei, however, are not wasted on mere oxygen carriers, but are entirely used to form the endothelium of the capillary wall; and non-nucleated red corpuscles are developed by a simple differentiation of the central part of the protoplasmic mass, the parts of the protoplasm between the corpuscles again appearing to furnish the material for the fluid plasma.

We have no evidence to tell us how long a red corpuscle lives, or how long it can carry on its functions before it is broken up in liver or spleen and cast out of the body. Experiments, such as injection of the blood of a bird into a mammal, when the introduced blood-corpuscle can be always identified, naturally give us no idea of the duration of activity of a normal corpuscle.

Since iron is an essential constituent of hæmoglobin, it is evident that our food must contain enough iron to restore the loss of it in the corpuscles. This, however, need be very small, if it were all assimilated, for the whole blood of an average-sized man only contains about 2·5 grms. Fe.

Inorganic forms of iron, such as the iron salts, are however only absorbed in very small quantities, and there is some probability that a good deal of the hæmoglobin is reintegrated from an organic form of iron contained in the food, called hæmatogen—a proteid belonging to the group of nucleo-albumens, and containing iron in a state of intimate chemical combination.

Chemistry of White Blood-corpuscles

The white corpuscles consist chiefly of proteids, which include a body similar to myosin, paraglobulin, and possibly other proteids. The nuclei contain nuclein. The salts are similar to those of the red corpuscle, there being a preponderance of potassium salts and phosphates. They contain in addition lecithin, fats, and glycogen, and nitrogenous extractives.

Origin of White Blood-corpuscles

The various kinds of leucocytes probably differ in their mode of origin. There seems little doubt that the hyaline corpuscle is derived from the lymphocytes, which are found in the lymphatic glands and enter the blood with the lymph-stream by way of the thoracic duct.

Many authorities ascribe a similar mode of origin to the chief or polynuclear leucocyte. These corpuscles occur mainly in the blood, and have been seen in a state of division, so that it is most probable that they reproduce themselves by direct cell-division in the blood-stream itself.

The eosinophile corpuscles are found in large numbers in the connective tissue in various parts of the body. They probably represent a migratory tissue *sui generis* (perhaps of a glandular nature), and are derived from similar cells by division in the blood-stream or in the connective tissues.

Estimation of Blood-corpuscles

In order to count the corpuscles, a known small volume of blood is diluted with some indifferent fluid (such as 1·0 per cent. NaCl solution), and a drop of this placed in a small cell on a glass slide, the bottom of which is ruled with squares. The depth of the cell and the size of

the squares being known, it is easy to count the corpuscles lying on each square under the microscope, and from this to estimate the number present in a cubic millimetre of undiluted blood.

Thus the graduated glass cell in Gowers' hæmocytometer is $\frac{1}{5}$ millimetre deep, and each square is $\frac{1}{10}$ millimetre each way.

5 c.mm. of blood are drawn into a graduated capillary tube, and then blown into a 'mixing vessel' containing sodium sulphate solution (sp. gr. 1025). The mixture is well stirred and a drop placed in the middle of the cell, and the cell covered. In a few minutes the corpuscles have sunk to the bottom of the cell, and rest on the squares. The number of corpuscles in ten squares is counted, and this multiplied by 10,000 gives the number of corpuscles in a cubic millimetre. In normal blood there are from four to five million corpuscles in a cubic millimetre (*i. e.* an average of forty or fifty to each square of Gowers' instrument).

Estimation of Hæmoglobin.

To estimate the amount of hæmoglobin in a given sample of blood, 20 cubic mm. are taken and diluted with water, until the mixture is equal in tint to a permanent standard coloured solution, made with glycerin and carmine and corresponding in tint to blood diluted 100 times (Gowers' hæmoglobinometer). Thus, the number of times the blood must be diluted to bring it to a standard tint divided by 100 gives the percentage amount of hæmoglobin present, the normal amount being taken as 100.

In von Fleischl's hæmoglobinometer the specimen of blood is always diluted to the same extent; but the standard of comparison is a wedge of coloured glass, which can be slipped to and fro till its tint exactly equals the tint of the sample of diluted blood placed in a glass cell by the side of the wedge for comparison. The sliding

wedge is graduated to indicate the percentage amount of hæmoglobin present compared with normal. Thus, if the tint of the blood is equal to the wedge at 100, the blood contains the normal amount of hæmoglobin ; if at 50, half that amount, and so on.

Coagulation

The most striking property of blood is that of clotting when it is shed. If blood be drawn from an artery or vein into a vessel, in from two to three minutes it becomes rather viscid. This viscidity increases till the whole mass of blood solidifies to form a jelly-like mass, exactly occupying the volume of the original fluid blood.

After about an hour, yellowish drops exude from the surface of the clot, and this exudation continues till the clot has shrunk to half its former dimensions, and floats in a clear yellow fluid (the serum).

Thus, as a result of standing, the blood has been resolved into solid clot and fluid serum. On examining the clot under the microscope, we find that it consists of all the corpuscles enclosed in a meshwork of fine fibrils.

If, however, directly the blood is drawn, it be whipped with a bundle of twigs, or anything presenting a large rough surface, the latter becomes covered with a stringy mass, and we find that the blood has lost its power of setting to form a jelly. This stringy mass is called fibrin, and it is evident that the coagulation of the blood is due to the appearance in it of these fibrils of fibrin, which form a network enclosing in its meshes the corpuscles and the remaining fluid part of the blood. This network then contracts, squeezing out the fluid, which appears on the surface of the clot as the serum.

Fibrin obtained by whipping fresh blood, or by washing away the corpuscles from a clot, exhibits the following properties :

It is insoluble in water or in dilute saline solutions. In stronger solutions, such as 10 per cent. potassium nitrate, it is very slowly dissolved, but is altered in the process, the solution containing not fibrin, but proteids belonging to the globulin class.

It swells up in dilute HCl (·2 per cent.), and if digested with it at a temperature of 40° C. slowly dissolves, with the formation of acid albumen or syntonin. If shreds of fibrin are suspended in water and heated to boiling, they are converted into coagulated proteid, losing the property of swelling up in dilute HCl.

The general reactions and constitution of fibrin show that it belongs to the class of proteids.

We have now to consider the processes which lead to the formation of fibrin in shed blood. In order to analyse these processes it is necessary to slow the process of coagulation.

Clotting is favoured by the following influences:

Exposure to high temperature (up to 50° C.).

Contact with foreign surfaces (as when it is whipped with a bundle of twigs).

It is retarded or prevented by—

Exposure to cold (blood may be kept fluid almost indefinitely at a little above 0° C.).

Mixture with various salts, such as magnesium or sodium sulphate, or common salt. The blood is received into one third its volume of a saturated solution of magnesium sulphate.

Injection of albumoses (peptone) or of leech extract (also an albumose) into the veins before the blood is drawn.

Contact with the lining membrane of a living blood-vessel. Thus if we ligature the jugular vein in a horse at two points, the blood in the intervening part will remain fluid for many hours. In fact, two such "living test-tubes" may be prepared, and the blood poured in a thin stream from one to the other without coagulating.

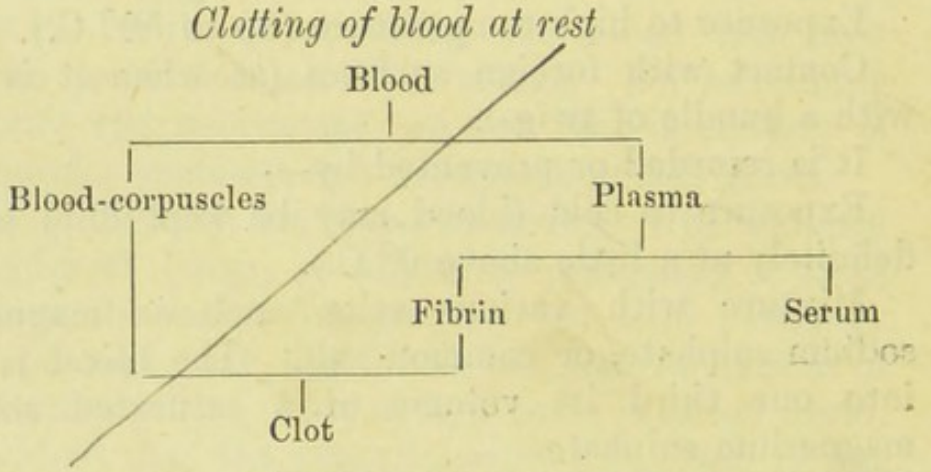
If blood which has been prevented from coagulating by one of these methods be allowed to stand in a cool place, the blood-corpuscles, which are heavier than the plasma, gradually sink to the bottom, leaving a clear supernatant layer of plasma, which can be pipetted or siphoned off.*

Plasma prepared in this way perfectly free from formed elements can be easily made to clot. Cooled plasma clots directly its temperature is allowed to rise; salt-plasma on simple dilution; peptone-plasma on dilution and passage of a current of CO_2.

The clot formed is colourless, and contracts after formation just like the clot formed in the whole blood. It only differs from the latter in containing no corpuscles; in fact, it is pure fibrin.

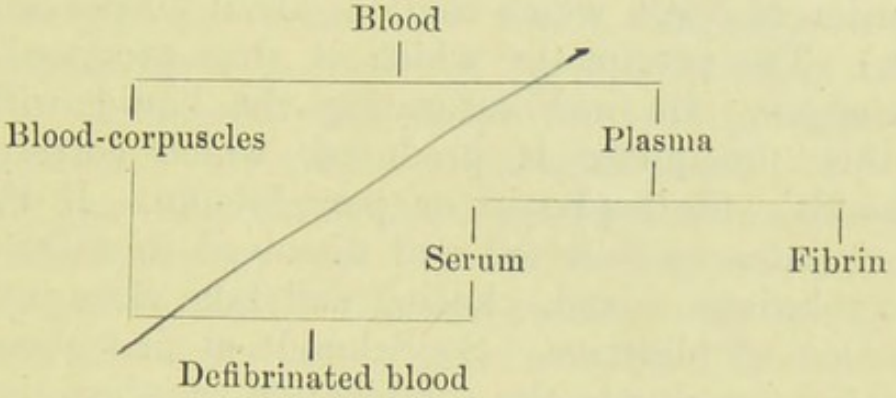
Hence it is evident that the *blood-plasma contains within itself the precursors of fibrin.*

We may therefore represent the processes occurring in coagulation schematically as follows:



* This process is much shortened by using a centrifugal machine. This consists essentially of a horizontal wheel, with slots cut in it in which tubes are suspended. These tubes are filled with the blood, and the wheel made to revolve about 2000 times per minute. The tubes swing out to a horizontal position, and the centrifugal force causes all the heavier particles to collect at the ends of the tubes, so that in half an hour the blood-corpuscles form a compact mass at the bottom of the tubes.

Clotting of whipped blood



What are these precursors? If plasma prepared in either of the foregoing methods be saturated with common salt, a sticky white precipitate is produced. This may be collected on a filter and washed with saturated salt solution to remove all traces of adhering plasma. If we dissolve this substance in dilute salt solution, the solution (at the ordinary temperature) soon becomes viscid and clots, the clot after a while contracting and separating out a serum, which is found to contain a proteid belonging to the globulins. Denis, the discoverer of this precipitate, called it *plasmine*, and supposed that clotting consisted essentially in a splitting up of this simple soluble body into two bodies, one of which was insoluble (fibrin) and the other soluble (serum globulin).

Later on Alexander Schmidt found it possible to separate this plasmine into two substances, which he called fibrinogen and fibrinoplastin. The separation may be effected in either of the two following ways.

Plasma is diluted with ten times its volume of ice-cold water, and a stream of CO_2 passed through it for several hours. A white precipitate, which is thus produced, consists of fibrinoplastin or paraglobulin. If the plasma is still further diluted and the stream of CO_2 continued, fibrinogen is precipitated. The separation, however, is much better effected by a modification of Denis' original method.

Common salt is added to the plasma till it reaches 15 per cent. (This is better effected by adding to each

volume of the plasma an equal volume of a saturated solution of NaCl, which contains about 30 per cent. of the salt.) The precipitate which is thus produced is pure fibrinogen. On now saturating the liquid with salt a further precipitate is produced, which corresponds to Schmidt's fibrinoplastin or paraglobulin. If these two precipitates be collected and dissolved in water, and the two solutions mixed, clotting will take place just as in a solution of plasmine. So Schmidt at first thought that clotting was due to the combination or interaction of two proteids, which together yielded fibrin.

In many cases, however, it is possible to prepare pure solutions of fibrinogen and paraglobulin which when added together have no power of clotting, although the mixture will clot rapidly if a little ordinary serum or blood, or the washings of a blood-clot, be added. In fact, one is constantly seeing this experiment performed in the wards of a large hospital. Nearly all pathological effusions into the large serous cavities, especially the pleural cavity and the tunica vaginalis, contain these two proteids. If a pleuritic effusion be removed by tapping, it is almost invariably noticed that the first portions which are mixed with blood, clot rapidly and firmly, while the later portions which are quite colourless, either do not clot at all or at most very late, and then only imperfectly.

Hence it is evident that a third substance is necessary to clotting, and that this substance is only sometimes present in the precipitates obtained in plasma, but is invariably present in blood after it has clotted, and in serum. Schmidt showed that this substance partook of the nature of a ferment; that is to say, a very small quantity of it was able to effect the conversion of fibrin factors into fibrin, without itself being altered or used up in the process. So his theory of blood-clotting in its amended form was—Fibrin is produced in shed blood by the interaction of fibrinogen and paraglobulin (or fibrinoplastin) under the influence of a ferment.

Hammarsten has shown, however, that paraglobulin is not necessary to the formation of a clot, and, according to this observer, fibrin is produced by the action of fibrin ferment on fibrinogen, which is split up to form fibrin and a soluble proteid very similar to paraglobulin.

A fairly pure solution of the fibrin ferment may be prepared in the following way. Serum, or chopped-up blood-clot, is allowed to stand with about twenty times its volume of absolute alcohol for two or three months. The proteids by this means are precipitated and rendered insoluble in water, so that an aqueous extract of the dried precipitate contains very little proteid matter, but is rich in fibrin ferment; that is to say, it possesses the power of converting solutions of fibrinogen into fibrin; for we can never recognise ferments except by their action.

What is the origin of this fibrin ferment? It is not present in the circulating blood, but is formed after the blood has left the vessels. If blood be received straight from an artery into a large quantity of absolute alcohol, and the precipitate extracted with water after two or three months, the extract is not found to have any power of causing clotting in solutions of fibrinogen.

Schmidt was of opinion that the colourless corpuscles break down as soon as they leave the vessels and liberate the ferment. If horse's blood be received into a vessel placed in ice, and allowed to stand, it soon separates into three layers: an upper layer of pure plasma, a thin layer of leucocytes and granules, and a layer of red corpuscles. If the temperature of the blood be allowed to rise, it clots throughout, but the clotting begins soonest in the layer of leucocytes, and is firmest there. If the clot be divided into three portions, and treated for the extraction of ferment, the extract from the part of the clot enclosing the leucocytes and granular matter is much more active than that from either of the two ends of the tube. Of course the significance of this experiment depends on the view we take of the origin of the granular matter.

Schmidt looked on it as the *débris* of exploded corpuscles, while Wooldridge regarded it as a precipitate produced by the effect of cold on the plasma. This latter observer therefore considered that the ferment was produced, not from the leucocytes but from the plasma, and that in fact the plasma contained all the fibrin factors.

According to the views just enunciated, the clotting of the blood would seem to be a fairly simple process. The circulating blood-plasma contains fibrinogen, a proteid belonging to the class of globulins, and coagulating at 56° C. When the blood leaves the vessels, fibrin ferment is formed, either by the breaking up of the white blood-corpuscles, or in consequence of changes taking place in the blood-plasma, and the ferment thus produced acts on the fibrinogen, altering this into an insoluble proteid—fibrin. There are, however, many difficulties in the way of accepting this hypothesis. If the blood-plasma contained fibrinogen which clots with fibrin ferment, one would expect, on the injection of a solution of fibrin ferment into the veins, to obtain intravascular clotting. This, however, does not happen, injections of solutions of pure fibrin ferment being quite innocuous for animals. In this respect the intravascular plasma resembles plasma obtained from blood which has been prevented from clotting by the injection of peptone. On the other hand, intravascular clotting can be brought about by the injection of extracts of cellular tissues, the active ingredients of such extracts being those described earlier as tissue-fibrinogens or nucleo-albumens. Now these substances also cause clotting when added to peptone plasma, but have no action on diluted magnesium sulphate plasma, or on pure solutions of fibrinogen. It is evident, then, that peptone plasma much more nearly resembles intravascular plasma than do the salt plasma, and the various exudations which were studied by the earlier observers; and this form of plasma was therefore used in a long series of researches carried out by Wooldridge.

Peptone plasma, perfectly free from all formed elements, although incoagulable, can be made to clot by simple means, such as free dilution and passage of CO_2, *i. e.* without the addition of any fibrin factor; after clotting has taken place, both clot and serum are found to contain fibrin ferment, which is therefore formed *in the process of clotting*. This modified coagulability can be entirely abolished by cooling the plasma for some time to 0° C. Under these circumstances a precipitate is formed, consisting of discoid granules. After this precipitate has been separated off, the supernatant fluid still contains somesubstance which may give rise to fibrin, but this changeinto fibrin only occurs on the addition of substances such as tissue-fibrinogen or leucocytes. It seems, therefore, that the power of peptone plasma to coagulate on simple dilution is due to the presence of the body precipitable by cold, and Wooldridge concluded that the chief event in clotting consisted in an interaction between the body precipitable by cold, which he named A. fibrinogen, and the proteid remaining in solution (B. fibrinogen), the process of coagulation being normally inaugurated by the changes occurring in A. fibrinogen. Both A. and B. fibrinogen may be precipitated by the addition of common salt, thus resembling Hammarsten's fibrinogen described above. They differ, however, from this fibrinogen in giving a precipitate on gastric digestion, and also in the fact that fibrin ferment has no action on them. If these bodies are precipitated by common salt, and redissolved two or three times in order to purify them, it is found that they have undergone a marked change. They now no longer give a precipitate on gastric digestion; they are unaltered by the addition of leucocytes or tissue-fibrinogen, but clot on the addition of fibrin ferment. In the process of 'purification' they have been altered. According to this view, the earlier observers, and especially Hammarsten, were studying only the end stages in a complicated process. In coagulation we have the passage from life to death of the plasma. The

approximate constituents of the living plasma, just like those of the living cells, consist of highly complex proteids, giving the general reaction of nucleo-albumens. When the blood leaves the vessels, or loses its intimate continuity with the living endothelial wall, chemical interactions take place between these principles, resulting in a complete splitting off of the phosphorised part of the molecule, and probably in the production of the fibrin ferment and a comparatively simple form of fibrinogen; these interact with the production of fibrin.

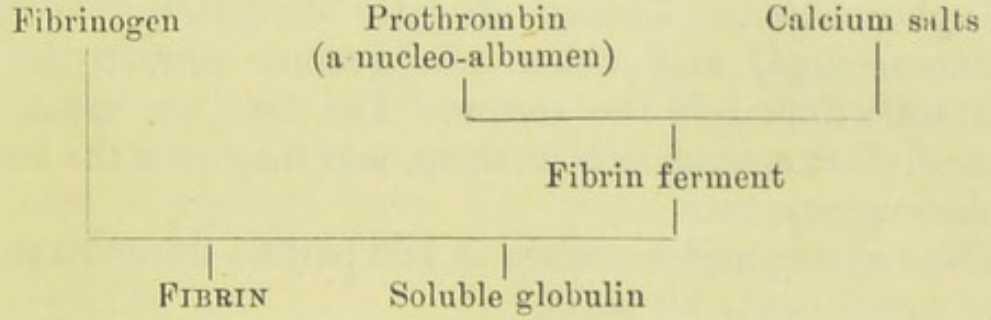
Certain histological observations support this view, that coagulation is normally inaugurated by the disc-like precipitate, called by Wooldridge A. fibrinogen, and which appears to be identical with the blood-platelets of other authors. If a small vessel be observed under the microscope, and a small part of the lining endothelium injured, it is noticed that blood-platelets are deposited on the injured spot, so as to form a little heap. The platelets seem to fuse into one another, and finally form a little white mass of fibrin (white thrombus), which effectually occludes any opening in the wall of the vessel. This process in the living body always occurs when a vessel is injured, and is a means by which the animal is protected from bleeding to death from any small wound.

There is one important factor in clotting which we have not yet mentioned, and that is the presence of lime-salts. If blood be received direct from the vessels into a weak solution of potassium oxalate, so that the blood contains 1 per mille of this salt, it will not coagulate. If, however, excess of some calcium salt, such as calcium sulphate, be added, clotting takes place rapidly.

It was at first thought that in this case the chemical changes go on in the plasma up to the formation of a soluble fibrin, which, however, needs the presence of a lime-salt for its separation in the insoluble form which we generally know as fibrin (Arthus).

It has been recently shown by Hammarsten, however,

that fibrinogen can be converted by fibrin ferment into fibrin, even in the presence of an excess of oxalates; so that it seems certain that fibrin is not merely a combination of fibrinogen with calcium salts. On the other hand, fresh plasma (including oxalate plasma) contains a precursor of fibrin ferment, which has been called *prothrombin*. This prothrombin is precipitated by the action of cold, and is a nucleo-albumen, apparently identical with the body called by Wooldridge A. fibrinogen. On adding prothrombin to a pure solution of Hammarsten's fibrinogen, no clotting takes place If, however, some soluble calcium salts be present clotting takes place. It seems, therefore, that calcium salts are necessary for the production of *fibrin ferment* from the nucleo-albumen known as prothrombin. The chemical changes which, according to Hammarsten, are involved in the clotting of blood, may be represented by the following schema:



Whether the fibrinogen and prothrombin are present in the circulating plasma as such, or are only formed after the blood is shed, by the disintegration of the plasma, or, in part, of the white corpuscles, must be left at present an open question.

Main Points in the Composition of the Blood

Specific gravity of whole blood about 1055;* of corpuscles about 1085; of serum about 1035.

* The specific gravity of the blood may be estimated clinically in the following way:—A series of mixtures of glycerin and water are prepared, with specific gravities varying from 1030 to 1070. A drop

The blood is slightly alkaline.

This is best demonstrated by placing a drop on a piece of delicate glazed litmus paper, and then wiping it off. The spot where the blood rested is found to be stained blue.

Blood contains from one third to half its weight of corpuscles. The plasma is resolved by clotting into serum and fibrin. The serum contains in 100 parts—proteids (consisting of serum-albumen and paraglobulin) 8 parts; salts about 1 part; water about 91 parts.

The paraglobulin and serum-albumen occur in varying proportions. The proportion of paraglobulin to albumen in one case was 1 : 1·5 (man).

The chief salt present is sodium chloride, which constitutes 60 per cent. of the ash. Next to this comes sodium carbonate (about 30 per cent.), and besides these two we find traces of potassium, sodium, and calcium chlorides and phosphates. Traces of fats, cholesterin, lecithin, dextrose, urea, and other nitrogenous extractives are constantly found in the serum. The fats are much increased after a meal rich in them, and may give the serum a milky appearance.

The red corpuscles contain in 100 parts—water 70 parts, solid constituents 30 parts.

Of the solid constituents, hæmoglobin forms nine tenths; the other tenth corresponds to the stroma, consisting of globulins, lecithin and cholesterin, and salts. There is a striking contrast between the salts of the corpuscles and those in the serum; the former consisting chiefly of

of blood is then sucked up into a capillary pipette with its point bent to a right angle, and minute portions of this drop are expelled into a series of glasses containing glycerin and water mixtures of various strengths. The red drop expelled from the pipette will rise or sink in the fluid so long as its specific gravity differs from that of the fluid. The specific gravity of the mixture in which the blood neither rises nor sinks is equal to that of the blood, and is the number we want to know.

potassium phosphate, the latter of sodium chloride, which may be almost or entirely wanting from the corpuscles.

The Quantity of Blood in the Body

From a few observations on executed criminals it has been determined that the amount of blood in the human body forms about one thirteenth of the body-weight. Such is the delicate balance between the blood in the vessels and the tissues that this amount remains approximately constant. Thus, if the blood be increased by injection of saline fluids or water, although at first its specific gravity diminishes, showing that its quantity is increased by the injected fluid, this increase soon passes off, and the blood is restored, often in a few minutes, to its normal condition. The excess of fluid is got rid of partly by the kidneys (giving rise to a profuse secretion of watery urine), but it also is largely taken up by the tissues, which become more watery and swollen in consequence. The ability of the tissues to take up the superfluous fluid is shown by the fact that this disappears from the blood, even when both kidneys are cut out of the circulation by ligature of the renal arteries.

On the other hand, a deficiency of blood, brought about by small bleedings, is soon remedied by a transfer of fluid from the tissues to the blood, probably through the intermediation of the lymph.

The blood is said to be distributed as follows :

In heart, lungs, and large vessels . .	one fourth
In liver	,,
In skeletal muscles	,,
In other organs	,,

This computation is, of course, very roughly estimated ; and the distribution of blood varies enormously, according to the condition of the animal and the state of activity of its various organs.

Relations of the Blood to the Tissues

It is only in the spleen that the blood comes in actual contact with the living cells of the tissue. In all other parts of the body the blood flows in capillaries with definite walls consisting of a single layer of cells, and is thus separated from the tissue-elements by these walls and by a varying thickness of tissue. In some organs, such as the liver and lung, every cell is in contact with the outer surface of some capillary; while in others, such as cartilage (which is quite avascular), a considerable thickness of tissue may separate any given cell from the nearest capillary. A middleman is thus needed between the blood and the tissues, and this middleman is the *lymph* which fills spaces between all the tissue-elements, so that any tissue can be regarded as a sponge soaked with lymph.

These spaces, which have an incomplete lining of endothelial cells, are connected with definite channels—lymphatics, by which any excess of fluid in the part is drained off. The lymphatics all run towards the chest,

FIG. 23.

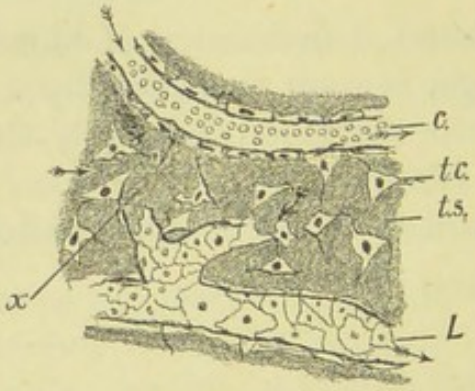


Diagram to show origin of lymphatics in connective-tissue spaces. *c.* Blood-capillary. *t.c.* Tissue-cell. *t.s.* Tissue-spaces filled with lymph, *x*. L. Lymphatic capillary.

where those of the limbs join a large vessel (the receptaculum chyli), which carries the lymph from the alimentary

canal to form the thoracic duct. This runs up on the left side of the œsophagus, to open into the great veins at the junction of the left internal jugular with the subclavian vein. A small vessel on the right side drains the lymph from the right upper extremity and side of the chest.

Thus the lymph may be looked upon as a part of the plasma which exudes through the capillary wall, bathes all the tissue-elements, and is collected by lymphatics into the thoracic duct, by which it is returned again to the blood.

It is easy to obtain lymph for examination by putting a cannula (a small tube of glass or metal) into the thoracic duct, and collecting the fluid that drops from it in a glass vessel.

We may also tap in a similar way one of the large lymphatic trunks of the limbs; but in the latter case we have to use artificial means to induce a flow of lymph, since little or none can be obtained in a normal animal from a limb at rest, the only part of the body where there is normally a constant flow of lymph, being the alimentary canal. And thus we see we cannot look upon the flow of lymph from a part as any index of the chemical changes going on at that part. In a limb at rest food-stuffs are being taken up from the blood and being burnt up by the muscles, with the production of CO_2, although we may not be able to obtain a drop of lymph from a cannula in one of the lymphatics.

The lymph is thus truly a middleman; as any substance, oxygen or foodstuff, is taken up by a tissue-cell from the lymph surrounding it, this latter recoups itself at once at the expense of the blood.

Thus there would seem to be no need for lymphatics to drain the limb, were it not that under many conditions, which we shall study directly, the exudation of lymph from the tissues is so excessive that, were it not carried off at once and restored to the blood, it would accumulate in the tissue-spaces, giving rise to dropsy, and by pressure on the cells and blood-vessels affect them injuriously.

Properties of Lymph

Lymph obtained from the thoracic duct of an animal varies in composition and appearance, according to the condition of the animal, whether recently fed or fasting. From a fasting animal the lymph is a transparent liquid, generally slightly yellowish, and sometimes reddish from admixture of blood-corpuscles. When obtained from an animal shortly after a meal, it is milky from the presence of minute particles of fat that have been absorbed from the alimentary canal. In the latter case, if the intestines be exposed, the small lymphatics are to be seen as white lines running from the intestine to the attached part of the mesentery. It is owing to this fact that these lymphatics have received the special name *lacteals*, the lymph in them being called the *chyle*. The fatty particles form the *molecular basis* of the chyle.

On microscopic examination the transparent lymph of fasting animals presents colourless corpuscles similar to those of blood, or perhaps we ought to say identical, since the leucocytes of the blood are probably derived from the corpuscles that have entered with the lymph through the thoracic duct.

All the lymphatic ~~glands~~ pass at some point of their course through lymphatic glands, which we may look upon as factories of leucocytes, since these are much more numerous in the lymph after it has traversed the gland than before. Leucocytes are also found in all the numerous localities where we find adenoid tissue, the tonsils, air-passages, alimentary canal (Peyer's patches and solitary follicles), Malpighian bodies of the spleen, and thymus.

The lymph is alkaline, has a sp. gr. of about 1015, and clots at a variable time after it has left the vessels, forming a colourless clot of fibrin, just like plasma. It contains about 6 per cent. of solid matters, the proteids consisting of fibrinogen, paraglobulin, and serum-albumen.

The salts are similar to those of the liquor sanguinis, and are present in the same proportions.

The flow of lymph is increased during muscular exercise or passive movements of the limbs. It is not altered in amount by digestion. The amount of lymph produced in any part depends on two factors, viz.—

1. The pressure at which the blood is flowing through the capillaries.

2. The permeability of the capillary wall.

The latter factor varies enormously in different regions of the body. The permeability is greatest in the capillaries of the liver, least in those of the limbs, so that an intracapillary pressure, which would cause a flood of lymph to transude through the hepatic capillaries, is without effect on the lymph production in the limbs.

We can therefore increase the flow of lymph in two ways. We may send up the intracapillary pressure, either locally as by ligature of the veins of an organ, or generally as by injection of a large amount of fluid into the circulation, or by injection of substances into the blood such as sugar and salt, which attract water from the tissues into the blood, so increasing the volume of the circulating fluid and raising the pressure in the capillaries.

On the other hand, we may increase the permeability of the capillary wall by injuring its vitality. We may thus produce a local increase of lymph flow by scalding the part, so giving rise to an inflammatory œdema; or we may cause a general increase in permeability by injecting certain poisonous substances, such as peptone, leech extract, decoction of mussels, &c. These latter bodies act chiefly on the capillaries of the liver.

Curare appears to have a similar action on the limb capillaries.

The substances which on injection into the blood give rise to increased lymph production have been named lymphagogues by Heidenhain, who first drew attention to their action.*

* This observer gives a somewhat different interpretation of their mode of action from that just described.

Emigration of Leucocytes

Besides this transudation of lymph from the vessels, it is probable that at all times some white corpuscles wander through the vessel wall into the surrounding tissues.

If any part of the tissue be injured or destroyed by some irritating lesion, this migration is much increased, and the tissue becomes infiltrated with leucocytes. These emigrated leucocytes have the power of taking up many irritant materials, such as bacteria or any bits of dead tissue, so that the other cells of the tissue are left free to proliferate and regenerate the part lost.

This power of leucocytes to take up foreign particles is probably of immense service to the organism in its strife with the environment. So we find that, wherever any surfaces are peculiarly exposed to infection by micro-organisms or inorganic particles, as in the air-passages and alimentary canal, there is, just under the delicate surface layer of cells, an almost continuous layer of adenoid tissue, in which leucocytes are formed ; and these leucocytes are always found enclosing bacteria (in the alimentary canal), or particles of dust or soot (in the air-passages).

In fact, the leucocytes may be looked upon as the scavengers of the body, devouring and destroying deleterious objects which have accidentally effected an entry. Their possible *rôle* in the absorption of fat need only be mentioned in this chapter.

CHAPTER IV

THE CONTRACTILE TISSUES

THE means by which the organism acts on its environment is furnished by the contractile tissues, under which term we include all the varieties of muscle, striated and unstriated.

All movements that require to be sharply and forcibly carried out are effected by means of striated muscular tissue, and as these movements are in nearly all cases under the control of the will, the muscles are often spoken of as *voluntary*.

Unstriated muscular fibres (often termed involuntary*) form sheets or closed tubes surrounding the hollow viscera, and by their slow prolonged contractions serve to maintain and regulate the flow of the contents of these organs.

Intermediate in properties between these two classes we find heart muscle; this, though striated, presents important histological differences from striated voluntary muscle. We shall study this form more fully when we come to consider the physiology of the whole vascular system.

The properties of contractile tissues have been most fully investigated in voluntary muscles, the most highly differentiated members of the group, and so we shall consider this part of the subject at length, merely indicating at the end in what points the unstriated involuntary muscles differ from the striated.

* The ciliary muscle furnishes an example of a muscle which, though unstriated, is under the control of the will. In birds this muscle is striated.

Voluntary Muscle

The voluntary or striated muscles form a large part of the body, and are known as the flesh or meat. Each muscle is embedded in a layer of connective tissue, and is made up of an aggregation of muscular fibres, which are united into bundles by means of areolar connective tissue. The individual fibres vary much in length, and may be as long as 4 or 5 cm. At each end of the muscle the fibres are firmly united to tough bundles of white fibres, which form the tendon of the muscle, and are attached, as a rule, to bones. Running in the connective tissue framework of the muscle we find a number of blood-vessels, capillaries, and nerves.

Most of our knowledge on the subject of muscle has been derived from the study of the gastrocnemius and sartorius muscles of the frog.

Two varieties of striated muscle are found in the higher Vertebrates, the red and the white muscles.

The former are distinguished by their red colour (due chiefly to hæmoglobin), and the fact that in them the cross striation is less marked and the nuclei more numerous than in white muscle. There is also a difference in the contraction of the two varieties, the red contracting much more slowly. In fact, in all its properties it appears to be less highly organised than the white.

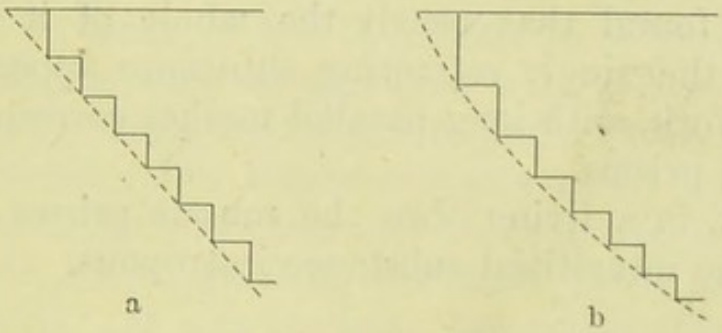
In some animals, such as the rabbit, we find muscles consisting almost entirely of one or other of these varieties; but in most animals (amongst which we may reckon frog and man) the two varieties occur together in one muscle, so that what we have to say about the properties of voluntary muscle, which rests nearly entirely on experiments made with frog's muscle, really has reference to a mixed muscle, *i. e.* muscle containing both red and white fibres.

Physical Properties of Resting Muscle

Living muscle is distinguished by its slight but perfect elasticity; that is to say, it is considerably stretched by a

slight force (in the longitudinal direction), but returns to its original length when the extending weight is removed. The length to which muscle is stretched is not proportional to the weight used, but any given increment of weight gives rise to less elongation, the more the muscle is already stretched. The accompanying curves show the elongation of muscle as compared with a piece of india rubber, when the weight on it is uniformly increased.

FIG. 24.



Extensibility of elastic (a) compared with that of a frog's gastrocnemius muscle (b).

Dead muscle is less extensible and its elasticity is less perfect. A given weight applied to a dead muscle will not stretch it so much as when the muscle was alive; but, on the other hand, the dead muscle does not return to its original length when the weight is removed.

Optical Properties

On examination of a living muscle, each fibre is seen to consist of a series of alternate light and dark striæ, arranged at right angles to its long axis, and enclosed in a structureless sheath—the sarcolemma. Each band may be considered to be made up of a number of prisms (sarcomeres) side by side, with interstitial substance between them. The muscle prisms of adjacent discs are connected to form long columns (primitive fibrillæ, or sarcostyles). Each muscle prism is more transparent at the two ends than in

the middle, thus giving rise to the appearance of light and dark striæ. In the middle of the light band is a line or row of dots, called Krause's membrane.

When a muscle fibre, killed by osmic acid or alcohol, is examined under the microscope by polarised light, it is seen to be made up of alternate bands of singly and doubly refracting material. The doubly refracting (*anisotropous*) substance corresponds to the dark band, and the singly refracting (*isotropous*) to the light band.

If, however, the living fibre be examined in the same way, it is found that nearly the whole of it is doubly refracting, the singly refracting substance appearing only as a meshwork, with long parallel meshes corresponding to the muscle prisms.

In short, in a living fibre the muscle prisms are anisotropous, the interstitial substance isotropous.

Chemical Composition of Muscle

It is impossible to speak with any certainty about the chemical composition of any living tissue, since in the act of analysis we destroy the life of the tissue; all we can do, in most cases, is to find the proximate principles present in the dead tissue. But, by using certain precautions, we may learn some interesting facts about the chemistry of living muscle. Muscle of cold-blooded animals may be frozen and thawed again, without at once losing its irritability, and therefore, we may say, without its life being destroyed. If living frog's muscle be frozen, then minced with ice-cold knives as finely as possible, and pounded in a mortar with four times its weight of snow, containing 1 per cent. of common salt, and the mixture thrown on to a filter and kept a little over 0° C., an opalescent fluid filters through. The filters soon get clogged, and therefore require to be frequently changed. Their temperature must not be allowed to rise above 1° C. This fluid is called *muscle-plasma*. If its temperature be allowed to rise to

that of the room, it clots, and the clot soon contracts, squeezing out a serum, just as in the case of blood-plasma.

The clot consists of a substance called *myosin*. It differs from fibrin in being more granular and not so stringy. It is soluble in 10 per cent. solutions of $MgSO_4$, NH_4Cl, or KNO_3. It is also easily soluble in dilute HCl, forming syntonin or acid albumen. From its solutions in neutral saline solutions it is precipitated by the addition of large quantities of distilled water, or by saturation with magnesium sulphate or common salt. In solution it is coagulated by heat at 56° C. Thus it is marked out as belonging to the class of globulins by the facts that it is coagulable by heat, insoluble in pure water, soluble in saline solutions. The serum contains an albumen similar to serum albumen (myalbumen), and a globulin similar to paroglobulin, but coagulating at a rather lower temperature (myoglobulin). It also contains the extractives and pigments of the muscle.

The muscle plasma is neutral or slightly alkaline. When coagulation takes place, however, it becomes distinctly acid, and this acidity has been shown to be due to the formation of sarcolactic acid in the process.

Arguing chiefly from analogy with the blood-plasma, the muscle-plasma has been said to contain a body, myosinogen, which is converted when clotting takes place (? under the influence of a very hypothetical ferment) into myosin, and perhaps other bodies, of which lactic acid may be one.

It is probable that a very similar change takes place normally when a muscle dies. All muscles, within a short time of their removal from the body, or if left in the body, after general death, lose their irritability, and this is succeeded by an event which occurs rather suddenly, and is known as rigor mortis. The muscle, which was before translucent, supple, extensible, becomes more opaque, rigid, and inextensible, and shortens. The shortening is not very powerful, and can be prevented by loading the muscle moderately. Chemical changes also take place. The

muscle, which was previously alkaline, becomes distinctly acid, the acidity being due to the formation of sarcolactic acid. At the same time there is a production of CO_2 and an evolution of heat.

After rigor has occurred it is impossible to extract muscle-plasma from the muscle, although the greater part of it may be dissolved in 10 per cent. $MgSO_4$, and is found to be myosin, exactly similar to the clot from muscle-plasma.

A rigid muscle never recovers. It is dead, and, in dying, chemical and physical changes have taken place, giving rise to shortening and rigidity, and converting a fluid complex substance into a solid clot of myosin, with the formation of CO_2 and lactic acid. The unstable living molecule has broken down into dead stable molecules, the potential energy of the former appearing as heat and work.

The residue left after the expression of the muscle-plasma consists chiefly of connective tissue, sarcolemma and nuclei, and as such contains gelatin (or rather collagen), mucin, nuclein, and adhering traces of the proteids of the muscle-plasma itself.

The muscle-serum contains the greater part of the soluble constituents of muscle. These are—

A. *Colouring matters.*—All red muscles contain a considerable amount of hæmoglobin. In many, a special pigment, probably allied to hæmoglobin, is also present. This has been named *myohæmatin* (MacMunn).

B. *Nitrogenous extractives.*—Of these, the most important is creatin ($C_4H_9N_3O_2 + H_2O$), which occurs to the extent of 0·2 to 0·3 per cent. This substance only occurs in muscular and nervous tissues. Its significance we shall discuss later on when inquiring into the history of the formation of urea.

Other nitrogenous extractives are—

Hypoxanthin or sarcin, xanthin (both bodies allied to uric acid), carnin, and a trace of urea.

C. *Non-nitrogenous constituents* —Fats.

Glycogen. The amount of this is very variable. In the embryo the muscles may contain enormous quantities, but in the adult they contain only from ·4 to 1 per cent.

Inosit ($C_6H_{12}O_6 + 2H_2O$), or muscle-sugar, which is present in minute quantities, is non-fermentable, does not rotate polarised light, and does not reduce Fehling's solution.

Dextrose. It is doubtful whether this is present in fresh resting muscle.

D. *Inorganic constituents.*—Muscle contains about 75 per cent. of water. The ash forms 1 to 1·5 per cent., and consists chiefly of salts of potassium and phosphoric acid. There are small traces of calcium, magnesium, chlorine, and iron.

Contraction of Muscle

A muscle may be caused to contract in various ways. Normally, it only contracts in response to impulses starting in the central nervous system and transmitted down the nerves. But contraction may be artificially excited in various ways in a muscle removed from the body. If we make a muscle-nerve preparation (*i. e.* a muscle with as long a piece of its nerve as possible attached to it), such as the gastrocnemius of the frog with the sciatic nerve, we find we can cause contraction by various forms of stimuli —mechanical, thermal, or electric—applied to the muscle or the nerve (direct and indirect stimulation). Thus the muscle responds with a twitch if we pass an induction shock through it or its nerve, or pinch either with a pair of forceps. Or we may use chemical stimuli, and cause contraction by the application of strong glycerin or salt solution to the nerve.

These experiments do not prove conclusively that muscle itself is irritable. It might be urged that when we pinched or burnt the muscle, we stimulated, not the muscle substance itself, but the terminal ramifications of the nerve

in the muscle, and that these, in their turn, incited the muscle to contract. But the independent excitability of muscle is shown clearly by the following experiment.

A frog, whose brain has been previously destroyed, is pinned on a board, and the sciatic nerves on each side exposed. A ligature is then passed round the right thigh, underneath the nerve, and tied tightly so as to effectually close all the blood-vessels supplying the limbs, without interfering with the blood-supply to the nerve. Two drops of a 1 per cent. solution of curare are then injected into the dorsal lymph-sac. After the lapse of a quarter of an hour it is found that the strongest stimuli may be applied to the left sciatic nerve without causing any contraction of the muscles it supplies. On the right side, however, stimulation of the nerve is as efficacious as before.

Both gastrocnemii respond readily to direct stimulation, showing that the muscles are not affected by the drug. Now, since both sciatic nerves have been exposed to the influence of the curare, it is evident that the difference on the two sides cannot be due to any deleterious effect on them by the curare.

We have also excluded the muscles themselves; so we must conclude that the curare paralyses the muscles by affecting the terminations of the nerve within the muscle, and probably the end-plates themselves.

This experiment therefore teaches us that muscle can be excited to contract by direct stimulation, even when the terminal ramifications of the nerve within it are paralysed, so that stimulation of them would be without effect.

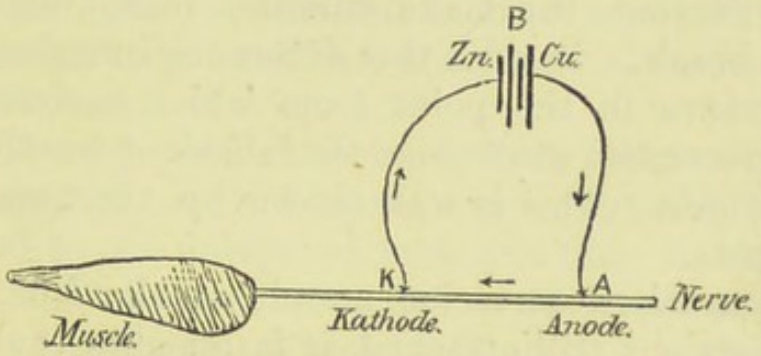
Of all the different stimuli that we have mentioned as capable of exciting muscular contraction, the electrical is that most frequently used. It is easy using this form to graduate accurately the intensity and duration of the stimulus. At the same time the stimulus may be applied many times to any point on the muscle or nerve without killing the part stimulated, whereas with other forms of

stimulus it is difficult to obtain excitatory effects without injuring to a greater or less extent the part stimulated.

Two forms of electrical stimuli are employed,—the make and break of a constant current, and the induction currents of high intensity and short duration.

Constant current.—As a source of constant current a Daniell's cell is generally employed (*vide* Appendix). In this cell the copper is the negative, and the zinc the

FIG. 25.



positive *element*. The current therefore passes in the cell from zinc to copper, and outside the cell from copper to zinc. If, therefore, wires be attached to the zinc and copper, the wire attached to the former will be the negative, and that to the latter the positive *pole*. If we connect such wires with the nerve or muscle of a nerve-muscle preparation (as in Fig. 25), the current will flow from copper to the nerve at A, and along the nerve from A to K. At K the current will leave the nerve to flow to the zinc of the battery, so completing the circuit. The point at which the current enters the nerve (*i. e.* the point of the nerve connected with the positive *pole* of the battery) is called the *anode*, and the point at which the current leaves the nerve is called the *kathode*. The wires by which the current is conducted to and from the nerve are called the *electrodes*.

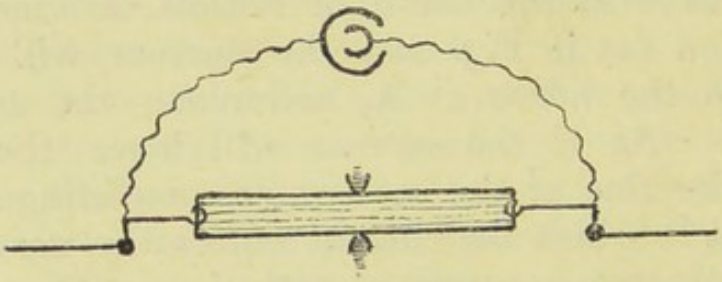
If a weak current from a Daniell's cell (or any other form of battery) be passed through a muscle, or any part

of its nerve, we find that at the make of the current the muscle gives a single sharp contraction—a *muscle-twitch.* No effect is produced during the passage of the current or when it is broken, the muscle remaining perfectly quiescent. If the current is now increased we find that the muscle responds to both make and break, remaining however quiescent during the passage of the current. Using a current of moderate strength, we find the contraction due to make is more energetic than that due to break.

Thus stimulation is caused by the make and break of a constant current, the make stimulus being more effective than the break. Besides this difference in intensity, there is a difference in the point from which excitation starts. *A make contraction starts from the kathode, a break contraction from the anode.* This is well shown by the two following experiments.

a. A curarised sartorius muscle of the frog, with its bony insertions still attached, is fastened at the two ends to two electrodes, which are able to swing when the muscle contracts, and are attached by threads to levers which serve to record the contraction. The middle of the muscle is then fixed by clamping it lightly. A circuit is arranged

FIG. 26.



Sartorius clamped in middle and attached to levers at either end.

so that a constant current can be sent through the electrodes and the whole length of the muscle. It is found, on making the current, that the lever attached to the kathode, that is, to the electrode by which the current

leaves the muscle—rises before the other lever. On the other hand, on breaking the current, the lever at the anode rises first, showing that the anodic half of the muscle contracts before the kathodic half.

b. The irritability of a muscle, *i. e.* its power of responding to a stimulus by contracting, is intimately dependent on the life of the muscle. If the muscle be injured or killed at any spot, its irritability at this spot will be therefore diminished or destroyed. Hence, if we stimulate a muscle at the injured spot, no contraction will ensue. This fact may be used to demonstrate the production of excitation at kathode on make, and at anode on break of a constant current.

A muscle with parallel fibres, such as the sartorius, is injured at one end, and a constant current passed, first from the injured to the uninjured end, and then in the reverse direction. It is found in the former case, when the anode is on the injured part (which is therefore less excitable), that break of the current is ineffective, and in the latter, when the kathode is on the injured surface, that the make stimulus is ineffective, showing that the part excited corresponds to the kathode at make and to the anode at break.

Induced currents.—In using these the muscle or nerve is stimulated by the current of momentary duration produced in the secondary circuit of an induction coil, by the make or break of a constant current in the primary. The strength of the shock is graduated by moving the secondary nearer to or farther away from the primary coil.

It is found, using this mode of stimulus, that the contraction on break of the constant current is much stronger than that on make. It must not be imagined, however, that there is any contradiction between this and the fact that the make of a constant current is a stronger stimulus than the break.

When we put a muscle in the secondary circuit and make a current in the primary, there is a current induced

in the former of momentary duration; so that there is a current *made and broken* through the muscle, and the same thing takes place again when the primary circuit is broken.

It has been shown that, when we use currents of such short duration, the break stimulus is ineffective; so in both cases, whether we make or break the current in the primary circuit, we are dealing with a *make* stimulus in the muscle. The difference in the efficacy of make and break induction shocks is purely physical, and depends on the fact that the current induced in the secondary coil on make is of slower rise and smaller potential than that produced at break. (See Appendix.)

A *minimal* stimulus is the weakest stimulus that will produce a contraction. A *maximal* stimulus is one that produces the strongest contraction a muscle is capable of under the effects of a single stimulus. A *submaximal* stimulus is any strength of stimulus between these two extremes.

The Changes that a Muscle undergoes when it Contracts

A. Physical Changes

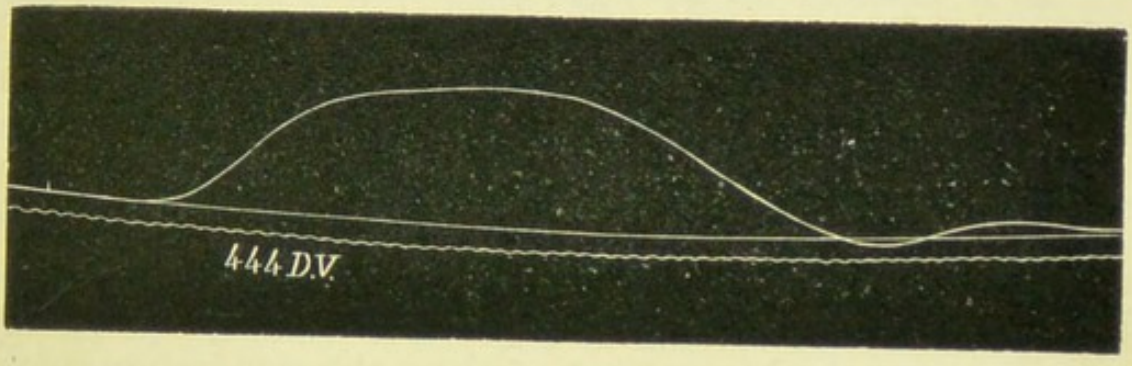
The most evident change about a muscle when it contracts is of form. It becomes shorter and thicker, its bulk remaining unaltered.

To study this change more closely, it is necessary to obtain a graphic record of the contraction. For this purpose the femur, to which the gastrocnemius of the muscle-nerve preparation is attached, is clamped firmly, and the tendo Achillis attached by a thread to a light lever, free to move round an axis at one end. The point of this lever is armed with a bristle (anything that is stiff and pointed will do), which just touches the blackened surface of a piece of glazed paper. This paper is stretched round a cylinder (drum) which can be made to rotate at any con-

stant speed required. If the drum is moving, the point of the bristle draws a horizontal white line on the smoked paper.

If, however, a single induction shock be sent through the nerve of the preparation, the lever is jerked up, falling again almost directly, and a curve is drawn like that shown in Fig. 27.

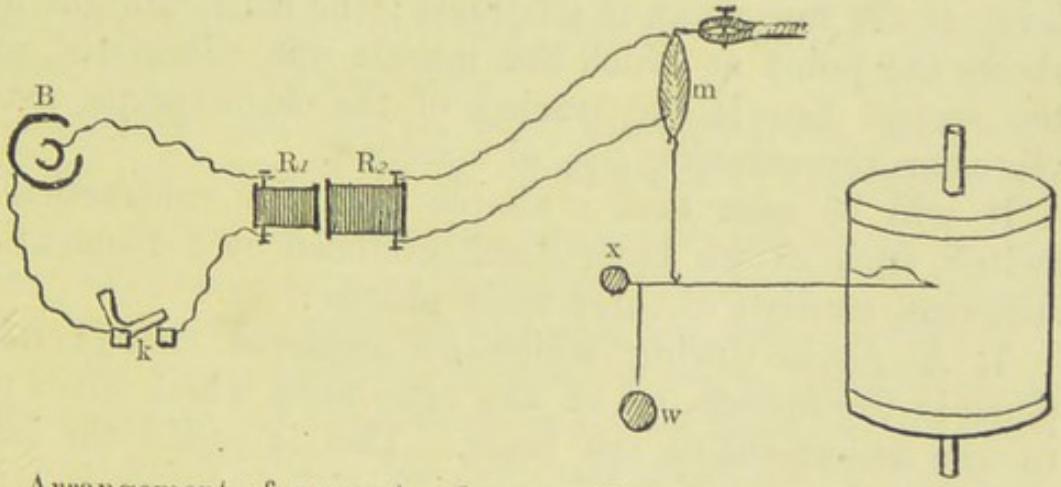
FIG. 27.



Curve of single muscle-twitch taken on a rapidly moving surface (pendulum myograph) (from Yeo).

A similar curve is obtained if the muscle be stimulated directly.

FIG. 28.



Arrangement of apparatus for recording simple muscle-twitch.

In all such graphic records we should have also—

1. *A time record.*—This is furnished by means of a small

electro-magnet, armed with a pointed lever writing on the smoked surface. This electro-magnet (time-marker or signal) is made to vibrate 100 times a second (more or less as may be required) by putting it in a circuit which is made and broken 100 times a second by means of a tuning-fork vibrating at that rate. The tuning-fork is maintained in vibration in the same way as the Wagner's hammer of an induction coil.

2. *A record of the exact point at which the nerve or muscle is stimulated.*—This may be obtained in two ways.

a. When using the pendulum or trigger myograph, in both of which the recording surface is a smoked flat surface on a glass plate, this latter is so arranged that it knocks over a key as it shoots across, and so breaks the primary circuit, and excites the nerve or muscle of the preparation. As we know the exact point that the plate reaches when it knocks over the key, we can mark on the contraction curve the exact moment at which stimulation took place.

b. If we wish to make and break the primary circuit at will by means of a key, a small electro-magnet signal, interposed in the circuit, is arranged to write on the revolving drum, and so mark the point of stimulation.

In the figure the upper line is the curve drawn by the lever of the muscle as it contracts ; the small upright line shows the point at which the muscle was stimulated, and the second line is the tracing of the chronograph, every vibration representing $\frac{1}{444}$ of a second.

It will be seen that a simple muscular contraction or twitch, such as we have here, produced by a momentary stimulus, consists of three main phases :

1. A phase during which no apparent change takes place in the muscle, or, at any rate, none which gives rise to any movement of the lever. This is called the *latent period.*

2. A phase of shortening, or contraction.

3. A phase of relaxation, or return to the original length.

The small curves seen after the main curve are due to elastic vibrations of the lever, and do not indicate any changes occurring in the muscle itself. From the time-marking below the tracing, we see that the latent period occupies about $\frac{1}{100}$ of a second, the phase of shortening $\frac{4}{100}$, and the relaxation $\frac{5}{100}$ second.

Thus a single muscle-twitch is completed in about $\frac{1}{10}$ of a second. It must be remembered, however, that this number is only approximate, and varies with the tempe rature of the muscle and its condition, being much longer in a fatigued muscle.

It is generally said that, during the latent period, invisible preparatory changes are taking place in the muscle, and these changes are supposed to be indicated by the electrical change accompanying a muscular contraction, which is generally described as taking place during the latent period. But recent experiments have tended more and more to shorten the latent period, and it now seems probable that nearly the whole of the latent period is due partly to instrumental inertia, and partly to the mechanical inertia of the muscle itself. For living muscle is elastic and very extensible, and the effect of contraction of any given part of it will be, first, to stretch the adjacent part, and only after that to move the part of the muscle to which the lever is attached.*

Sanderson and Burch have measured the mechanical latency of muscle by a photographic method. The

* The effect of the extensibility of muscle in lengthening the latent period will perhaps be more intelligible if illustrated by an example. If we have a weight supported by a rigid wire, and suddenly pull the upper end of the wire so as to raise the weight, the latter will rise instantaneously. If, however, the weight be suspended by a piece of elastic, it will not follow the pull exactly, but will lag behind, the first part of the pull being occupied with stretching the india rubber, and only when this is stretched to a certain degree will the weight begin to rise. The same retardation of the pull would be observed if, instead of india rubber, we used a piece of living muscle.

thickening of the muscle at the point stimulated was recorded graphically by photographing the outline of the muscle on a slit, behind which was a moving sensitive plate. Thus avoiding all instrumental inertia, and diminishing the inertia of the muscle to a minimum, the mechanical latent period was found to be only ·0025 second, and to coincide with the electrical latent period.

As we should expect from the preceding paragraph, the latent period is much increased by increasing the load. It is also lengthened by cold and fatigue. It is much longer in the red than in the white muscles.

The *height* of the contraction depends—

1. On the strength of the stimulus.

2. On the load; the height being smaller, the greater the weight the muscle has to raise. If the load is gradually increased, a point is reached when the muscle can no longer raise it. This weight represents the 'absolute force' of the muscle. In determining it the muscle is 'after-loaded,' that is to say, the lever is supported by a screw in its unweighted position, so that the weight cannot act on the muscle till the latter begins to contract.

The relaxation of muscle is helped by a moderate load, and in a normal condition is complete. It is not active—that is to say, is not due to a contraction in the transverse direction—but is a passive effect of extension and elastic rebound.

Summation of Contractions

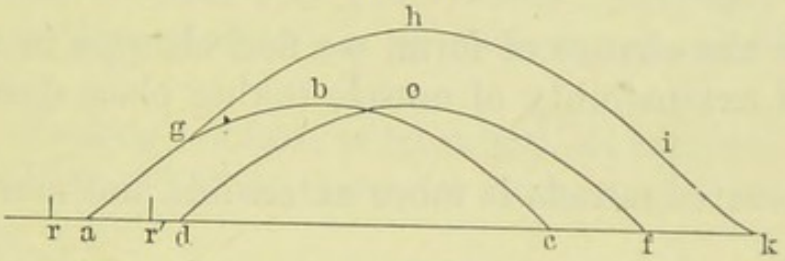
If a muscle is stimulated twice in succession, so that the second stimulus follows the first before the muscle has reached its maximum shortening, we get a combination of the effects of the two, which results in a stronger contraction.

The second stimulus has the same effect on the muscle as if the condition of contraction, which this latter has

attained when the stimulus reaches it, were its normal length.

Thus it is evident that if the period that elapses between the two stimuli is equal to the duration of the first part of the contraction (from its beginning to the maximum height), the shortening of the muscle may be doubled. Fig. 29

FIG. 29.



Muscle curves, showing summation of stimuli. r and r′, the points at which the stimuli were sent into the nerve. From the first stimulus alone the curve a b c would be obtained. From r′ the curve d e f is obtained. These two curves are *summated* to form the curve a g h i k when both stimuli are sent in at the interval r r′.

shows the effect of two successive stimuli at an interval of about $\frac{1}{20}$ second. The two lower curves represent the contractions which would have resulted from either of the stimuli alone.

This piling up of one contraction on the other is spoken of as *summation.*

Tetanus

If a muscle be stimulated so many times in a second (*e. g.* with the interrupted current of an ordinary induction coil) that it has no time to relax between each stimulus, we get a prolonged steady contraction, which is much stronger than the maximal muscle-twitch, owing to the summation of the rapidly following stimuli. This condition is called *tetanus.*

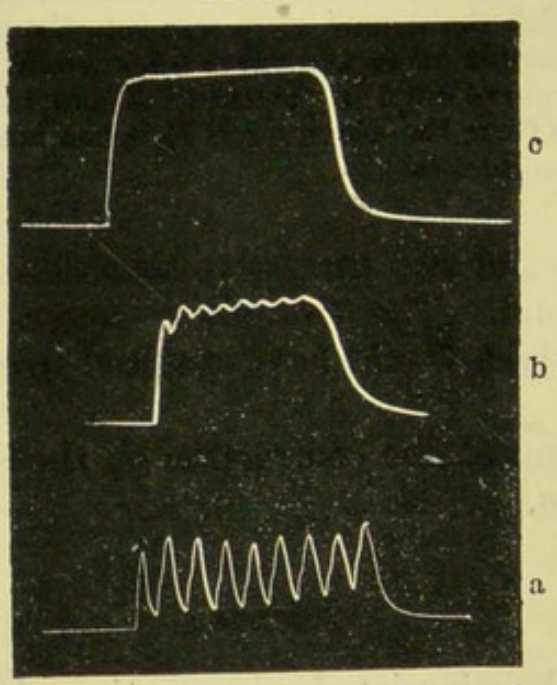
The rapidity of stimulation needed to produce an un-

broken tetanus depends on the duration of a single muscle-twitch, therefore according to the variety and condition of the muscle. Thus the rapidity need only be small in the case of cooled and tired muscles, or of the red muscles of the rabbit and tortoise. The rate varies from about 15 in the case of red muscles to 30 or 40 for white muscles. For the much more highly differentiated muscles of insects the rate is probably very much higher.

Besides the change of form, we find changes in the elasticity and extensibility of muscle taking place during contraction.

A contracted muscle is more extensible and more elastic

FIG. 30.



Curves showing formation of tetanus (from frog's gastrocnemius). a. Six stimuli per sec. b. Ten stimuli per sec. c. Thirty stimuli per sec.

than a muscle at rest. A gram applied to a tetanised gastrocnemius will cause greater lengthening than if it were applied to the same muscle at rest. At the same time the elasticity is more perfect,—that is to say, when the weight

is removed, the muscle returns more quickly and completely to its original length.

Production of Heat

The experience of every-day life teaches us that muscular exercise is associated with increased production of heat. A man walks fast on a frosty day to keep himself warm; and we find this observation confirmed when we investigate the contraction of an isolated muscle outside the body.

Thus, if a frog's muscle is tetanised, its temperature rises from 0·14° to 0·18° C., and for each single twitch from 0·001° to 0·005° C.

It is evident that such small changes in temperature as ·001° cannot be estimated by ordinary thermometric methods. For this purpose a thermopile must be used.

The construction of a thermopile depends on the fact that, when the junctions of a circuit made of two metals are at different temperatures, a current of electricity generally flows through the circuit. This current can be measured by means of a galvanometer, and is proportional to the difference of temperature between the two junctions.

To measure the production of heat during muscular contraction, a small flat thermopile (containing four or six elements composed of iron and German silver) is fixed with one of its ends between two frogs' gastrocnemii. The other end containing the other junctions of the six pairs of metal discs is kept at a constant temperature. The terminals of the pile are connected by wires with a galvanometer.

The muscle is now tetanised or stimulated with single shocks, and it is found that every contraction causes a movement of the galvanometer needle in a direction that shows a production of heat at the end of the thermopile which is inserted between the muscles. The deflection of the galvanometer is measured, and from this the production of heat in the muscles can be calculated.

In large animals the production of heat in muscular contraction can be easily shown by inserting the bulb of a

thermometer between the thigh muscles, and stimulating the spinal cord. The rise of temperature produced in this way may amount to several degrees.

The following are the chief results of researches carried out in these ways:

A. More heat is produced when a muscle does no work than when it does work. Thus, if the muscle be excited several times and extended passively by the weight between each contraction, more heat will be evolved than if the weight be prevented from falling at the end of each contraction by means of an automatic catch.

B. The amount of heat produced is increased by increasing the tension of the muscle.

C. On increasing the strength of stimulus the amount of heat increases faster proportionately than the extent to which the muscle contracts.

Electrical Changes

If a current from a battery be passed between two plates of platinum immersed in acidulated water or salt solution, *electrolysis* of the water takes place, bubbles of hydrogen appearing on the negative plate (kathode), and bubbles of oxygen on the anodal plate. If now we remove the battery, and connect the two plates (electrodes) by wires with a galvanometer, it will be seen that a current is passing through the galvanometer and water in the reverse direction to the previous battery current. This current is called the polarisation current, and is due to the electrolysis of the water that has taken place. The vessel in which the electrodes are immersed has, in fact, become a galvanic cell, the platinum covered with oxygen bubbles being the negative *element*, and that covered with hydrogen bubbles the positive *element*. Exactly the same process of electrolysis or polarisation takes place when we pass currents through the tissues of the body by means of metallic electrodes.

Hence before we can study accurately the delicate electrical changes that may occur normally in living tissues, it is necessary to have some form of electrodes in which this polarisation will not occur. The 'non-polarisable' electrodes which are most generally used for this purpose are made in the following way. A glass tube (Fig. 31) is closed at one end with a plug of kaolin made into a paste with a saturated solution of zinc sulphate. The rest of the tube is filled with a similar solution. Dipping into the zinc sulphate solution is a rod of pure zinc, amalgamated. Just before use, a plug of china clay made with normal saline solution, is put on the end of the tube, so as to effect a connection between the zinc sulphate clay and the nerve or muscle which it is desired to stimulate or lead off. In these electrodes there is no contact of metals with fluids that can produce dissimilar ions (*e. g.* hydrogen or oxygen bubbles) at the surface of contact, and hence they may be regarded as practically non-polarisable.

FIG. 31.

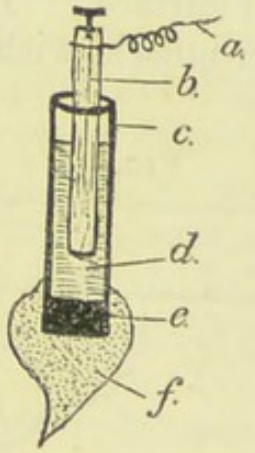


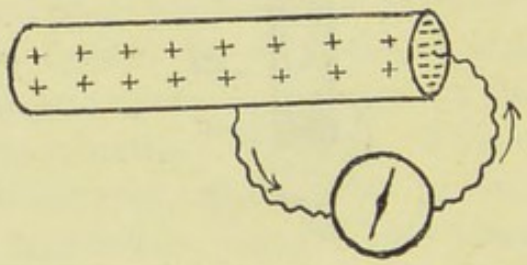
Diagram of non-polarisable electrode. *a*. Covered wire. *b*. Amalgamated zinc rod. *c*. Glass tube. *d*. Saturated $ZnSO_4$ solution. *e*. Plug of zinc sulphate clay. *f*. Plug of normal saline clay.

If a muscle, such as the sartorius, be removed from the body, and two non-polarisable electrodes connected with a

delicate galvanometer be applied to two points of its surface, there will be a deflection of the mirror attached to the galvanometer, showing the presence of a current in the muscle from the ends to the middle, and in the external circuit from the middle (or equator) to the ends. It was formerly thought that this current was always present in all normal muscles, and it was spoken of as the "natural muscle current;" the muscle was said to be made up of a series of electromotive molecules, the equator of each molecule being positive to the two poles (Du Bois Reymond). It has been conclusively shown, however (by Hermann and others), that this current of resting muscle is not a natural current at all, but is due to the effects of injury in making the preparation. The less the preparation is injured, the smaller is the current to be obtained from it, and in some contractile tissues, such as the heart, there may be absolutely no current during quiescence.

The latter observer describes the fact of the existence of currents of rest thus:—"In partially injured muscles every point of the injured part is negative towards the points of the uninjured surface." Fig. 32 shows the direction of the current in a muscle with two cut ends.

FIG. 32.



Current of rest.

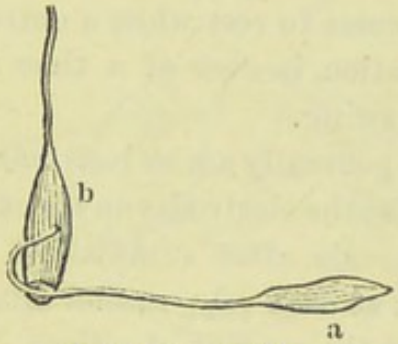
When the muscle is quite dead, this current of rest, or "demarcation current" (Hermann), disappears.

The existence of this current may be demonstrated without using a galvanometer.

If the nerve of a sensitive muscle-nerve preparation

(a, Fig. 33) be allowed to fall on an excised muscle (b), so that two points of the nerve are in contact with the cut end of the surface of the second muscle (b), the muscle (a) will contract each time the nerve touches (b) so as to complete the circuit.

FIG. 33.



Rheoscopic frog.

Whatever be the explanation of this current of resting muscle, there is no doubt that a very definite electrical change occurs in a muscle when it contracts.

To show this change, we may lead off two points, one on the cut end and one on the surface of the muscle of a muscle-nerve preparation, to a galvanometer. We shall then obtain a certain deflection of the mirror of the magnet, due to the current of rest or demarcation current. If now the nerve be stimulated with an interrupted current, so as to throw the muscle into a tetanus, the ray of light from the galvanometer mirror is observed to swing back towards the zero of the scale, showing that the current that was present before is diminished.

When the excitation of the nerve is discontinued, the galvanometer indicates once more the original current of rest. This diminution of the current of rest during activity of a muscle is spoken of as the '*negative variation.*'

The negative variation may also be observed, by means of a very lightly moving galvanometer, to accompany a single twitch of the muscle. It has been found to occupy

about $\frac{1}{200}$ second, and to occur almost immediately after stimulation, either before or at the very commencement of contraction.*

To analyse more fully the electrical change accompanying each separate twitch of the muscle, recourse must be had to other methods than the direct galvanometric method. Since a delicate galvanometer takes some seconds to come to rest when a current is sent through it, the whole of the variation is over at a time when the magnet has hardly commenced its swing.

For this purpose we generally use an instrument called the rheotome, by which we can connect the electrodes on the muscle with the galvanometer at varying intervals after stimulation, and by observing the galvanometer readings at each $\frac{1}{1000}$ second after stimulation, can map out the exact course of the current of action.

The instrument is represented diagrammatically in Fig. 34.

By means of a clock or motor the rod, a b, is made to rotate at any required rate round a vertical axis at its centre. On either end it carries two brushes made of fine wire and connected together. The brushes at each rotation come in contact with the pieces of copper, rr′, and when this happens the primary circuit, K, r, a, r′, p, is rapidly closed and broken again, thus giving rise to a momentary current in the secondary coil, s, and exciting the muscle, m. In the same way

---

* It was formerly thought that the negative variation took place immediately after stimulation, and ended before contraction began,—that is to say, was confined entirely to the latent period (Bernstein). But more recent observations seem to show that the electrical and mechanical latency are the same, and that, in fact, as stated in the text, the negative variation accompanies the first part of the contraction.

The negative variation or current of action accompanying a single twitch of the muscle may also be investigated by means of the capillary electrometer, which is peculiarly adapted for this purpose, since it has no instrumental delay, and the characters of the electrical change may be deduced from those of the curve on the photographic record of the excursion of the meniscus (*vide* Appendix for description of capillary electrometer).

the brushes, b, close the galvanometer-electrode-muscle circuit, G, t, b, t′, l, m, q, each time they brush on the copper banks, tt′. By turning the disc, A, round, the interval at which the brushes, b, pass tt′, after the brushes, a, pass rr′, can be altered at will, and therefore

FIG. 34.

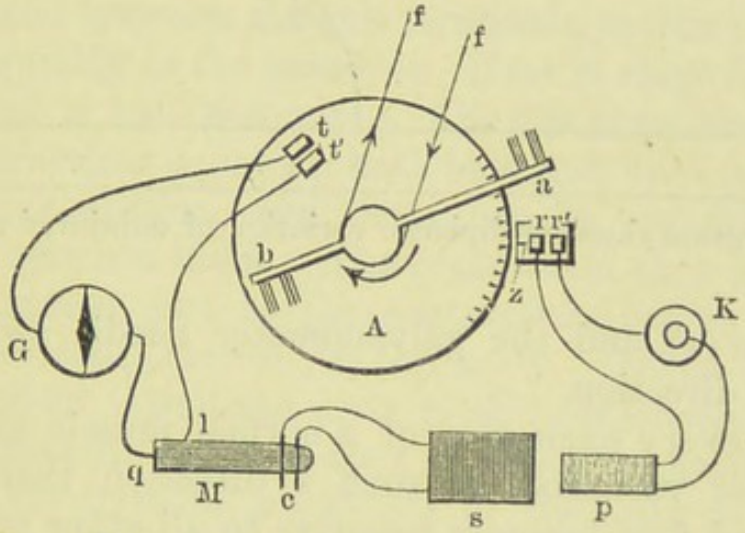


Diagram of rheotome (Hermann).

the interval between stimulation and leading off the current to the galvanometer.

But there is no need for any demarcation current to be present in order to show an electrical change accompanying contraction. In fact, we learn much more about the nature of the excitatory change if we study the electrical behaviour of a perfectly normal (and therefore currentless) muscle on stimulation. This can be easily done by means of the rheotome or capillary electrometer.

If a perfectly uninjured regular muscle (such as the sartorius) be stimulated with a single induction shock at one end (x), and the relative electrical conditions of the points (a) and (b) investigated, it will be found that as soon as the excitatory process reaches (a), this point becomes negative to (b), and there is thus a current in the galvanometer from (b) to (a). A moment later the two points are equipotential, as shown by the fact that no

current passes through the galvanometer. A thousandth of a second later this balance is upset, and now (b) is ne-

FIG. 35.

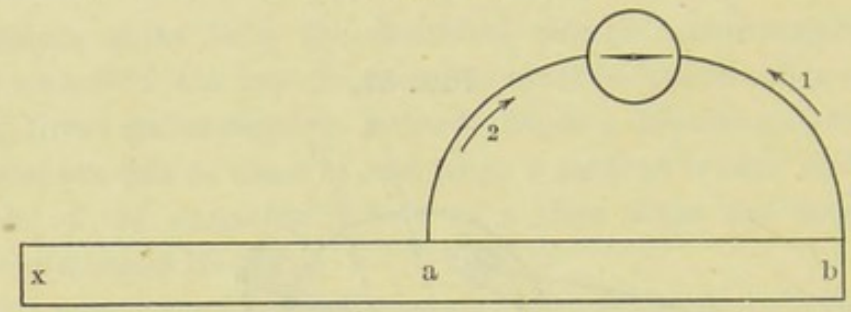


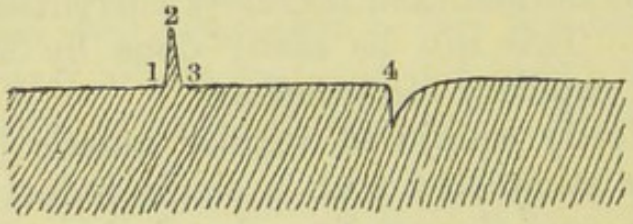
Diagram showing diphasic variation of uninjured muscle.

gative to (a), and the galvanometer needle swings in the opposite direction.

Thus every excitation of a normal muscle gives rise to a diphasic variation, of such a direction that the point stimulated first becomes negative to all other points of the muscle, and this 'negativity' (to use a loose but convenient expression) passes as a wave down the muscle, accompanying (preceding ?) the wave of contraction, and travelling at the same rate.

This diphasic current of action is shown much more clearly and easily on a slowly contracting tissue such as the frog's ventricle.

FIG. 36.



Tracing of diphasic variation of frog's heart taken with capillary electrometer.

Fig. 36 represents the photograph of variation of a capillary electrometer, one terminal (acid) of which is con-

nected with the base of the ventricle, and the other (Hg) with the apex.

The contraction of the ventricle begins at the base. The base, therefore, becomes negative, and the column of mercury moves up (1 to 2). A moment later the contraction has extended to the apex. Hence there is now an equalisation of the potential between the two terminals, so the mercury comes back quickly to the base line. Here it stops for some time (one and a half seconds). All this time the whole heart is contracting equally; both base and apex are thus in a similar condition, and there can be no difference of potential between them. The contraction then goes off, but the relaxation, just as the contraction, begins at the base, and proceeds thence to the apex. There is thus a small period in which the apex is still contracted while the base is relaxed, and the apex is therefore negative to the base. This terminal negativity of the apex is shown on the photograph by the excursion of the column of mercury away from the point of the capillary at (4).

The only difference between the electrical change in this case and in that of voluntary muscle is that in the former all processes are very much quicker, so that as a rule, the point (a) (Fig. 35) has ceased to be negative before the negativity of (b) has attained its full height, and there is thus no prolonged equipotential stage.

We may now return for a moment to the consideration of the current of rest observed in injured muscle.

Hermann considers that muscle (or contractile tissue) becomes negative under two conditions:

(1) In activity.

(2) When dying.

But it must be confessed that the second may be easily placed under the first head. Section or injury of a muscle causes a constant stimulation of the adjacent parts. These parts, therefore, become negative to the other parts that are further away from the seat of injury, and we thus get a demarcation current. Hence we come to the con-

clusion (only paradoxical in terms) that the currents of rest are currents of action, and are due to excitation around the injured spot.*

Secondary Contraction. Rheoscopic Frog

The negative variation of one muscle may be used to make another contract.

If the nerve of the preparation (a) (in Fig. 33) be laid so as to touch at two points the cut end and surface of the muscle (b), and the nerve of (b) then stimulated with single induction shocks, every contraction of (b) will be attended by a contraction of (a), excited by the negative variation of the current passing through its nerve from the point touching the cut end to that in contact with the equator of (b).

If the nerve of (b) is tetanised, (a) as well as (b) enters into a continued contraction. This '*secondary tetanus*' is of interest as showing that, although the contractions of (b) are fused, the excitatory process and negative variations are still quite distinct.

B. Chemical Changes

When a muscle contracts there is an increased formation of sarcolactic acid and of carbon dioxide, and increased consumption of oxygen.

The two latter changes may be considered first. The increased production of CO_2 may be proved by hanging the excised muscle in a chamber, and analysing the surrounding

* If the demarcation current is really only due to excitation, we would expect to find it weaker than the action current obtained by exciting the whole muscle to contract. And this is, in fact, the case. The E. M. F. of the demarcation current of a sartorius equals about ·05 of a Daniell. The action current of the same muscle may attain to an E. M. F. = ·08 of a Daniell cell (Gotch).

air before and after tetanisation of the muscle, or by estimating the amount of CO_2 contained in the venous blood flowing from a muscle before and during contraction.

In both these cases this production of CO_2 is attended with increased consumption of oxygen, and it might be thought that the energy for the contraction was furnished by the direct combustion of certain constituents of the tissues to form CO_2 and perhaps other products. But this view is at once disproved by the facts that the absorption of oxygen is not nearly sufficient to account for the amount of CO_2 giveno ff, and that a frog's muscle may be tetanised again and again in a vacuum or atmosphere of nitrogen, and each time will give off a certain quantity of CO_2.

So we must come to the conclusion that the energy of the contraction is furnished by the breaking down of an unstable body of high potential energy, which contains carbon and oxygen. In the breaking down, a rearrangement of the constituent atoms takes place, resulting in the formation of simpler stable bodies, such as CO_2 and lactic acid, with little or no potential energy. The energy thus set free appears as heat, work, and electrical differences of potential.

These chemical changes force immediately a comparison between contraction and rigor mortis. In both cases there are shortening of the muscle, doing of work, and evolution of heat. In both cases there is formation of CO_2 and lactic acid. Perhaps we should mention also the electrical changes incident upon contraction and dying of muscle (*v.* p. 105).

Here, however, the analogy must cease. For a muscle in becoming rigid becomes opaque, less extensible, and less elastic. When it contracts it remains as translucent as before, and is more extensible and elastic. So it is evident that, although probably the initial changes of rigor are similar to those of contraction, they lead to a more profound breaking down of the complex muscle molecule, from which there is no recall. We may conceive of the living proto-

plasm of the muscle during contraction as using stored-up carbohydrate, or allied substances, and oxygen to furnish the necessary energy ; but it is also possible that the whole living molecule breaks down with the formation of a still living proteid residue, and waste products such as CO_2 and lactic acid. Immediately afterwards this living residue takes up oxygen and carbon-containing substances from the surrounding lymph or interstitial substance of the muscle, and is ready once more to break down and furnish energy in the process.

A hypothetical muscle molecule of this nature is spoken of as *inogen.*

The fate of the extractives of muscle during contraction is still a matter of dispute. Kreatin is probably neither increased nor diminished, and, in fact, no nitrogenous extractive seems to be produced during contraction. This fact supports what we have already stated about the ultimate origin of the energy of contraction from the oxidation of carbon alone.

Glycogen is said to be converted into sugar in rigor mortis, and possibly in tetanus. Sugar (dextrose) is looked upon by many authorities as of great importance in muscular contraction. It is stated that analyses of blood going to and coming from contracting muscle show a consumption of this substance during contraction ; and it is possible that it is the special carbohydrate food of muscle, and its oxidation the chief source of the energy set free when a muscle contracts and does work. The estimation of sugar in blood, however, is liable to so many errors, that we cannot at present regard this as definitely proved by the analyses just mentioned.

Conditions modifying the Irritability and Contraction of Muscular Tissue

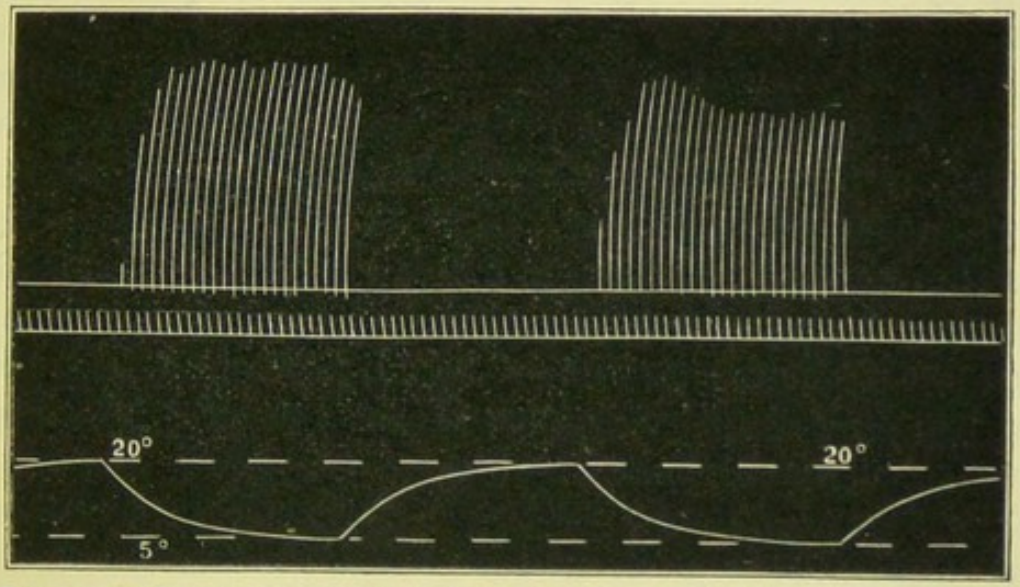
A. *Temperature.*—Speaking generally, the effect of warming a muscle is to quicken all its processes. The

latent period becomes shorter and the muscle curve steeper and shorter.

If a muscle be heated gradually (without stimulation) up to about 45° C., it undergoes no apparent change till that point is reached, when it suddenly contracts and enters into rigor mortis.

Cold has the reverse effect. The intramolecular processes which lie at the root of the muscular activity are

FIG. 37.



Tracing of muscle contractions to show effect of cooling a nerve on its excitability. The lower line indicates the changes in temperature of the excited part of the nerve. The muscle only responded when the nerve was cooled, the stimulus becoming ineffectual when the nerve was warmed (Gotch).

slowed, so that the latent period as well as the contraction period are prolonged. Curiously the action of cold on the excitability of muscle is to increase it, so that any form of stimulus is more effective at 5° C. than at 25° C. Moreover when maximal stimuli are being used, the first effect of the application of cold is to increase the height as well as the duration of contraction.

If, however, a muscle be cooled for a short time to zero or a little below, it loses its irritability, which returns if the muscle be gradually warmed again.

Prolonged exposure to severe cold destroys irrevocably its irritability. Warming the muscle now will simply bring about rigor mortis.

B. *Fatigue.*—A muscle will not go on contracting indefinitely. If it is repeatedly stimulated, changes soon become apparent in the curve of contraction. The latent period is prolonged, as well as the length of the contractions; the absolute height and work done are diminished. At the same time the muscle does not return to its original length; the shortening which remains is spoken of as '*contraction remainder.*'

After an initial rise during the first few contractions, these diminish uniformly in height till they are no longer apparent, so that the muscle is now said to have lost its irritability.

If left to itself, the muscle which has been exhausted by repeated stimulation will recover. The recovery is hastened by passing a stream of blood, or even of salt solution, through the blood-vessels of the muscle. Recovery, however, in a muscle outside the body is never complete.

The phenomena of fatigue probably depend on two factors:

(1) The consumption of the contractile material or the substances available for the supply of potential energy to this material.

(2) The accumulation of waste products of contraction. Of these waste products the lactic acid is probably of great importance. Fatigue may be artificially induced in a muscle by 'feeding' it with a dilute solution of lactic acid, and this again removed by washing out the muscle with normal saline solution containing a small percentage of alkali. After a certain time the mere removal of waste products by means of an artificial circulation of salt solution becomes inadequate to restore contractile power to the muscle. In this case the muscle can be made to contract once more by supplying it with fresh food material, as by the circulation of serum or salt solutions containing serum albumen.

Of the drugs that have a direct action on muscle, the most remarkable is veratrin, which causes an excessive prolongation of a muscular contraction (produced by a single stimulus). Thus the 'twitch' of a muscle poisoned with veratrin may last fifty or sixty seconds, instead of the normal one tenth of a second.

Barium and calcium salts have a similar though less marked effect.

Voluntary contraction.—We have now to inquire, in the light of our knowledge gained chiefly by electrical excitation of muscles, what is the nature of ordinary voluntary contraction as it occurs in the muscles in the body.

The fact that it is impossible to get an artificial prolonged contraction in excised muscles except by repeated stimulation—that is, by summation of single twitches to form a tetanus—inclines us to view almost every voluntary contraction as a tetanus. What further evidence is there for this view?

Muscle-sound.—If we place the end of a stethoscope over the biceps muscle, and listen while we voluntarily contract the muscle, a low sound is heard. This is the muscle-sound, and invariably accompanies any voluntary contraction. Its tone corresponds to about thirty-six vibrations a second, and it was thought to be the first overtone of a note of eighteen vibrations per second, which, therefore, was looked upon as the rhythm of 'voluntary tetanus.'

But one hears exactly the same note when listening to any irregular sound of low intensity. The roar of London that we hear in the middle of Hyde Park has the same pitch as the muscle-sound of our contracting biceps. And really this muscle-sound proves nothing about the number of contractions composing voluntary tetanus, for it is the natural resonance-tone of the ear, and therefore selected and intensified in the ear when we listen to any irregular mixture of tones and noises.

Tracings of most voluntary contractions show superficial vibrations of eight to twelve per second, and this

rhythm is seen in many movements, such as the clonic convulsions of epilepsy, and some diseases of the spinal cord. This irregularity would quite well account for the muscle-sound.

But we can get tracings of natural contractions showing eight or ten complete twitches in the second (contraction and relaxation), or a continued contraction with eight or ten superficial waves.

So it is not sufficient to say that voluntary contraction is a tetanus of eight or twelve per second. If it is a tetanus, there must be some means by which each individual contraction can be shortened till it is distinct, or lengthened till it fuses with the next contraction to produce an unbroken tetanus. And we must remember that the electric stimulus differs in many of its effects from the natural stimulus, and so not transfer all our results of electrical stimulation too unreservedly to the contraction of muscles in the living body in response to the will.

Other Forms of Contractile Tissue

Smooth or unstriated muscle.—The little we know about the physiology of unstriated muscle is derived from experiments on the intestine, ureter, bladder, and retractor penis. This tissue differs from voluntary muscle in containing numerous plexuses of nerve-fibres (non-medullated) and ganglion-cells, so that in all our researches it is difficult to be certain whether the results are due to the muscle-fibres themselves, or to the nerves and nerve-cells which are so intimately connected with them, especially as we have as yet no convenient drug like curare by aid of which we might discriminate between action on muscle and action on nerve.

The contraction of smooth muscle is so sluggish that the various stages of latent period, shortening and relaxation, can be easily followed with the eye. The latent

period may be from ·4 to ·8 second, and the contraction may last from half to three minutes.

If we stimulate any point of a tube of smooth muscle (such as ureter or small intestine), which contains two layers, one circular, the other more scanty, of longitudinal fibres, a circular contraction takes place at the point stimulated, so that a ring-like constriction of the intestine is produced. This constriction lasts some time at the spot, and then slowly passes along the tube in both directions, upwards and downwards, at the rate of 20 to 30 millimetres a second.

This advancing wave of constriction normally takes place only in one direction, and so serves to drive on the contents of the tube. It is spoken of as 'peristaltic action.'

The stimuli for smooth muscle are essentially the same as for striated. Single induction shocks are often ineffectual to produce excitation, and smooth muscle is always more susceptible to the make or break of a constant current. When the latter form of stimulation is used, response occurs at the make sooner than at the break, and just as in voluntary muscle, make excitation starts from the kathode and break excitation from the anode.

The smooth muscles are very susceptible to changes of temperature, and soon lose their excitability on removal from the body.

It is possible by stimulating with slowly interrupted shocks to produce tetanus, but it is very doubtful whether in the body a tetanic contraction of this kind of muscle ever occurs. Much more important than this is the property these muscles have of entering into a prolonged contraction, which is spoken of as *tonus*. This tonic contraction is especially seen in the case of the plain muscular tissue of the arteries, and will be spoken of again when we deal with the vascular system.

One important difference between smooth and striated muscle lies in the fact that the former in very many cases

has the power of automatic movement; that is to say, it can contract of its own accord without any definite stimulus from without, or any impulse from the central nervous system. It is on this account that it is called involuntary.

Amœboid Movement

We have already described amœboid movement as seen in the amœba and the white blood-corpuscles. It only remains to enumerate the chief factors that influence its activity.

Amœboid movements can only occur within certain limits of temperature (about 0° C. to 40°); within these limits it is the more active the higher the temperature. At about 45° the cell goes into a condition resembling heat rigor.

The fluid in which the corpuscles are suspended is of great import. Distilled water, almost all salts, acids and alkalies, if strong enough, stop the action and kill the cell.

The movements are also stopped by CO_2 or by absence of oxygen.

Artificial excitation, whether electrical, chemical, or thermal, causes universal contraction of the corpuscle, which therefore assumes the spherical form.

Ciliary Movement

Cilia are met with in man in nearly the whole of the respiratory passages and the cavities opening into them, in the generative organs, in the uterus and Fallopian tubes of the female, and the epididymis of the male, and on the ependyma of the central canal of the spinal cord and its continuation into the cerebral ventricles.

The cilia are delicate tapering filaments which project from the hyaline border of the epithelial cells. There are about twenty or thirty to each cell. The hyaline border

is really made up of the enlarged basal portions of the cilia.

In action the cilia bend suddenly down into a hook or sickle form, and then return more slowly to the erect position. This movement is repeated many (twelve to twenty) times a second, and thus serves to move forward mucus, dust, or an ovum, as the case may be. The movement seems to be entirely automatic, and is quite unaffected by nerves, at any rate in all the higher animals.

There is, however, a functional connection between all the cells of a ciliated epithelial surface, so that movement of the cilia, started in one cell, spreads forward as a wave, just as, when the wind blows, waves of bending pass over a field of corn.

The conditions of ciliary action are exactly the same as those for amœboid movement of naked cells.

The minuteness of the object has, up to now, prevented us from deciding whether the cilium is itself actively contractile, or whether it is simply passively moved by the action of the basal part situated in the hyaline border of the cell.

CHAPTER V

THE GENERAL PROPERTIES OF NERVE-FIBRES (CONDUCTING TISSUES)

In the last chapter we studied incidentally some of the functions of nerve-fibres. We found that, when we stimulated the nerve of a nerve-muscle preparation at any part by electrical, thermal, or mechanical means, the stimulus was followed, after a very short interval, by a contraction of the muscle. This observation illustrates the two functions of nerve-fibres, irritability and conductivity,—that is to say, a suitable stimulus can set up changes in any part of the nerve, which are transmitted down the nerve without any visible effects occurring in it; and it is not until this nervous change has reached the muscle that a visible effect takes place in the shape of a contraction. Now in the human body a direct excitation of the nerve-fibre in its course never takes place under normal circumstances. The only function the nerve-fibre has to perform is that of conducting impulses from the sense-organs at the periphery to the central nervous system, and efferent impulses from this to the muscles and other of its servants. So we must first study the conditions on which the conduction of a nervous impulse depends.

In the first place, it is absolutely essential that there should be vital continuity along the whole length of the fibre. Damage to any part of it, such as by crushing, heat, or any other injurious condition, infallibly causes a block to any impulse.

The velocity of propagation along a nerve-fibre may be

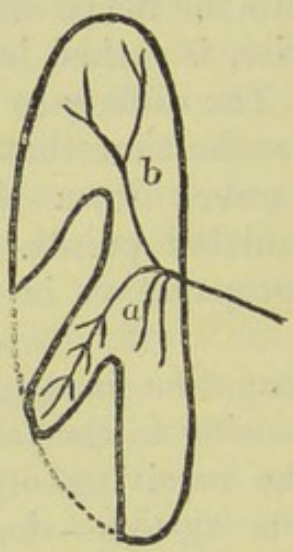
measured, although in early times it was thought to be as instantaneous as the lightning flash. To measure the velocity of propagation in a motor nerve, a frog's gastrocnemius is prepared, with a long piece of sciatic nerve attached. The muscle is arranged so that its contraction may be recorded on a rapidly moving surface, on which is also recorded, by means of electro-magnetic signals, the moment at which the stimulus is sent into the nerve, and also a time-marking showing $\frac{1}{250}$ sec. Tracings are now taken of the contraction of the muscle; first, when the nerve is stimulated at its extreme upper end; secondly, as close as possible to the muscle. It will be found that the latent period, which elapses between the point at which the stimulus is sent into the nerve and the point at which the lever begins to rise, is rather longer in the first case than in the second. The difference in the lengths of the two latent periods gives the time that it has taken for the nervous impulse to travel down the length of nerve between the two stimulated points. Calculated in this way, the velocity of propagation in frogs' nerve is about 28 metres per second.

The velocity of propagation in sensory nerves is more difficult to determine, owing to the fact that a sensory impulse, on arrival at the receiving organ—*i. e.* some part of the central nervous system—does not give rise at once to some definite, recordable, mechanical change, such as muscular contraction. There is another method of determining the velocity of conduction, which may be used also with sensory fibres. The passage of a nerve-impulse down a nerve, just as the passage of a wave of contraction along a muscle-fibre, is immediately preceded or accompanied by an electrical change, which also travels along the nerve as a wave of negativity. The velocity of propagation of this wave may be measured, and is found to give the same numbers as the velocity determined by the preceding method.

The existence of this electrical change enables us to

show that a nerve-impulse, excited at any point in the course of a nerve-fibre, travels *in both directions* along the fibre. The power of nerves to transmit impulses in either direction is shown further by the experiment known as Kühne's gracilis experiment. The gracilis muscle of the frog is in two portions separated by a tendinous intersection, so that there is no muscular continuity between the two halves. The nerve to the muscle divides into two branches, one to each half, and at the point of junction there is division of the axis cylinders themselves. It is found that if the section a in the diagram (Fig. 38),

FIG. 38.



Kühne's gracilis experiment.

which is quite isolated from the rest of the muscle, be stimulated, as by snipping it with scissors, the whole muscle contracts. If, however, the portion of the muscle which is free from nerve-fibres be stimulated in the same way, the contraction is limited to the fibres directly stimulated, showing that in the former case the stimulus excited nerve-fibres, which transmitted the impulse *up* the nerve to the point of division, and then *down* again to the other half of the muscle. Since nerves have this power of conduction

in both directions, it might be thought that a single set of nerve-fibres might very well subserve both afferent and efferent functions; at one time conducting sensory impulses from periphery to cord, at another time motor impulses from cord to muscles. But this is not the case. As a matter of fact, we find in the body a marked differentiation of function between various nerve-fibres.

We have already mentioned the division of nerves into afferent and efferent, and we find further that each of these afferent or efferent fibres has its own proper impulses to conduct, and only conducts these impulses. Thus some fibres in the anterior spinal roots conduct ordinary motor impulses to muscles, others impulses causing contraction or relaxation of the muscular walls of arteries, or which quicken or slow the contractions of the heart. We shall return to this question of restricted function of nerve-fibres when we come to treat of the special senses, under the heading of "Müller's law of specific irritability."

The rate of propagation of a nervous impulse is quickened by heat (up to about 38° C.) and slowed by cold. At a little over 0° C. the rate in frogs' nerve is only about one metre per second.

Excitation of Nerves

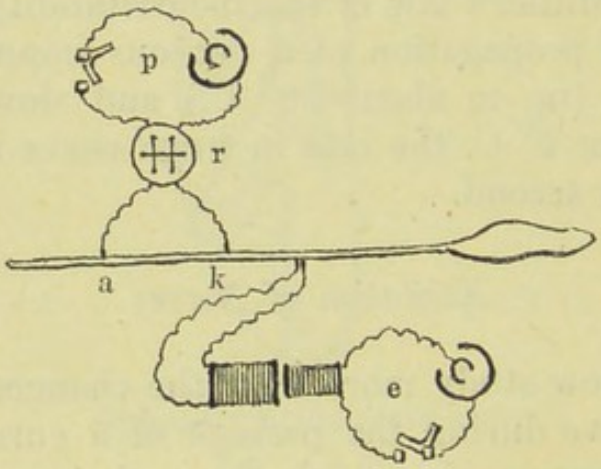
We must now study more fully the changes which take place in a nerve during the passage of a current through it, and the manner in which these changes are able to generate a nervous impulse. Under normal circumstances, if a constant current be passed through the nerve of a nerve-muscle preparation for a short time, the muscle responds only at the make and the break of the current, remaining perfectly quiescent all the time the current is passing. If the nerve be in a very excitable condition, it is possible that the muscle may be thrown into a tetanus or continued contraction during the whole time that the current is passing (closing tetanus). On the other hand,

if a strong ascending current be passed through the nerve for a considerable time, the muscle when the current is broken may go into continued contraction, which may last some time. Normally, however, the muscle simply responds with a single twitch at the make and break of the current; but, on investigating the condition of the nerve during the passage of the current, we find that it is considerably modified.

This modification in the condition of the nerve is spoken of as *electrotonus*, and includes changes in its irritability and its electrical condition.

To investigate these changes the following apparatus is necessary :—two constant batteries, induction coil, a reverser and keys, a pair of non-polarisable electrodes, and a pair of ordinary platinum electrodes. Fig. 39 represents

Fig. 39.



Arrangement of apparatus for showing electrotonic changes in irritability. e. Exciting current. p. Polarising circuit. r. Pohl's reverser.

roughly the arrangement of the experiment. A constant current from the battery is led through a part of the nerve by means of non-polarisable electrodes, which are about one inch apart. In this circuit we put a reverser, by means of which the direction of the current of the nerve may be changed at will, and a key to make or

break the current. This is the polarising circuit. The other battery is arranged in the primary circuit of the coil, a key being interposed, so that we may use make or break induction-shocks, which are applied to the nerve by means of the small platinum electrodes. The tendon of the muscle is connected by a thread with a lever, which is arranged to write on a smoked surface, so that the height of the contraction can be recorded.

We first find the position of the secondary coil, at which the break induction-shock is a submaximal stimulus, and we employ this strength of stimulus throughout the experiment. The make induction-shock is prevented from acting on the nerve by closing a short-circuiting key in the circuit of the secondary coil. The nerve is now stimulated at various points with a single break induction-shock, and the contractions recorded. The heights of these contractions serve to indicate the irritability of the nerve at the point stimulated. We now throw the polarising current into the nerve. At the make of this current the muscle will probably respond with a twitch which is not recorded. We then test once more the irritability of different points of the nerve, and we find that when the stimulus is applied near (a) the point where the current enters the nerve (anode), the stimulus, which before gave a moderately large contraction of the muscle, now has either no effect or else gives a very weak contraction. On the other hand, in the region of the kathode the stimulus, which before was submaximal, has now become maximal, as is shown by the increase in the height of the contraction evoked by the induction-shock.

We now reverse the direction of the polarising current, so that the current of the nerve runs from (k) to (a). With this reversal of current there is also a reversal of the changes in the nerve; that is to say, the normally submaximal stimulus is maximal when applied near (a), and minimal when applied near (k). On break of the polarising current the condition of the nerve returns to

normal, and the submaximal stimulus is once more submaximal throughout.

This experiment teaches us that when a constant current is passed through a nerve, there is increase in the irritability in the nerve near the kathode, and a diminution in irritability near the anode. These conditions of increased and diminished irritability are spoken of as *katelectrotonus* and *anelectrotonus* respectively. In the previous chapter we learnt that a make contraction always starts from the kathode, and a break contraction from the anode. Now the event that takes place at the kathode on make and at the anode on break of a constant current is, as the last experiment shows us, a rise in irritability, in the former case from normal to above normal, in the latter from subnormal to normal. Hence we may say that the excitation is caused by a sudden rise of irritability, which may be due either to a sudden appearance of katelectrotonus, or a sudden disappearance of anelectrotonus. I have said sudden, because the steepness of the rise of irritability is a necessary factor in causing excitation. If the polarising current passing through a nerve be slowly and gradually increased to considerable strength, it will give rise to no contraction. The degree of suddenness of the rise, which is most beneficial in causing contraction, varies with the nature of the tissue stimulated. Thus it is more rapid in nerve than in muscle, and in pale muscle than in red muscle, and in voluntary muscle than in unstriated muscle.

It is evident that there must be, somewhere between the anode and kathode, an indifferent point,—that is to say, a region where the irritability is neither increased nor diminished. We find experimentally that this indifferent point is nearer the anode when the polarising current is weak, and gets nearer to the kathode as the current is strengthened, so that with very strong currents nearly the whole intrapolar length is in a condition of anelectrotonus. When a strong polarising current is used, the depression of irritability at the anode is so marked that no impulse

can pass this region. Thus if we send a very strong ascending current through the nerve, there is no contraction at make. This is owing to the fact that the impulse started at the kathode on make of the current cannot reach the muscle, its passage down the nerve being blocked in the region of the anode.

These results, worked out chiefly on motor nerves, have been confirmed as far as possible experimentally on sensory nerves and muscle, and contractile tissues generally, and probable hold good for all irritable living tissues.

It is said that an anelectrotonus takes some time to attain its full height, and a katelectrotonus reaches its maximum almost directly after the current is made. Hence a current of very short duration probably only excites at the make, the break occurring before the anelectrotonus is developed enough for its disappearance to cause a stimulus. Thus induction-shocks (both make and break) may be looked upon as make excitations, the excitation, however, being stronger in the case of the break induction-shock than in that of the make.

Other things being equal, a current of given strength causes a stronger excitation the greater the length of nerve that it flows through. It must be remembered, however, that the nerve offers considerable resistance to the passage of the current, and so, to keep the current constant while increasing the length of intrapolar nerve, we must largely increase the electromotive force employed.

A nerve cannot be excited by currents passed transversely across it, since in such cases the anode and kathode lie so close to one another in a nerve-fibril as it is traversed by a current that their effects counteract one another.

The excitability of a nerve is, within certain limits, increased by cooling the nerve, and diminished by raising its temperature.* Thus, if a frog be cooled to 2° or 3° C.

* This is true for all stimuli except induction shocks and extremely short galvanic currents (less than ·005 secs.), with which the irritability of nerve is increased by warming and diminished by cooling.

for a day, it will be found that simple section of its sciatic nerve may suffice to send the gastrocnemius into continued contraction, and under these circumstances closing tetanus may be obtained with the greatest ease. The opposite effects of cooling on the conductivity and excitability of nerves show that probably these properties are independent, and are not affected by the same circumstances.

Other stimuli.—1. Heat. If the temperature of a nerve be gradually raised, no effect is noticed till about 40° C. is reached, when the muscle may enter into weak quivering contractions. Sudden warming of the nerve always gives rise to excitation. At about 45° C. the nerve loses its irritability and dies.

A nerve may be rapidly cooled without any excitation taking place. At about 0° C. the conductivity of mammalian nerve-fibres is absolutely abolished, and hence this method of cooling is of great value when it is required to divide a nerve physiologically without exciting it.

2. Mechanical. A nerve may be excited by crushing or cutting. These methods, however, destroy the nerve. It is possible to excite a nerve mechanically, without any serious injury to it, by carefully graduated taps, and this method has been used in investigating phenomena of electrotonus.

3. Chemical. All chemical stumuli applied to the nerve have a speedy effect in destroying its irritability. The chemical stimuli most used are strong salt solutions, glycerin, or weak acids. If any one of these means be applied to a motor nerve, the muscle enters into an irregular tetanus, which lasts till the irritability of the nerve is destroyed at the part stimulated. It is thus evident that we are justified in our choice of electrical stimuli in all ordinary experiments on nerves.

The same appears to be true for ventricular cardiac muscle, but in the case of voluntary muscle the excitability for *all* forms of stimuli is increased by cooling (Gotch).

Fatigue of Nerve and Muscle

It has been shown that it is absolutely impossible to fatigue a nerve-fibre. If a cat be curarised, and one of its sciatics dissected out and stimulated for several hours at intervals with induced currents, the animal being kept alive all the time by artificial respiration, it will be found that as soon as the effects of the curare begin to wear off the muscles of the leg respond to the stimuli.

Under normal conditions, as we have already seen, repeated stimulation of a motor nerve gives rise to a rapidly diminishing series of contractions, until at last the strongest stimulus applied to the nerve is inefficient to cause a contraction. It might be thought, therefore, that the absence of response was due to fatigue of the muscle-fibres themselves, as a result of the accumulation of waste products as well as the using up of contractile material. This, however, is only partly true. A stimulus applied to the muscle directly will cause a contraction almost, but not quite, as extensive as would be produced by a similar stimulus at the beginning of the experiment. It is evident, therefore, that the chief seat of fatigue must lie in the junction between nerve and muscle, *i.e.* in the motor end-plates.

That fatigue, as ordinarily experienced, is chiefly central (*i.e.* cerebral or spinal) in origin, is shown by the fact that after working a muscle until the strongest effort of the will is unable to evoke a contraction, the muscle may be still made to contract by an electrical stimulus applied directly to its motor nerve. In this case the fatigue may be of the nature of a reflex inhibition from the muscle itself.

Ritter-Valli Law

The irritability of the nerve of a muscle-nerve preparation is not equal in all parts of its course, but is greater at

the upper end, probably in consequence of the proximity of the cross-section.

Some time after a motor nerve is divided, the increased irritability at the upper end gives way to a decreased irritability, and this decrease goes on till the nerve is no longer excitable.

The diminution in excitability gradually extends down the nerve-fibre, so that the part of the nerve nearest the muscle remains excitable the longest. This progressive change in the irritability of a nerve after section is spoken of as the Ritter-Valli Law. It is soon followed by definite histological changes in the nerve, which we shall describe later on (see Chap. XII).

Events accompanying the Passage of a Nervous Impulse

In muscle we saw that the passage of an excitatory wave was accompanied or followed by electrical changes, evolution of heat, and mechanical change, all pointing to an evolution of energy from the explosive breaking down of contractile stuff.

In nerve, however, which serves merely as a conducting medium, we should not expect so much expenditure of energy, or, in fact, any expenditure at all. All that is necessary is that each section of the nerve should transmit to the next section just so much kinetic energy as it has received from the section above it. And, indeed, experiment bears out this conclusion. The most refined methods have failed to detect the slightest development of heat in a nerve during the passage of an excitatory process, and we know already that there is no mechanical change in the nerve. The only physical change in a nerve under these circumstances is the development of a current of action. A nerve becomes, when excited at any point, negative at this point to all other points of the nerve, and, just as in muscle, this negativity is propagated in the form of a wave in both directions along the nerve.

Thus, as in muscle, the current of action in an uninjured nerve is diphasic. If, however, the nerve be injured in one of the leading-off points, so as to give rise to a demarcation current, the current of action only appears as a negative variation of this current.

It has been a subject of much debate what the exact nature of the nervous impulse really is, and how it is transmitted down the nerve. Since we have no other evidence of the passage of an impulse down a nerve than the current of action accompanying the impulse, and the result of the arrival of the impulse at the terminal organ, whether it be contraction of muscle, secretion of gland, production of sensation in the central nervous apparatus—all of which effects may be produced by electrical stimulation of the end-organs themselves—it has been thought that the wave of negativity *is* the nervous impulse; that is to say, that the current produced in any given section of the nerve-fibre, when it is stimulated and so becomes negative, excites the adjacent segments or molecules, causing them to become negative, and thus setting up another current of action, which in its turn excites the molecules next in order, and that in this way the excitatory process travels the whole length of the nerve. A natural corollary of this view would be that the normal excitation of nerve-fibre in the brain or at the periphery is also brought about by electrical means. There are, however, considerable difficulties in the way of accepting this hypothesis. Although we can to a great extent imitate the results of the natural excitation of nerve-fibres by artificial electrical stimulation, yet the phenomena in the two cases do not run exactly parallel, and many differences are found to exist between the two forms of a stimulation. The electrical hypothesis, however, although so incomplete, affords us the best explanation of the largest number of phenomena, and so can be usefully adopted as the sign-post to further paths of research.

Electrotonic current.—In describing the effects of the

passage of a constant current through a nerve, we only mentioned mere alterations of irritability. There is a

FIG. 40.

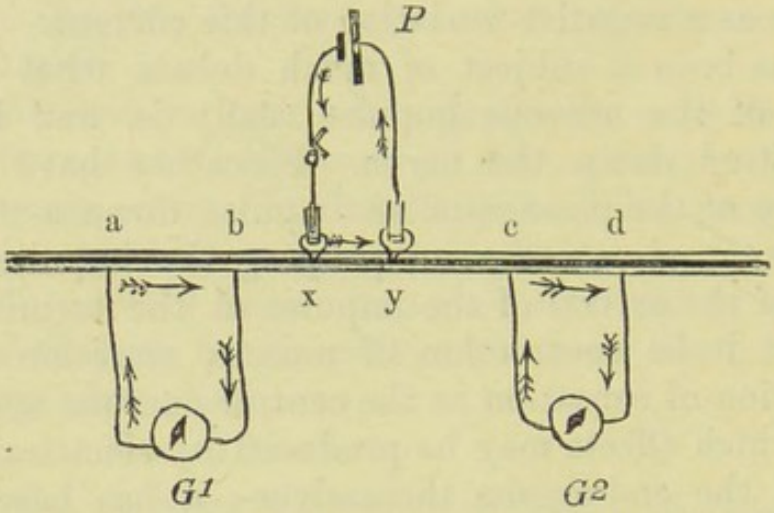


Diagram showing electrotonic currents. *P.* Polarising circuit. G^1, G^2. Galvanometers.

further phenomenon which is more purely physical in its nature.

If a constant current be passed through a nerve-fibre through the electrodes (x) and (y)—(x) being the anode and (y) the kathode—and the extrapolar portions of the nerve (a b c d) be connected with galvanometers, it is found that the needles of both are deflected, and the direction of the deflection shows the existence of a current in the extrapolar portions of the nerve (a) to (b), and from (c) to (d).

The galvanometers will indicate, before the passage of the polarising current, the ordinary demarcation current of the nerve resulting from the cross-section at the upper end. This current flows, in the outer circuit, from equator to cut end, and therefore in the nerve-fibre from (a) to (b), and from (d) to (c). The effect of closing the polarising current will be to increase the current of rest between (a) and (b), and to diminish that between (c) and (d). We thus see that the passage of a current through a part of a

nerve gives rise to a current flowing through a considerable portion of the nerve-fibre on each side of the polarising current and in the same direction. This current is called the electrotonic current. It must not be confounded with the current of action, which originates at one of the poles, only at make or break of the current, and is transmitted thence in the form of a wave with a measurable velocity of about 30 metres per second. The electrotonic current is developed instantaneously, and lasts the whole time that the current is flowing through the nerve. Its production is dependent on the occurrence of polarisation between the sheathing and conducting part of the nerve-fibre, and may be exactly reproduced on a model consisting of a core of zinc wire in a casing of cotton soaked with ordinary salt solution. Although thus physical in origin, its production is dependent on the vitality of the nerve, and so is not to be confounded with the simple spread of current.

Paradoxical contraction.—If the sciatic nerve of a frog be dissected out, and one of the two branches into which it

FIG. 41.

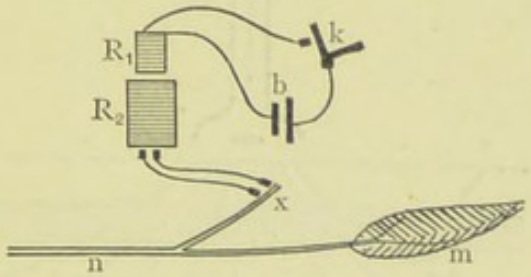


Diagram of arrangement for showing paradoxical contraction.

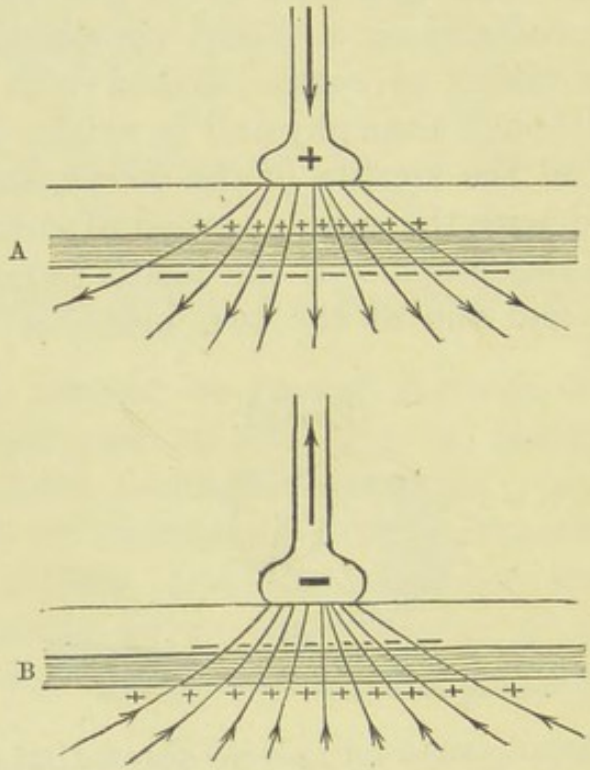
divides be cut, and the *central* end of this branch stimulated, the muscles supplied by the other half of the nerve contract to each stimulus. Ligature or crushing of the nerve (x) between the points stimulated and the point which joins the main trunk puts a stop to this effect, showing that it is not due to a mere spread of current. The fibres passing down (n) are in fact stimulated by the

electrotonic current developed in (x) during the passage of the exciting current.

Electrical Stimuli as applied to Human Nerves

When we attempt to apply results gained on frogs' nerves to man, we are met at once by the difficulty that we cannot dissect out the nerves and apply stimuli to them directly. So usually, unipolar excitation is used, one elec-

FIG. 42.



Electrodes applied to the skin over a nerve-trunk. In A the polar area is anelectrotonic and the peripolar katelectrotonic. The former condition therefore preponderates, since the current here is more concentrated. In B the conditions are reversed, the polar zone corresponding here to the kathode.

trode, anode or kathode, being applied to the nerve to be stimulated, and the other to some indifferent point, such as the back. It is evident, under these circumstances, that the current is concentrated as it leaves the anode and

reaches the kathode, and diffuses widely in the body, seeking the lines of least resistance. Thus it is impossible to get pure anodic or kathodic effects. If the anode be applied over the nerve, the current enters by a series of points (the polar zone), and leaves by a second series (the peripolar zone). The polar zone will thus be in the condition of anelectrotonus, and the peripolar zone in that of katelectrotonus. The current, however, will be more concentrated at the polar than at the peripolar zone, and so the former effect will predominate. These restrictions in the application of the current cause slight apparent irregularities in the law of contraction as tested on man.*

* Cf. Waller, 'Human Physiology,' chap. x.

CHAPTER VI

THE VASCULAR MECHANISM

We have now to study more fully the manner in which the continuous circulation of the blood through the body is carried on.

If an artery in the living animal be cut across, blood spurts from it to a considerable height, escaping in jerks corresponding to every heart-beat. This fact, which shows the existence of a certain amount of pressure on the blood in the artery, may be illustrated in another way. If a vertical glass tube be connected with the central cut end of the carotid artery, the blood will rise in it to a height of three feet (in the rabbit), or still higher in the case of the dog, and remain about this height, rising a little with every heart-beat, and falling again between the heart-beats.

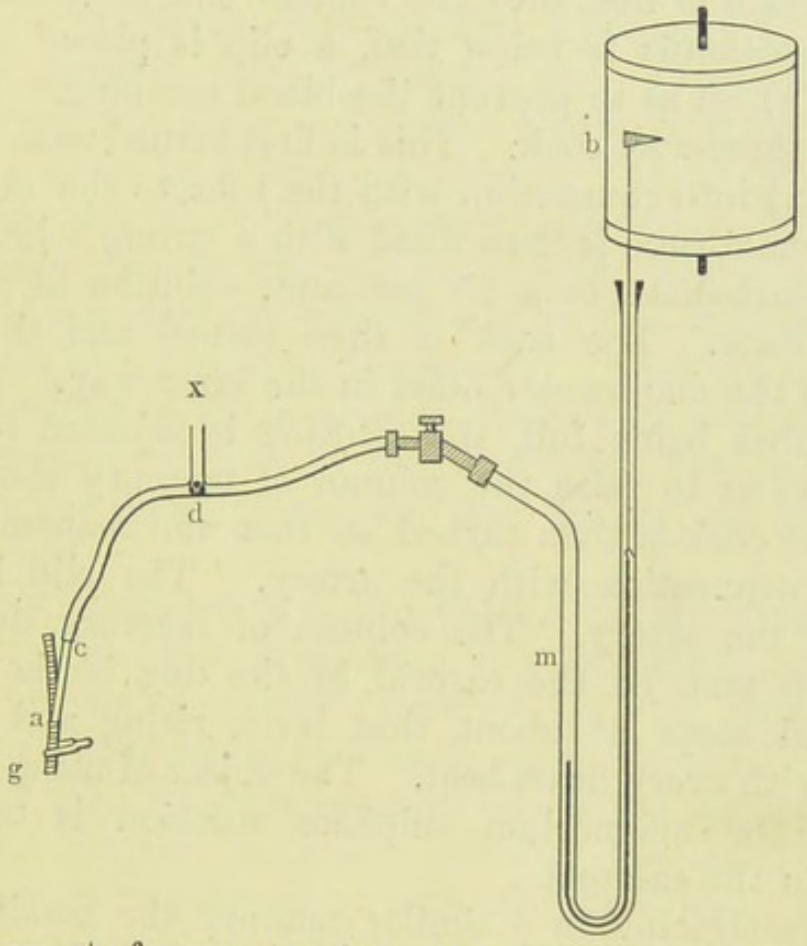
We thus see that the blood in the artery is under a constant pressure, which varies to a slight extent with the heart-beats, rising with and sinking between the beats, but never approaching the line of no pressure.

This blood-pressure may be more conveniently measured and its variations studied by means of an instrument called the manometer. If we simply measure the pressure by inserting a vertical tube into the cut central end of an artery, the animal is injured by the loss of the blood which is necessary to fill the tube, and the experiment is soon stopped by the clotting of the blood in the tube.

There are many different forms of manometer. The best for investigating changes in the mean arterial blood-pressure is Ludwig's mercurial manometer.

This instrument consists essentially of a U-tube with

FIG. 43.



Arrangement of apparatus for taking blood-pressure tracing. a. Artery (carotid). c. Cannula. d. Three-way cock. m. Mercurial manometer. b. Drum covered with smoked paper.

two vertical limbs about eighteen inches long. This is half filled with clean mercury. On the surface of the mercury in one limb is a float, from which a stiff fine rod (of steel or glass) rises, bearing on its upper end a writing point. This point is adjusted so as to record its movements by scratching a white line on the smoked paper of a kymograph. (A kymograph is merely an arrangement of revolving cylinders, moved by clockwork or other means, arranged to carry a roll of smoked paper). Instead of using the smoked paper, a pen may be fitted to the end of the vertical rod, and its excursions recorded in ink on a moving band of white paper.

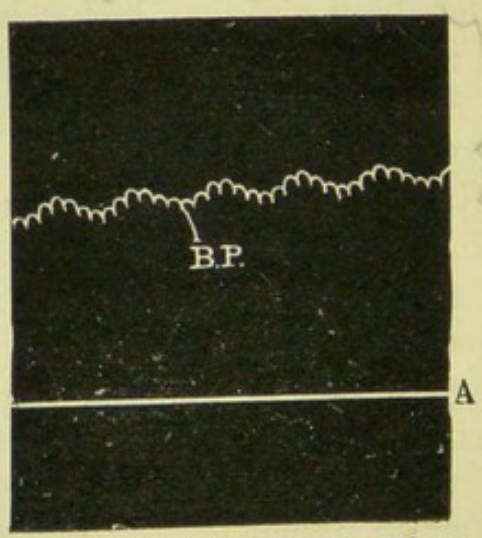
The other limb of the manometer is connected by a

flexible rigid tube (such as lead) with a small tube or *cannula*, which is tied into the central end of the artery While the cannula is being tied, a clip is placed on the artery at (g), so as to prevent the blood escaping. At (d) there is a three-way cock. This is first turned so as to put the tube (x) into connection with the tube to the cannula, and the whole tube is then filled with a strong solution of sodium bicarbonate, or a 25 per cent. solution of magnesium sulphate. The cock is then turned and the tube leading to the manometer filled in the same way.

Both tubes being full, the solution is injected forcibly into (x), so as to raise the column of mercury about 200 mm. The cock is then turned so that the manometer is put into connection with the artery. The clip is then taken off the artery. The column of mercury drops to about 120 mm. (if the carotid of the dog is the artery used), and stops at about that level, rising and falling slightly with every heart-beat. The object of using sodium carbonate or magnesium sulphate solution is to delay clotting in the cannula.

On investigating in a similar manner the condition of the veins, we find quite a different state of things. If a

FIG. 44.



Blood-pressure tracing taken with mercurial manometer (from carotid of rabbit). A. Abscissa or line of no pressure.

vein be ligatured in any part of its course, it swells up on the distal side and shrinks on the side towards the heart. If it be cut across, the bleeding that occurs takes place nearly entirely from the distal end. The hæmorrhage, moreover, is of quite a different character from that which occurs when an artery is divided. The blood, instead of spurting out to a distance, wells up and is not at all increased or in any way affected by the heart-beat. If we connect a manometer with a vein, we find that the pressure amounts to a few mm. of mercury. Thus we see that the blood which in the arteries is under high pressure and has an intermittent flow, by the time it has reached the veins is at a low pressure, and the flow has lost its intermittent character.

What is the cause of this change in the character of the flow? The blood in passing from arteries to veins has to traverse the capillaries. Every time an artery divides, although each separate branch is smaller than the original branch from which it springs, the united sectional area of the two branches is greater; so that the sectional area of the capillaries exceeds by many hundred times that of the aorta. If this increase in the sectional area took place without division, its effect would be to lower resistance to the flow of blood. But if we consider for a moment the condition of the circulation of the capillaries, we see that the friction-lowering effect of increased area is much more than compensated for by the increased surface, and therefore increased friction. Many of the capillaries are no wider than a single blood-corpuscle. The resistance of such a capillary system would be very large even to a stream of water, much more so then to a fluid which is somewhat viscid and has suspended in it a number of solid particles.

The main factors in converting an intermittent flow of the arteries into a constant flow through capillaries and veins and in maintaining a mean blood-pressure in the arteries are —

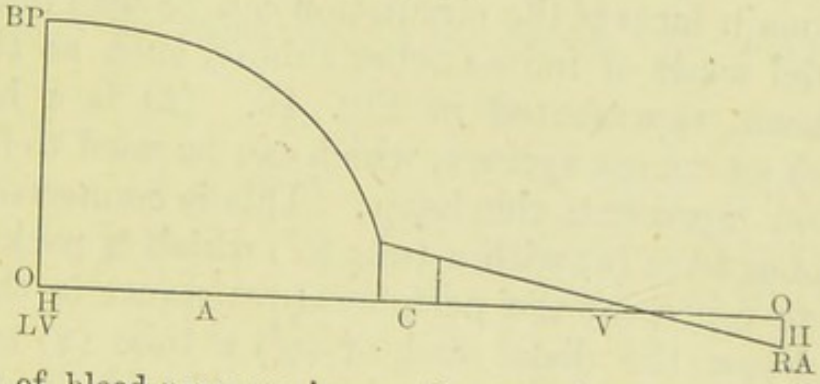
1. The contraction of the heart.
2. The peripheral resistance.
3. The elastic reaction of the arterial walls.

Since this is a purely mechanical question, it will be more easily understood by a simple illustration. The heart may be regarded as a pump, forcing a certain amount of blood (about 4 oz.) into the circulation at each stroke. If a pump be connected with a rigid tube, every time that a certain amount is forced into the beginning of the tube, an exactly equal quantity will be forced out at the other end at the same time. Increasing the peripheral resistance by partial closure of the end of the tube will not affect the intermittent character of the flow, but will merely serve to diminish the quantity thrown in, as well as the quantity which escapes at the other end of the tube, supposing that the work done by the pump is equal in both cases. If, instead of a rigid tube, we employ an elastic tube, and the end be left open so that no resistance is offered to the outflow of the fluid, the effect will be the same as when we use the rigid tube ; the outflow will correspond exactly to the inflow, and will be just as intermittent. But now, if the end of the elastic tube be partially clamped, so as to increase the resistance to the outflow, there will be a marked difference between this effect and that produced by the rigid tube. Each stroke of the pump forces a certain amount of fluid into the tube. Owing to the peripheral resistance, this cannot all escape at once, and so part of the force of the pump is spent in distending the walls of the tube, and part of the fluid that was forced in remains in the tube. The distended elastic tube, however, tends to empty itself, and forces out the fluid which over-distends it, before the next stroke of the pump occurs. So that now the outflow may be divided into two parts,—one part which is forced out by the immediate effect of the stroke of the pump, and another part which is forced out by the elastic reaction of the tube between the strokes. If the strokes be rapidly repeated before the tube has time to

thoroughly empty itself, it will get more and more distended. Greater distension means stronger elastic reaction, and therefore stronger outflow of fluid between each beat. This distension goes on increasing till the fluid forced out between each stroke by the elastic reaction of the wall of the tube is exactly equal to that entering at each stroke, and the outflow thus becomes continuous.

The same thing occurs in the living body. A man's heart at each beat or contraction forces about four ounces of blood into the already distended aorta. The first effect of this is to distend the aorta still further. The elastic reaction of the walls drives on another portion of blood, which distends the next segment of the arterial wall, and so the wave of distension is transmitted with gradually decreasing force along the arteries. This wave of distension is what we feel on the radial artery, or any exposed artery, as the pulse. Between each heart-beat the arteries tend to return to their original size, and so drive the blood on through the capillaries (the peripheral resistance) into the veins. By the time the blood has reached the veins, all

FIG. 45.



Scheme of blood-pressure in—A, the arteries; C, capillaries; and V, veins. OO. Line of no pressure. LV. Left ventricle. RA. Right auricle. BP. Height of blood-pressure.

trace of the heart-beat has disappeared, and the pressure has fallen to a few mm. of mercury.

The accompanying diagram represents roughly the dis-

tribution of pressure along the vascular system. The blood-pressure falls only slowly in the great arteries, as is shown by the line BP in the first part of section A. Towards the end of this section there is a sudden and extensive fall of pressure caused by the increase of resistance in the arterioles. In the capillaries (C) and in the veins (V) the blood-pressure once more falls gradually, till, in the big veins near the heart, it may be negative.

The following table may serve to give some idea of the probable average height of the blood-pressure at various parts of the vascular system in man. It must be remembered, however, that these pressures are all subject to considerable variations according to the physiological condition of the various parts and organs of the body.

Large arteries (*e.g.* carotid)	.	+ 140 mm. mercury.
Medium arteries (*e.g.* radial)	.	+ 110 mm. „
Capillaries . . .	about .	+ 15 to + 20 mm. mercury.
Small veins of arm . . .	.	+ 9 mm. „
Portal vein	.	+ 10 mm. „
Inferior vena cava . . .	.	+ 3 mm. „
Large veins of neck .	from 0 to	− 8 mm. „

These main facts of the circulation can be well illustrated on a model made of india-rubber tubing, such as the artificial schema represented in Fig. 46. (B) is a basin of water, (e) an enema syringe, which can be used to force on water, and represents the heart. This is connected by an india-rubber tube (a) with a tube (C^2) which is packed with sponges to represent the peripheral resistance in the capillaries. From the distal end of (C^2) a tube (V) serves to conduct the fluid back to the basin. To side branches of (a) and (v) two mercurial manometers (m^1 and m^2) are connected, and these are arranged to write one below the other on a smoked surface of a kymograph. Another route for the fluid from (a) to (v) is afforded by the tube (c^1), which may be clamped at will. Tracings are first

FIG. 46.

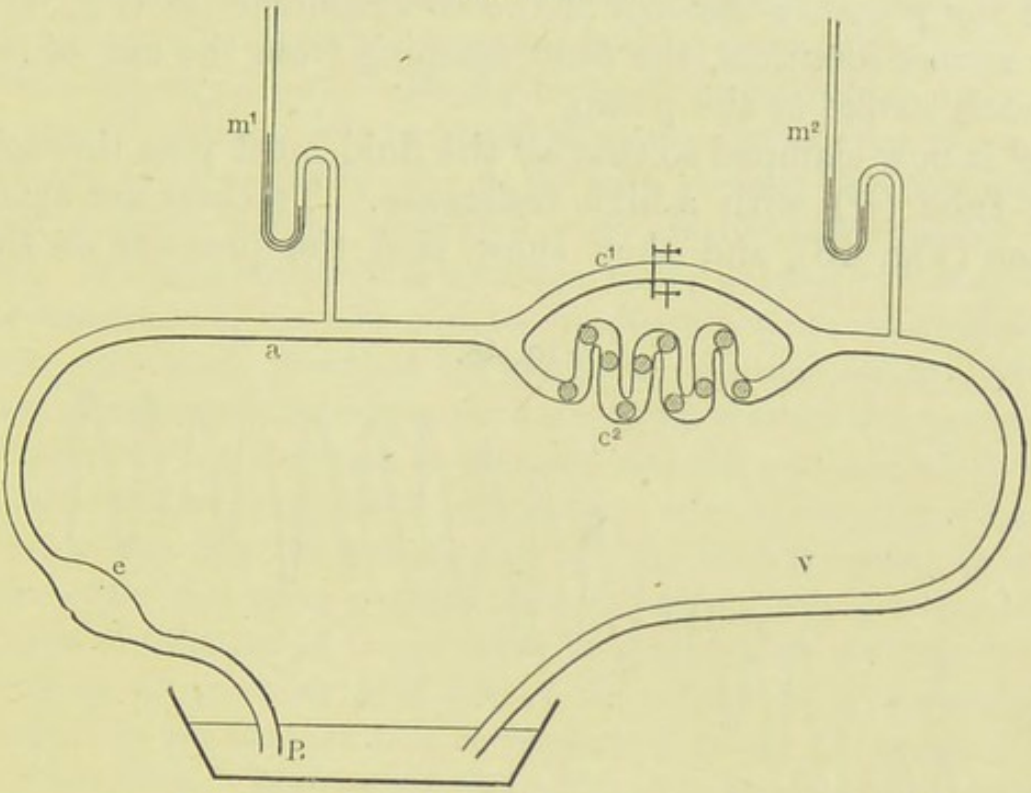
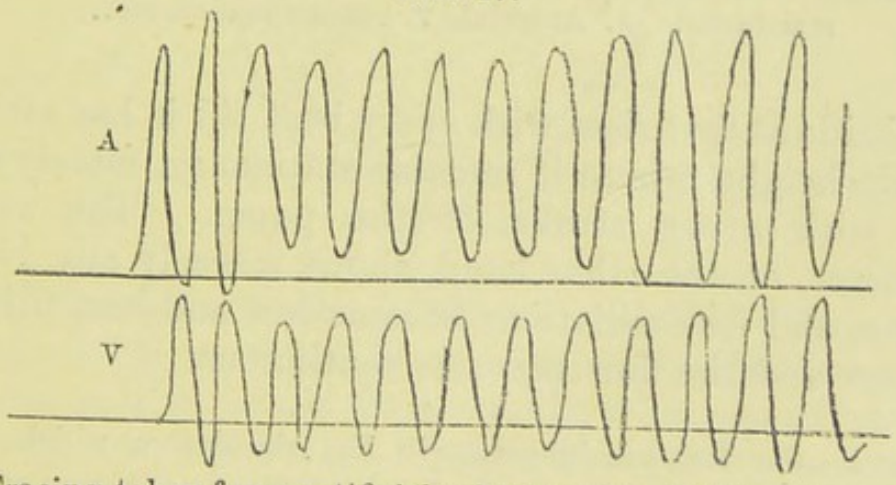


Diagram of artificial circulation schema.

taken of the pressures on the arterial and venous sides with the tube (c^1) open, while the fluid is forced through the system by rhythmical compression of the bulb of the enema. The fluid in passing from (a) to (v) has now practically no resistance to overcome, and accordingly we

FIG. 47.

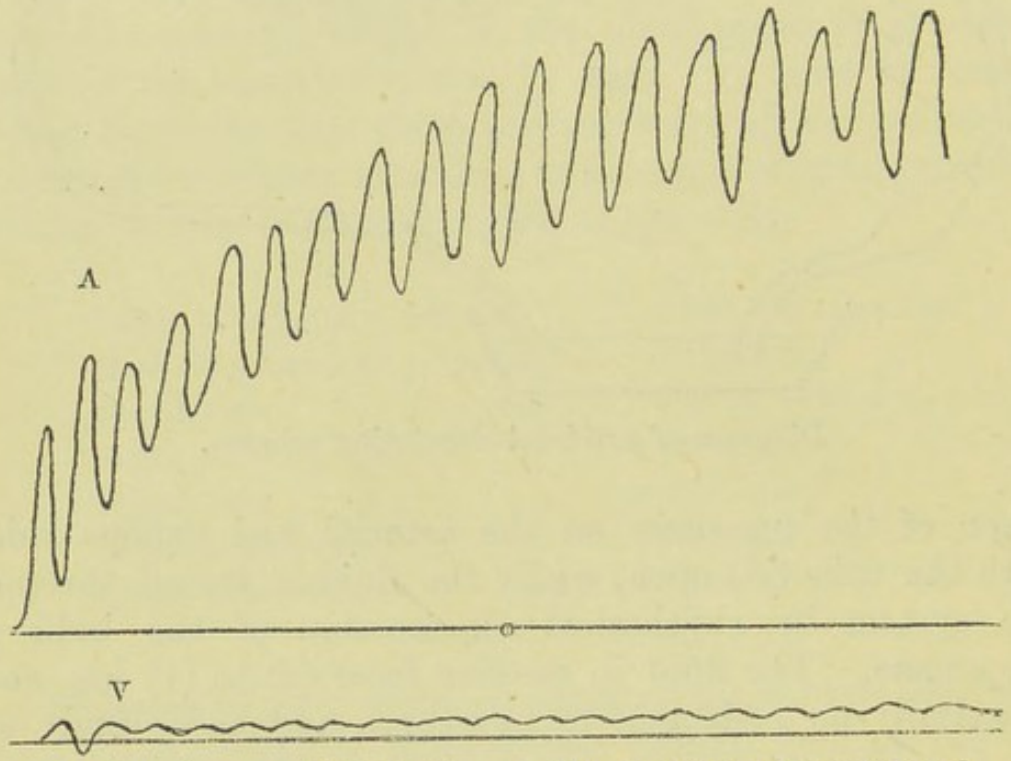


Tracing taken from artificial schema with slight peripheral resistance (Foster). A. Arterial, V. venous manometer.

find the pressure-tracings of the two manometers (Fig. 47) are almost identical, the fluid escaping from the end of (v) at each stroke of the pump.

c^1 is now clamped so that all the fluid must pass through the tube (c^2) with a high resistance. Tracings are again taken (Fig. 48), and they show that the pressure on the

FIG. 48.



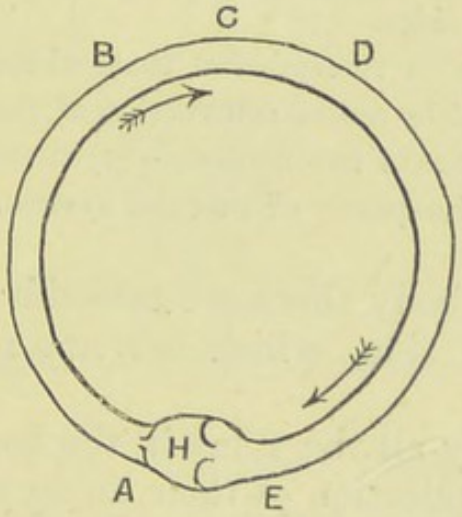
Tracing from artificial schema with considerable peripheral resistance. A. Arterial, V. venous manometer.

arterial side at first rises with every beat till it has attained a certain height, where it remains stationary, merely oscillating with every stroke of the pump. The venous manometer, on the other hand, shows scarcely any rise of pressure, and its oscillations become less and less, till they disappear and the flow becomes continuous.

There is one feature, however, in the circulation which is not represented in the above schema. In the latter the system of tubes is open at both ends, and the amount of fluid supplied to the con-

tracting heart-model is constant. In this model, therefore, so long as the resistance in the circuit is constant, the pressure in all parts of the circuit will vary directly with the force of the heart-beat, and a rise of arterial pressure will be attended with a smaller rise of venous pressure, as shown in Fig. 48. In the body, however, the blood-vessels form a closed circuit, containing a certain invariable quantity of fluid. We may imitate this condition in the schema by connecting the venous end of the tube with the supply-tube of the enema syringe, having previously overfilled the system to a slight extent. Under these circumstances, so long as the heart is not beating, the pressure in all parts of the system will be the same, and this pressure, which may be called the mean general blood-pressure, amounts in a large dog to about 10 mm. Hg. It will be seen at once that the pump or heart cannot alter this mean general pressure, but can only give rise to an unequal distribution of the pressure by diminishing the pressure in the veins by pumping fluid out of them, and by increasing the pressure in the arteries to a corresponding extent by pumping the fluid into them. Thus we may take Fig. 49 to represent the vascular

FIG. 49.



system, which has a definite capacity and contains a definite quantity of blood. If the heart (A E) is not acting, and the fluid is motionless, the pressures at all parts of the system will be the same (10 mm. Hg.). If now the heart begins to act, it pumps blood from the veins into the arteries, so that the latter become distended at the expense of the former, and the arterial pressure rises above, and the venous pressure

sinks below, the mean pressure of the system. It must be remembered that in the body the tubes forming the veins are much more distensible at low pressures than are the tubes on the arterial side. Hence, when the heart begins to beat, we get a large rise of pressure on the arterial side (from 10 mm. to 120 mm.) and only a small fall of pressure on the venous side (from 10 mm. to 5 mm., 0 mm., or near the heart about − 5 mm.). It is evident that, in such a system, while the resistance remains constant, the venous pressure will vary inversely with the arterial pressure, and not directly with the latter, as is the case with an open circuit.

There is one other important fact arising from the closed condition of the circulatory system. In the body, changes in the peripheral resistance are effected by contractions of the smaller arteries and of some of the veins. Now the contractions of these vessels not only increase the peripheral resistance, but also diminish the total capacity of the system, so that now we have the same amount of fluid as before enclosed in a smaller cavity. This must mean an increased elastic distension of the walls of the cavity and a rise of the mean general pressure, so that a general contraction of the arterioles, the heart-beat being unchanged, may cause a rise of pressure, both on arterial and venous sides.

It must therefore be remembered that, whenever a rise in arterial pressure is produced by active contraction of the smaller arteries, it is due to the coincidence of two factors,—(*a*) increased peripheral resistance, (*b*) diminished capacity of vascular system.

In the living body there are two aids to the circulation on the venous side, which are not represented in our schema.

Firstly, nearly all the veins in the body possess valves, formed by reduplication of their lining membrane. These valves are so placed that they only allow the passage of the blood in one direction, viz. towards the heart. Thus any muscular contraction pressing on the veins can only squeeze their blood in one direction, and in this manner it assists the onward flow of blood.

Secondly, as we shall see in treating of respiration, the movement of the chest-walls at every inspiration causes a

suction of the blood towards the thorax, and it is this aspiration of the thorax which gives rise to the negative pressure found in the big veins near the heart.

Rate of flow.—Since the area of the blood-vessels increases progressively from aorta to capillaries, it is evident that the rate of flow must decrease in like proportion. There are several methods by which the rate of flow in the larger arteries may be measured.

Of these we need only mention that in which the 'Stromuhr' is used. This (Fig. 50) consists of two oval

FIG. 50.

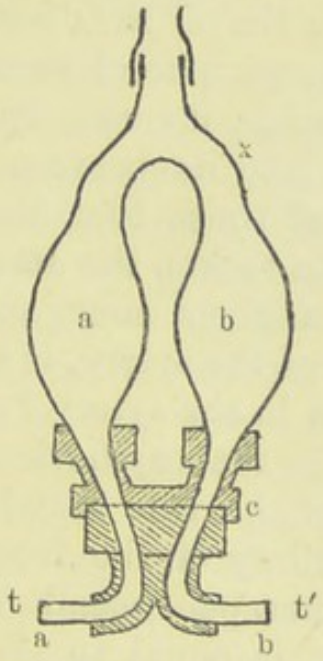


Diagram of Ludwig's Stromuhr.

glass vessels (a) and (b), connected above by means of a glass tube. The capacity of these vessels is accurately known. They are fixed at their lower ends in a metal disc (c), which is fitted on to another disc. The upper disc can be turned round on the lower disc. Through the latter run two tubes (t) and (t′), the upper ends of which are continuous with the vessels (a) and (b), and the lower ends, which are bent outwards in a horizontal direction, can be connected with the central and peripheral ends of

a cut artery such as the carotid. In using this instrument the vessel (a) and connecting tube as far as the mark (x) and the two tubes (t) and (t′) are filled with defibrinated blood. The vessel (b) is filled up to the mark (x) with oil. The (t′) is now fixed into the central and (t) into the peripheral end of a cut artery. As soon as the clips on the artery are released, blood flows from the artery through (t′) into (b′), displacing the defibrinated blood in (a), which flows into the peripheral end of the artery. As soon as the inflowing blood has reached the mark (x), the whole upper part of the instrument is turned suddenly round 180°, so that (b) now is in communication with the tube (t). The blood, which is still flowing steadily into (t′), now rises into (a), driving the oil back into (b), and the blood at (b′) onwards into the peripheral parts of the artery. As soon as the oil reaches its own level, the instrument is turned round again into its previous position, and so on. From the number of times that the Stromuhr has been turned round, we can reckon the amount of blood that has flowed through in a given time, and from this number, knowing the calibre of the artery, it is easy to compute the velocity of the blood in the artery.*

The rate of flow in the capillaries may be measured by direct observation of the rate at which a blood-corpuscle moves along a capillary of the frog's web. It probably varies from $\frac{1}{2}$ to 1 mm. per second. The area of the large veins near the heart is equal to about twice that of the arteries, and this relationship between veins and arteries holds good for the entire system. The veins of one area (the portal area) could contain almost the whole of the blood in the body. Hence, since the same amount of blood enters the heart as leaves it at each beat, the rate of

* If we take v for velocity, m for volume of blood that has flowed through in a unit of time, and a for the sectional area of the artery, then $v = \frac{m}{a}$.

flow in the veins must be about half that in the corresponding arteries.

It is also possible to measure the time taken up by the blood in traversing the whole of the circulation at once. To this end a solution of sodium ferrocyanide is injected into the jugular vein on one side, and the time in seconds is noted that elapses before the salt can be detected in the samples of blood taken from the carotid of the other side. This time in the horse is thirty-one seconds, and in the dog seventeen seconds. In man it has been computed to be about twenty-three seconds.

The Changes occurring in the Heart at each Contraction

If we expose the heart of a mammal, as the rabbit, by opening the chest, the animal being kept alive by artificial respiration, it is possible to observe the sequence of events which occurs at each contraction. The first thing to be noticed is a contraction of the great veins near the heart, which occurs simultaneously on the two sides. When the wave of contraction reaches the auricles, these also contract shortly and sharply towards the ventricles, dragging down with them the auricular appendages, which also take part in the contraction and become pale and bloodless. This is followed almost immediately by the contraction of the ventricles, which is more prolonged and forcible. Contraction of both ventricles occurs synchronously. As we shall show later, contraction of the ventricles begins at the base and extends thence to the apex, but the propagation of this contraction-wave occurs so rapidly that it is impossible to follow it with the eye, all parts of the ventricle appearing to contract simultaneously. During contraction, the ventricle undergoes changes in shape, size, and position, becoming shorter from above downwards and changing in cross-section from an elliptical to a circular form, *i.e.* the heart becomes more conical. There is at the same time a twisting of the inferior parts of the ventricle, owing to the

oblique course of the muscular fibres. If the pericardium is opened, this torsion causes a tilting of the apex forward and to the right with each contraction. In the normal condition, when the pericardium is intact, the apex remains almost stationary during contraction. This is owing to the fact that the pericardium is fixed externally, and the apex could not rise without causing a vacuum between it and the pericardium. The shortening of the long axis of the heart is rendered possible by a change in the position of the auriculo-ventricular groove, which descends with every contraction, the large arteries elongating at the same time as they are stretched by the amount of blood thrown into them.

The contraction or systole of the ventricles is followed by a rapid relaxation, and they remain for some time at rest, being simply passively filled with the blood flowing in through the great veins and auricles. This period of relaxation and rest is called the diastole.

We may now consider the effect of these cardiac events on the contained blood. During diastole the blood is flowing in a steady stream from the inferior and superior venæ cavæ into the right auricles and thence into the right ventricles, the propelling force being supplied by the systemic blood-pressure and the auxiliary forces we mentioned before, *i. e.* muscular movement and aspiration of the thorax. As the great veins contract, they simply hurry on their contained blood into the auricle, which immediately contracts on its contents, driving them through the open tricuspid valves into the right ventricle. It must be remembered that there are no valves at the mouths of the great veins (except in the great coronary sinus) to prevent reflux of blood into them during the auricular contraction. They are, indeed, unnecessary, the exclusive flow of blood into the ventricles being determined by the way in which the auricles contract towards the ventricles, and the low pressure in the ventricles during diastole. The ventricles during the whole of diastole have been getting more and

more distended by the gradual inflow of blood. This distension is suddenly increased by the auricular contraction, and then follows almost immediately the contraction of the ventricles. As the blood is flowing from auricles to ventricles, reflux currents or eddies must be formed on the ventricular side of the tricuspid valves, tending to keep these from being widely opened. Directly the pressure rises in the ventricles, in consequence of the contraction of their walls, the valves are forced back till their edges come in contact and effectually prevent any reflux of blood into the auricles. The close apposition of the edges of the valves is further provided for by the attachment of the chordæ tendinæ of the papillary muscle to the adjacent valves. As the ventricle shortens, the papillary muscles contract, thus preventing the valves being forced backwards and rendered incompetent. The effect of this contraction of the papillary muscles is that the auriculo-ventricular valves, which, during the diastolic period, form a truncated cone, open towards the ventricle, are dragged still nearer to the ventricular wall, so that the blood is, as it were, expressed between two cones (heart-wall and valves). At the same time the contraction of the circular fibres at the base of the heart constricts the auriculo-ventricular orifices, so bringing the valves at their origin close together, and enabling their inner surfaces as well as their free edges to be apposed for a considerable extent (*v.* Fig. 51). The valves being thus closed, the pressure rises higher and higher in the ventricle, till it exceeds that in the pulmonary artery. Directly this is the case, the semilunar valves open and allow the ventricle to discharge its contents. The flow of blood from ventricle to artery goes on during the whole systole of the ventricle; during this time the semilunar valves are pressed outwards, but not close to the arterial wall, since they are probably kept in an intermediate position by the reflux currents or eddies set up in the blood on their arterial side. They thus form an orifice, triangular in shape with

curved sides, presenting but little resistance to the onward flow of blood.

FIG. 51 A. FIG. 51 B.

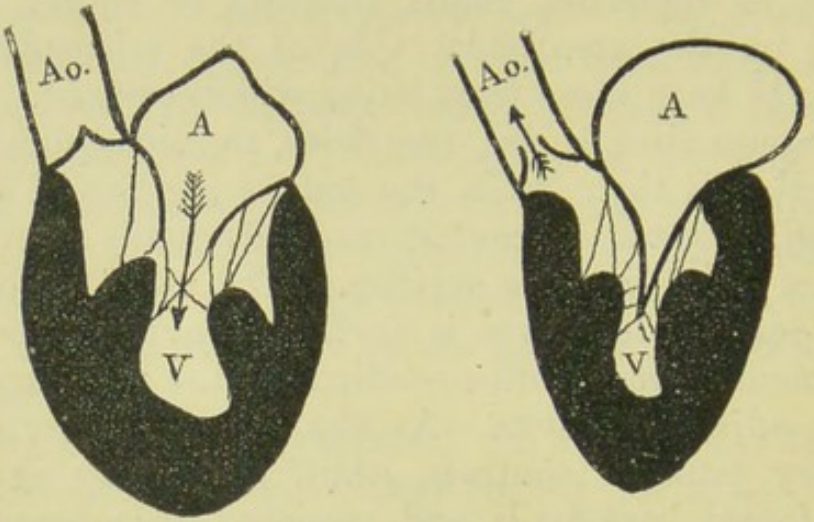


Diagram to show position of mitral valves in diastole (51 A) and systole (51 B). A. Auricle. V. Ventricle. Ao. Aorta.

Directly the ventricular contraction ceases and the blood stops flowing, these reflux currents tend themselves to bring the valves together. At the same time the pressure in the right ventricle falls quickly to nothing, and the sudden difference in the pressures on the two sides of the valves causes them to shut tightly and sharply, giving rise to a click which is distinctly audible on listening with one's ear closely applied to the chest-wall, and represents the *second heart-sound*. The lunulæ of two adjacent valves are closely pressed together, thus preventing the possibility of the leakage of even a single drop of blood back into the ventricle.

While these events are occurring on the right side of the heart, an exactly similar series is taking place on the left. During the diastole blood flows from the pulmonary veins to the left auricle and ventricle. The left auricle then contracts, and this is followed by the contraction of the left ventricle. The only difference between right and left sides consists in the fact that the pressure which has to be

overcome in forcing blood into the aorta is much greater than that in the pulmonary artery, and so the left ventricle, having much more work to do, is much thicker, and contracts more forcibly than the right. The closure and opening of the mitral and aortic valves occur in just the same way as the corresponding events affecting the tricuspid and pulmonary valves.

Heart-sounds

If we apply our ear to the front of a person's chest, (it is more convenient to use the stethoscope for the purpose,) we hear two distinct sounds accompanying each beat of the heart, followed by a pause corresponding to the diastole. The sounds are compared to the syllables *lubb*, *dup*, the first sound being low-pitched and prolonged, the second sound high and sharp.

Thus the heart-sounds may be represented :

lubb, *dup* (pause), *lubb*, *dup* (pause).

The causation of the second sound is very simple, and may be considered first. It is heard just over the second right costal cartilage, *i. e.* the place where the aorta lies nearest the surface.

It comes at the end of the systole, as determined by the hardening of the apex of the heart, felt as the apex-beat, and can be shown to be synchronous with the closure of the aortic valves. It is, in fact, caused by the sudden shutting and stretching of these valves that occur directly the heart ceases to contract and to force blood into the aorta. If the valves be hooked back (by means of a wire passed down a carotid artery) in an animal, the second sound disappears, and is replaced by a murmur caused by the blood rushing back into the ventricle at the end of the systole. The same disappearance of the normal second sound is often observed in cases where the valves are prevented from closing by diseased conditions.

The pulmonary and aortic valves generally close simultaneously. In some cases, however, the aortic may close slightly before the pulmonary, giving rise to a 'reduplicated second sound.' The pulmonary element of this sound is best heard over the second *left* cartilage.

The first sound has probably a twofold origin, viz. from the sudden closure of the auriculo-ventricular valves, and from the contraction of the thick muscular wall of the ventricle.

If the veins going to the heart be clamped, so that the heart can no longer be distended with blood nor the valves put on the stretch, the sound is altered in character but not abolished. The first sound may, indeed, be heard on listening with a stethoscope to the beat of an excised heart. It is said that two notes may be detected in the first sound—a high note of short duration due to closure of the valves, and a long low-pitched note due to the muscular contraction. This muscular element of the first sound has the same pitch as the sound produced by voluntary contracted muscle, and therefore as the resonance-tone of the ear.

This consideration prevents our arguing from the tone that a cardiac contraction is a tetanus. As we shall show later on, each ventricular contraction is analogous to a simple muscle-twitch, and not to a tetanus.

By means of these sounds we are able to determine to a certain extent the amount of time taken up by each phase of the cardiac cycle. The heart beats in a healthy man about seventy-two times per minute. So we may say that each systole with its corresponding diastole (cardiac cycle) is completed in about $\frac{8}{10}$ of a second.

This time is divided up in the following way :—Systole of auricle $\frac{1}{10}$ sec., systole of ventricle $\frac{3}{10}$ sec., diastole $\frac{4}{10}$ sec.

The relationship between the phases and heart-sounds is represented by Fig. 52.

We arrive at a clear idea of the events occurring during

the ventricular systole by a study of the endocardiac pressure-curve.

FIG. 52.

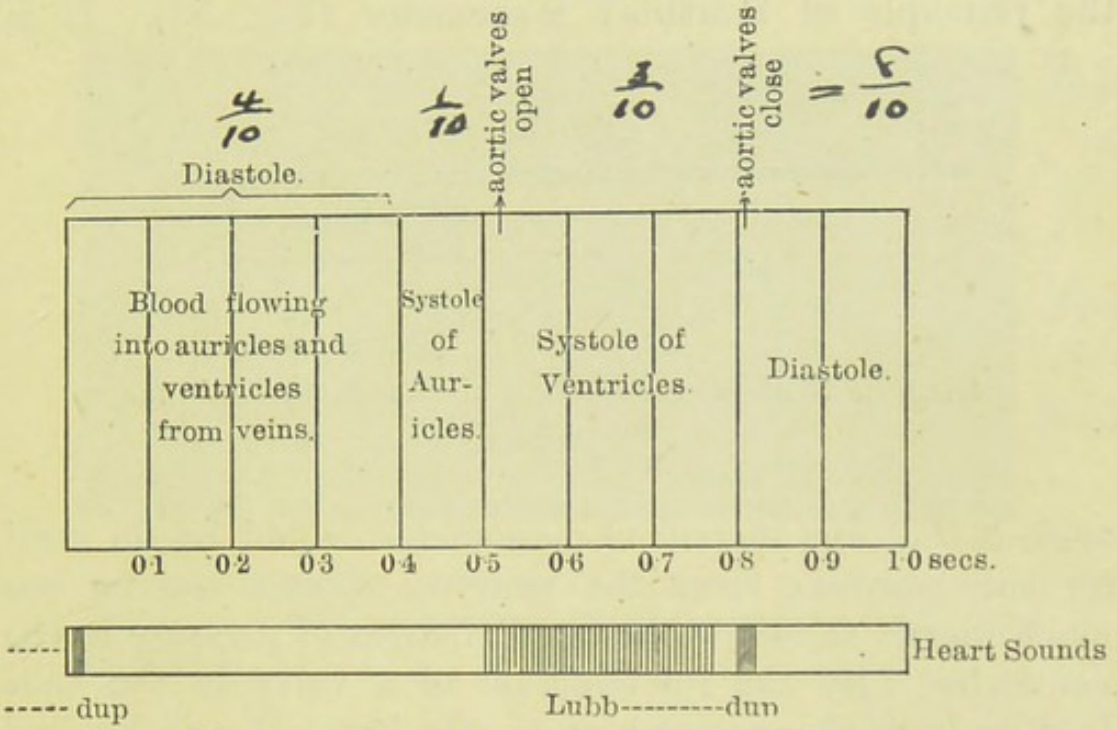


Diagram of events constituting a cardiac cycle.

There are several methods by which the endocardiac pressure may be recorded. In one (Chauveau and Marey) a cardiac sound is put down the jugular vein into the right auricle or ventricle, or down the carotid into the left ventricle. The cardiac sound is a stiff tube, having an elastic bag or 'ampulla' at the end that is to be inserted into the heart. The upper end of the tube is connected with a tambour, which is a small round metal tray covered with delicate elastic membrane. To the top of the membrane a writing lever is attached. Any change of pressure on the ampulla causes a corresponding movement of the lever on the tambour, which may be recorded on a moving smoked surface.

Since this instrument is very easily set into vibrations, it is often difficult to know whether a given rise or depression on the tracing is to be taken as of cardiac oe instrumental origin. Hence it is better to make thr

tambour very small, with thick rubber, so as to limit the movements, and to fill it with saline fluid, which is also used to fill the tube connecting it to the heart. This is the principle of Hürthle's manometer (Fig. 53). It is

FIG. 53.

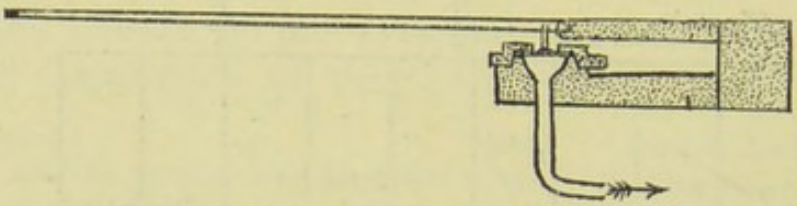


Diagram to show construction of Hürthle's membrane manometer.

evident that the mercurial manometer would be no good for this purpose, since the mercury column has far too much inertia to follow the rapid changes of pressure in the ventricles. By the introduction of a valve in the tube leading from the manometer to the heart, it may be used as a maximum or minimum manometer. If the valve permits fluid to go only towards the heart, the manometer will indicate the minimum pressure ever attained during the cardiac cycle. If it be turned the other way it will indicate the maximum pressure.

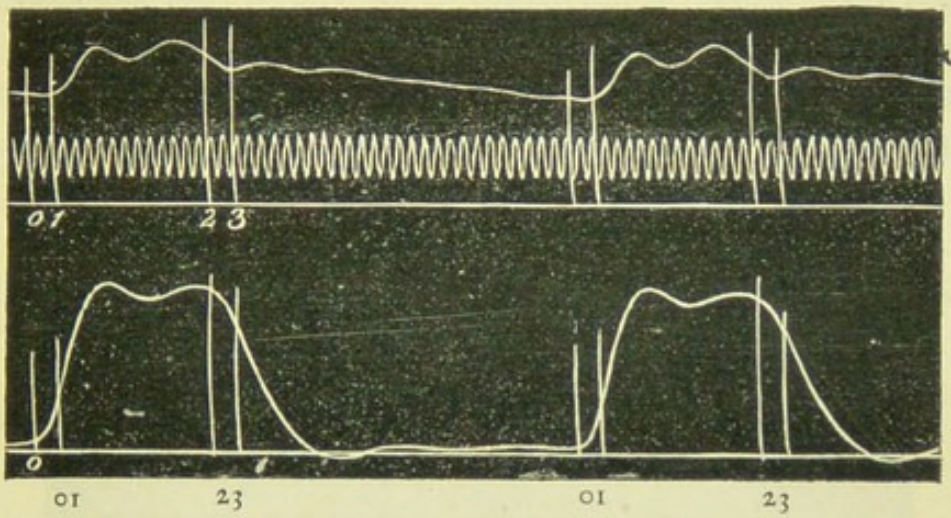
In the dog the maximum pressure in the left ventricle may be 140 mm., in the right ventricle 60 mm., and in the right auricle about 20 mm. Hg.

The use of the minimum manometer reveals the striking fact that, at some period of the cardiac cycle, there is a negative pressure in the ventricle; that is to say, the mercury is sucked up in the limbs of the manometer towards the heart. This negative pressure may amount to 30 or 40 mm. Hg. in the left ventricle, to 15 mm. in the right ventricle, and to 7 or 8 in the right auricle.

If, however, we register the variations of endocardiac pressure by means of a manometer which is sufficiently accurate to record quick changes in pressure that occur in

the ventricle with each heart-beat, we get a curve like Fig. 54. By registering this curve simultaneously with that of

FIG. 54.



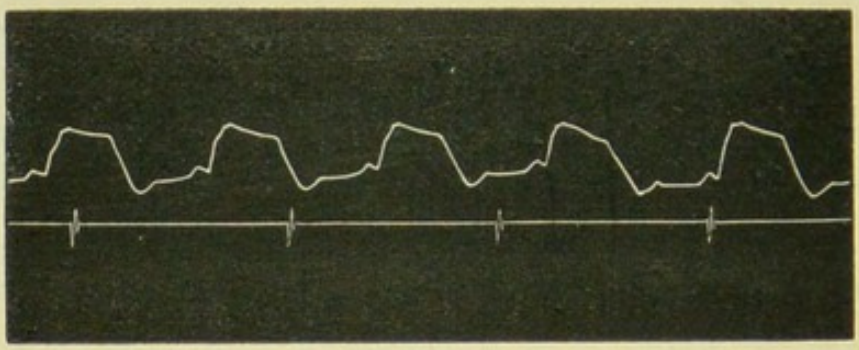
Curve of endocardiac pressure, V, compared with pressure in aorta, A. Each vibration of time-marker = $\frac{1}{100}$ sec. (Hürthle).

the blood-pressure in the aorta, we may determine what events are occurring during each phase of the curve. The auricular systole in some tracings gives rise to a small rise of endocardiac pressure represented by an elevation on the curve which would occur before the ordinate 0. It generally lasts about ·05 second. It is not represented in the curve reproduced in Fig. 54. This is immediately followed by the ventricular contraction, which lasts from 0 to 2. From 0 to 1 the ventricle is getting up pressure, so that at 1 the intraventricular pressure is equal to the aortic pressure. This process takes from ·02 to ·04 second. Directly the intraventricular pressure rises above this point the aortic valves open and blood is driven into the aorta. The outflow of blood lasts from 1 to 2, about ·2 second. At 2 the ventricle suddenly relaxes, the period of relaxation occupying about ·05 second. The flat part of the curve is often spoken of as the systolic plateau, and on an average occupies about ·18 second. According to the condition of the heart and peripheral resistance, this plateau

may present a gradual ascent or descent (*v.* Fig. 59). Almost immediately afterwards relaxation commences, the intraventricular pressure falls below the aortic, so that the aortic valves close somewhere near the upper part of the descent (at 3).

Cardiogram.—We may get a somewhat similar curve by applying a tambour, armed with a button, over the

FIG. 55.



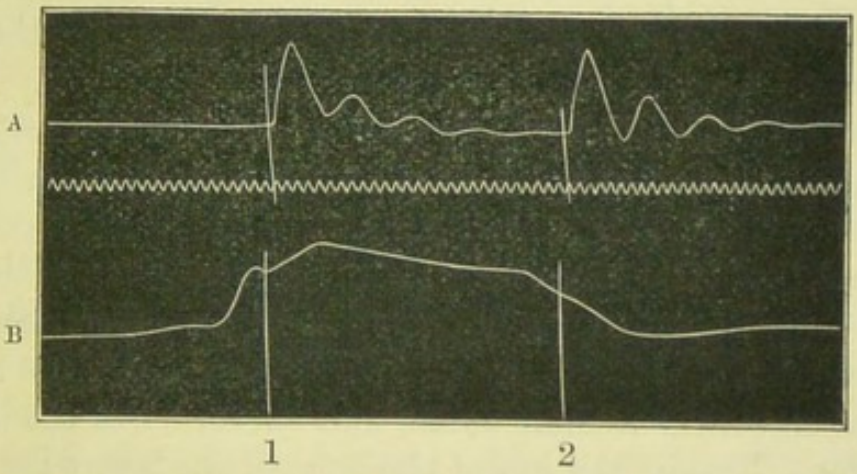
Card'ogram (Hürthle).

apex-beat, though this curve may vary considerably in the same subject, according to the pressure employed and the exact spot at which the tambour is applied. Fig. 55 represents a cardiographic tracing or cardiogram, which may be spoken of as typical. In order to interpret this curve, we must record at the same time either the intraventricular pressure in animals, or the heart-sounds in man.* Applying the latter method we may obtain the

* This mechanical record of the heart-sounds has been successfully accomplished by Hürthle. His method consists in an application of the microphone. A special form of stethoscope is so arranged that by its means the vibrations corresponding to the heart-sounds are transmitted to a contact between silver and carbon. Through this contact a strong current is passing. This also passes through an electro-magnet, which attracts an iron disc attached to the membrane of a Marey's tambour. Any vibration transmitted to the carbon-silver contact alters its resistance, and so the strength of the current passing

curve shown in Fig. 56. In this curve it will be seen that the first heart-sound, corresponding to the ventricular systole, begins, not at the commencement of the rise of the cardiogram, but at the notch near the top of the ascent. From this fact we may conclude that the first part of the ascent is caused by the auricular systole forcing blood into the ventricle, the ventricular systole being marked by the notch near the top of the curve. In Fig. 55, taken from the dog, the auricular curve is more distinct as a slight elevation preceding the rise due to the contraction of the ventricles. Other forms of curve, however, are often obtained, which show considerable differences from the

FIG. 56.



Cardiogram (B) with simultaneous record of heart-sounds (A) (Hürthle). 1. Position of first heart-sound. 2. Position of second heart-sound.

endocardiac pressure, and are spoken of as atypical. They are often conditioned by a faulty position of the cardiograph.

through the electro-magnet. In this way the heart-sounds can affect the pull exerted by the electro-magnet on the membrane of the tambour, and the change in the volume of the contained air recorded by means of an ordinary registering tambour.

Negative Pressure

It will be noticed in the curve of endocardiac pressure that the line drawn by the lever descends slightly below the base line at the end of systole. This is the period at which the negative pressure occurs. This is, however, of such short duration that the most delicate manometers fail to show its maximum value. Several explanations have been suggested for the production of this negative pressure. When the flow of fluid through a tube is suddenly interrupted, the column of fluid, which has a certain degree of inertia, tends to go on, so that a negative pressure is produced in its rear. If, however, the negative pressure in the ventricle were due to the sudden cessation of flow through the first part of the aorta, we ought to obtain with the minimum manometer a negative pressure at the root of the aorta equal to that found in the ventricle. This, however, is not the case, so that the cause of the negative pressure must be sought in the ventricle itself. It is probably due to the fact that during ventricular contraction the base of the heart, including the orifices of the pulmonary artery and aorta, is constricted. Directly the ventricle relaxes, the pressure of blood in these two trunks causes a dilatation of their bases, and therefore of the base of the heart. This dilatation of the base of the heart increases its capacity, and so creates a negative pressure in the ventricular cavities. This mode of production of the negative pressure may be illustrated experimentally by connecting a manometer with the interior of either of the ventricles of an excised heart that has ceased beating and forcing fluid into the aortic and pulmonary arteries. With each distension of the arteries so produced the mercury in the manometer sinks, showing the production of negative pressure in the ventricles.

It is possible also that the ventricles exert some expanding force as they return from a contracted to an uncontracted condition.

The Pulse

If a finger be placed on some artery, such as the radial, we feel an expansion of it occurring at regular intervals corresponding to the heart-beats. On the tracing of a mercurial manometer we saw a similar rise and fall produced by each heart-beat. So the pulse may be defined as the expansion of the artery under the increased blood-pressure caused at each ventricular systole. Just as the blood-pressure diminishes from heart to periphery, so the pulse diminishes in size as we get farther away from the heart. If the arterial system were perfectly rigid, the increased pressure due to the forcing of blood into it by each ventricular systole would occur almost simultaneously over every point of it. In the elastic distensible arteries, however, the first effect of the inflow of blood into the aorta is to distend a section of the aorta nearest to the heart. The elastic reaction of this forces a portion of blood on into the next section, distending it in its turn. And so the increased pressure is transmitted from segment to segment of the arteries, in the form of a wave, at a velocity of about five metres per second. We must be careful not to confuse the velocity of the pulse-wave with that of the blood. The velocity of the blood in the aorta is not more than half a metre per second, and gets less and less towards the periphery. The pulse-wave may be compared to a wave produced by the wind travelling rapidly down a sluggishly flowing river.

We will make this difference clearer by an illustration. If the hindmost of a row of billiard balls be struck sharply with a cue, the foremost ball flies off and the others stop still. In this case the energy imparted to the first ball by the stroke has been transmitted from ball to ball, just as the effect of the ventricular contraction is transmitted from section to section of the arterial blood-stream. If the balls are struck so that the cue continues pressing on

the hindmost after the stroke is delivered, the front balls fly off, while the others move slowly along in the direction of the stroke. In the arteries this continuous pressure is furnished by the elastic reaction of the arterial wall, and we see how the impact of the blood may travel quickly along as a wave of increased pressure, while the blood itself is moving slowly along, impelled by the elastic reaction of the arterial wall.

To study the pulse more fully it is necessary to obtain a graphic record of the expansion of the arteries, or, what comes to the same thing, of the exact changes in pressure which produce this expansion. The curve obtained with the mercurial manometer shows elevations corresponding to the pulse; but the instrument is far too sluggish to record the finer variations of pressure. For this purpose a manometer such as Hürthle's, which has very little inertia, must be used.

The expansion of the artery is registered by means of a lever which may be made to rest more or less heavily upon the artery, and the movements of which are recorded on a blackened surface. Such an instrument is called a

FIG. 57.

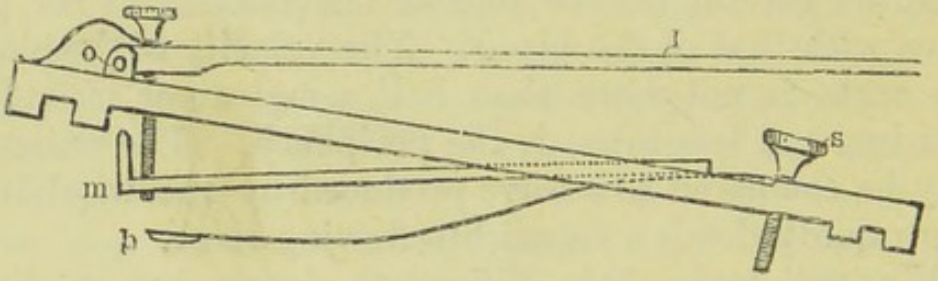


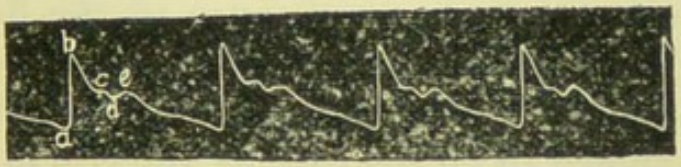
Diagram showing principle of Marey's sphygmograph. The button (b) is adjusted so as to press on the radial artery. Its movements are transmitted to a lever (m). The screw on this works on a small cogged wheel at (o), which is also the axis of the writing lever (l). The movements of the button (b), thus transmitted to a point near the axis of (l), are reproduced by this lever highly magnified, and as such are recorded on a blackened surface. The pressure on the artery can be adjusted by means of the screw (s).

sphygmograph. Of the many forms of sphygmographs, Dudgeon's or Marey's is perhaps the most convenient for clinical purposes (Fig. 57).

It is generally applied to the radial artery, since this is near the surface and is supported by bone, and the arm is well adapted for the application of the sphygmograph. The pulse curve obtained by means of a sphygmograph varies according to the artery employed and the force with which the lever presses on the artery, but all the curves present the same general features.

Fig. 58 represents a pulse-curve taken from the radial artery.

FIG. 58.



Pulse-curve from radial artery.

It will be noticed that the elevation due to the expansion of the artery is sudden and uninterrupted. We have already explained that this is due to the sudden pumping of blood into the first part of the aorta, whence the impulse is transmitted as a wave along the arteries. The curve descends gradually till the next beat occurs, since the elastic reaction of the arteries, which tends to keep up the pressure, acts more constantly and steadily than the heart-beat. On this descending part of the curve occur two or three secondary elevations. b is the primary or percussion wave, c the pre-dicrotic or tidal wave, and e the dicrotic wave. Elevations may occur on the curve after e, which are called post-dicrotic waves. It is better, however, for reasons which we shall see presently, to class the elevations before the dicrotic notch d as systolic elevations, and those afterwards, including the dicrotic

elevation itself, as diastolic. For the exact understanding of these elevations it is necessary to take simultaneous tracings of the pressure in the left ventricle and the aorta. In this way we may dissociate the waves caused by the ventricular systole from those having their origin in the aorta. In Fig. 59 is represented typical tracings of cardiogram, intraventricular pressure and aortic pressure taken simultaneously. The dotted lines are drawn through synchronous parts of the curves. Considering first the dotted part of Curve II and Curve IV,* we see that the contraction of the ventricle begins at A; the rise of intraventricular pressure from A to B is without effect on the aortic pulse; at B the intraventricular is exactly equal to the aortic pressure, and then rapidly rises above it. Since the aortic valves offer no resistance to the flow of blood from ventricles to aorta, it is evident they must open so soon as the intraventricular exceeds the aortic pressure, and this is shown to be the case by the rise of pressure in the aorta. From B to C the ventricle is still contracting and forcing the blood into the already distended aorta, so causing a rise of pressure. At C the ventricle relaxes, the intraventricular pressure falls quickly, and at D has fallen below the aortic pressure. The aortic valves must now close, since the pressure is greater on their aortic side. The fall of pressure in the ventricle now goes on uninterruptedly, but in the aorta there is a sharp elevation immediately after D. This elevation is the dicrotic wave. We thus see that it comes immediately after closure of the aortic valves.

There are several factors at work tending to produce a secondary wave at this point.

* Curve IV in Fig. 59 must be compared with the pulse-tracing taken from the radial artery in Fig. 58. It will be seen that, apart from the fact that Fig. 59, IV, is more lengthened out than Fig. 58, owing to the great rapidity of the recording apparatus, the curves are practically similar.

FIG. 59.

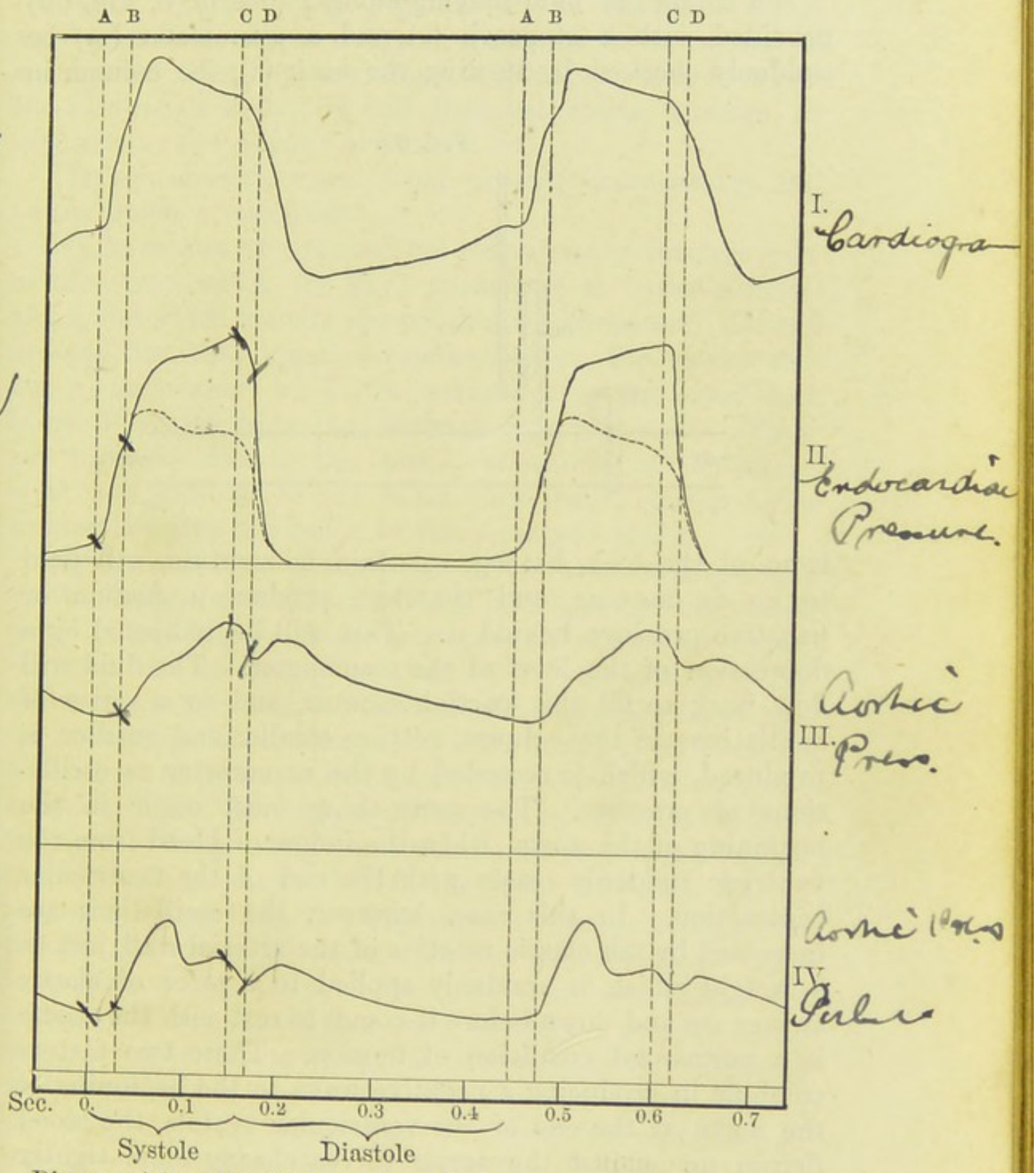
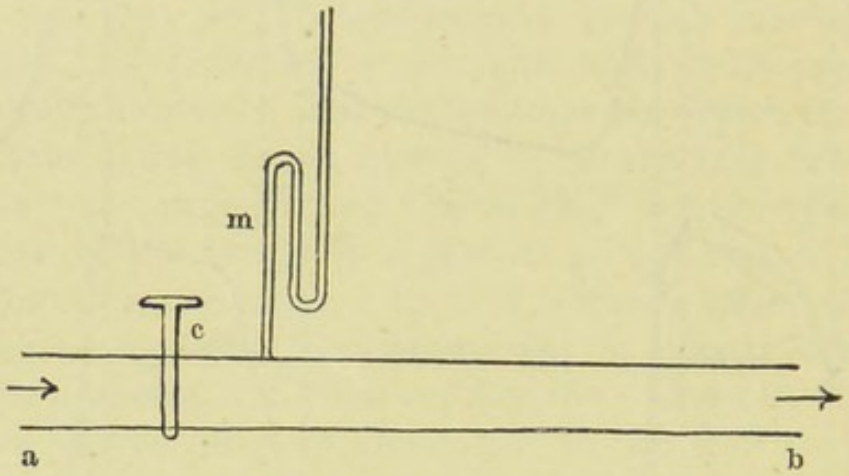


Diagram (after Hürthle) showing simultaneous cardiographic, endocardiac, and aortic curves. I. Cardiogram. II. Endocardiac pressure. III. Aortic pressure. IV. Aortic pressure, corresponding to dotted endocardiac curve in II.

If a column of fluid moving along a tube (a, b, Fig. 60) provided with a stopcock (c) and a manometer (m) be suddenly checked by turning the cock (c), the column in

FIG. 60.



front of the cock, having a certain momentum, will tend to go on moving, and therefore produce a suction or negative pressure behind it. This will be indicated by a depression of the level of the manometer. The fluid will flow back to fill this partial vacuum, and so a series of oscillations in the column, getting smaller and smaller, is produced, which is recorded by the manometer as oscillations of pressure. The same thing must occur in the beginning of the aorta, when the inflow of blood from the ventricle suddenly ceases with the end of the ventricular contraction. In this case, however, the oscillations are increased by the elastic reaction of the arterial wall, just as a weight which is suddenly applied to a piece of elastic swings up and down before it comes to rest with the elastic in a permanent condition of tension. These two factors combine in producing a negative wave in the beginning of the aorta at the end of the ventricular systole, the blood driven up against the aortic valves closing them tightly and putting them on the stretch. The negative wave, even in the rigid tube, is followed by a positive wave in the opposite direction. In the aorta this positive wave is

increased by the elastic reaction of the stretched aortic valves, so that we may regard the blood as being driven up against them by the negative pressure, and then rebounding like a billiard ball from the elastic cushion, to give rise to the dicrotic elevation.

The post-dicrotic waves, when present, are probably due to the waves of oscillation.

We have now to consider the elevations in the first part of the curve, which we have spoken of as systolic elevations, and which include the pre-dicrotic elevation. It will be seen that they are also represented on the ventricular curve, and occur while the aortic valves are open and blood is flowing from the ventricle into the aorta. They are probably due to the elastic vibrations of the aortic wall, and perhaps of the heart wall itself, started by a sudden increase of tension in the aorta and heart.

The general form of the pulse curve varies with changes in the heart, in the arteries, and in the peripheral resistance. Thus some curves may present secondary elevations on the ascending part, as in Fig. 59, III, and are called *anacrotic*, while in others all the secondary elevations occur on the descending part. This latter type is called *katacrotic*, and is the tracing usually obtained from a normal radial artery. By comparing these two types of curves with the corresponding intraventricular pressures, we find that in both cases blood is flowing into the aorta during the whole time, from the beginning of the primary elevation to the notch just before the dicrotic elevation. This is shown by the fact that the intraventricular pressure is all this time slightly higher than the aortic pressure. So long as this is the case blood must flow from ventricle into aorta. (This fact shows that there is normally no part of the cardiac cycle during which the ventricle remains contracted and empty, the ventricle in all cases relaxing before it has completely emptied itself of blood.)

Now it is easy to see the conditions which determine whether the systolic plateau shall be ascending or descend-

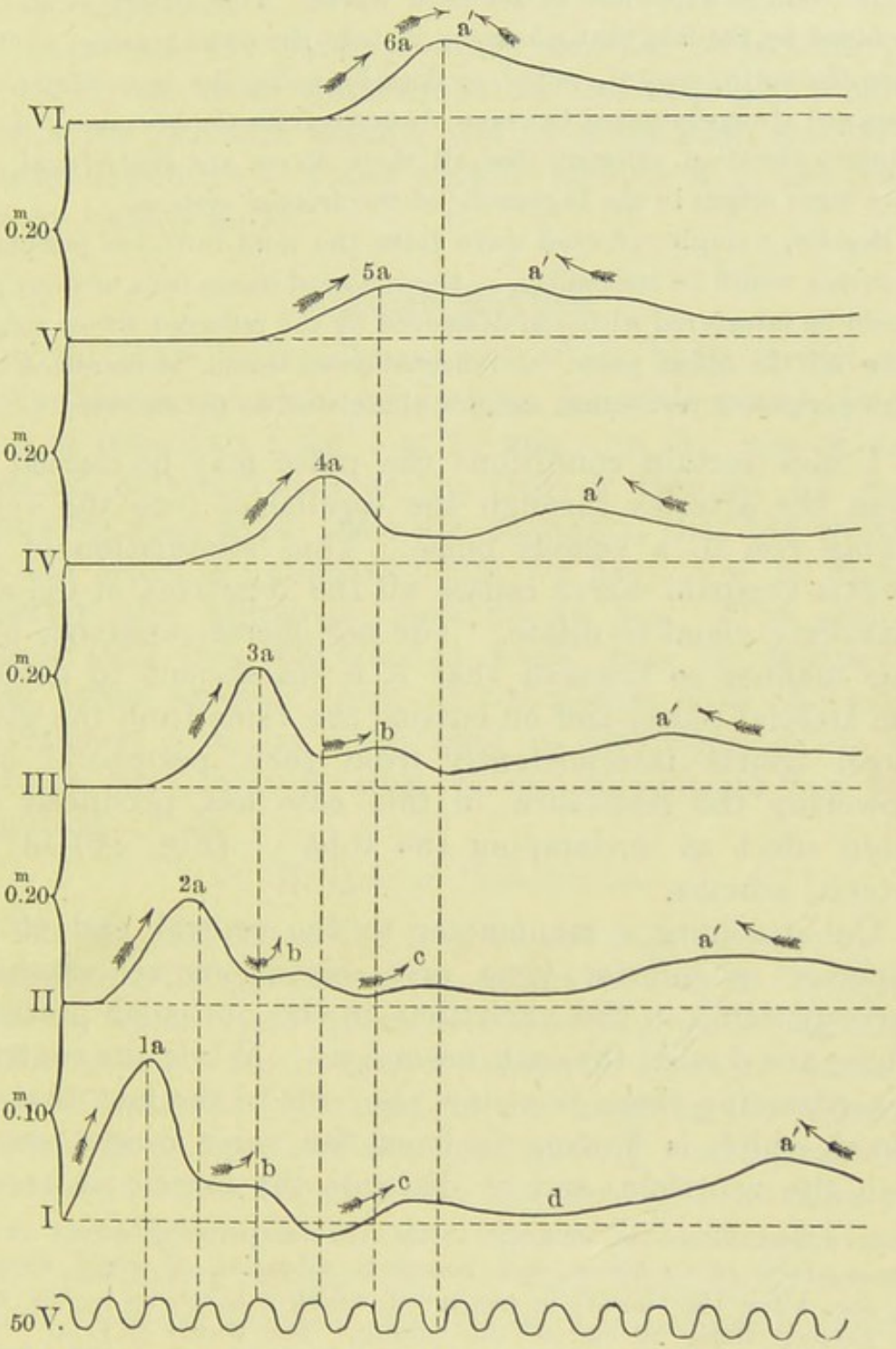
ing, and therefore when the pulse shall be anacrotic or katacrotic. If, after the first sudden rise of pressure in the aorta, the blood can escape more rapidly through the peripheral resistance than it is thrown into the beginning of the aorta, the systolic plateau will sink, and a katacrotic pulse tracing is obtained.

If, on the other hand, the peripheral resistance is high, or an extra large amount of blood be thrown into the aorta at each stroke of the heart (*e. g.* by prolongation of the diastole), the aortic pressure will rise so long as blood is flowing in, and we get an ascending systolic plateau and an anacrotic pulse. Thus we obtain an anacrotic pulse in old people with Bright's disease, in whom the peripheral resistance is very high, and also in animals when the heart is slowed by vagus action.

The production of the dicrotic elevation is favoured by any influence which increases the elastic resiliency of the arteries or causes the primary elevation of the pulse to be rapid and sharp. Thus it is much more pronounced in young people than in old people, whose arteries have become rigid. Where the peripheral resistance is low through relaxation of the arterioles, and the heart is beating forcibly, as in many cases of fever, and also to some extent after a good meal with alcohol, the dicrotic elevation becomes very marked. Under such circumstances it may be easily felt with the finger at the wrist, and in many cases the mistake has been committed of taking the dicrotic wave for a normal beat, and so doubling the rate of the pulse.

In tracings of the artificial pulse obtained from the arterial schema, secondary elevations are observed on the descending part of the curve, which are not explained in any of the above-mentioned ways. These waves are the reflections of the primary wave from the peripheral resistance. This is shown by the fact that the nearer to the peripheral resistance we record the pulsation, the nearer is the secondary to the primary wave. Near the pump the two waves may be separated by a considerable interval (Fig. 61).

FIG. 61.



Pulse-curves described by a series of sphygmographic levers placed at intervals of 20 cm. from each other along an elastic tube, into which fluid is forced by the sudden stroke of a pump. The pulse-wave is travelling from left to right, as indicated by the arrows over the primary (a) and secondary (b, c) pulse-waves. The dotted vertical

It has been thought that some of the elevations in the normal pulse curve could be explained as reflected waves. This theory is at once excluded by the fact that wherever we take the pulse tracing, whether from the aorta, carotid, radial, or dorsalis pedis, the secondary elevations are always situated the same distance from the beginning of the primary elevation, showing that all these waves are centrifugal, and have their origin in the beginning of the arterial system.

Besides, a single reflected wave from the multitudinous peripheral divisions would be impossible, as the reflected waves from any one part would be interfered with and destroyed by the reflected waves coming from all the other parts. A reflected wave would be increased by a high peripheral resistance, and not diminished as the dicrotic is.

Under certain conditions the pulse may be carried on from the arteries through the capillaries into the veins, giving rise to a venous pulse. Thus stimulation of the chorda tympani nerve causes all the arterioles of the submaxillary gland to dilate. The peripheral resistance is in this manner so lowered that it is insufficient to destroy the arterial pulse, and on cutting the veins from the gland blood spurts intermittently from their peripheral end. Lowering the resistance in this case has produced the same effect as unclamping the tube C^1 (Fig. 46) in the arterial schema.

On attaching a manometer to the central end of the superior or inferior vena cava, elevations are observed corresponding to the variations in the auricular pressure. These are double for each heart-beat. While the ventricle is contracting there is a slow rise, due to the fact that the blood which is flowing in from the veins cannot escape into the ventricle, and so distends the auricle; a second

lines drawn from the summit of the several primary waves to the tuning-fork curve below, each complete vibration of which occupies $\frac{1}{50}$ sec., allow the time to be measured which is taken up by the wave in passing along 20 cm. of the tubing. The waves (a′) are waves *reflected* from the closed distal end of the tubing; this is indicated by the direction of the arrows. It will be observed that in the more distant lever (VI) the reflected wave, having but a slight distance to travel, becomes fused with the primary wave. (From Foster, after Marey.)

short sharp elevation of pressure is produced by the auricular systole.

Alterations of venous pressure are also to be observed in the great veins, determined by the respiratory movements, the pressure sinking during inspiration and rising during expiration. These may be spoken of as the respiratory venous pulse.

Cardiac Rhythm

If the heart be rapidly cut out of the body, it will continue beating in a normal fashion for some time,—in the case of mammals from 5 to 10 min. ; in the case of cold-blooded animals, such as the frog or tortoise, for some hours, or even days. We say, therefore, that the rhythm of the heart is automatic ; and we have now to discuss wherein this automatic rhythmicity lies. The circumstance that the cold-blooded heart goes on beating so long, when severed from all connection with the body, has caused it to be much used in investigations on the subject, and from it most of our knowledge has been acquired.

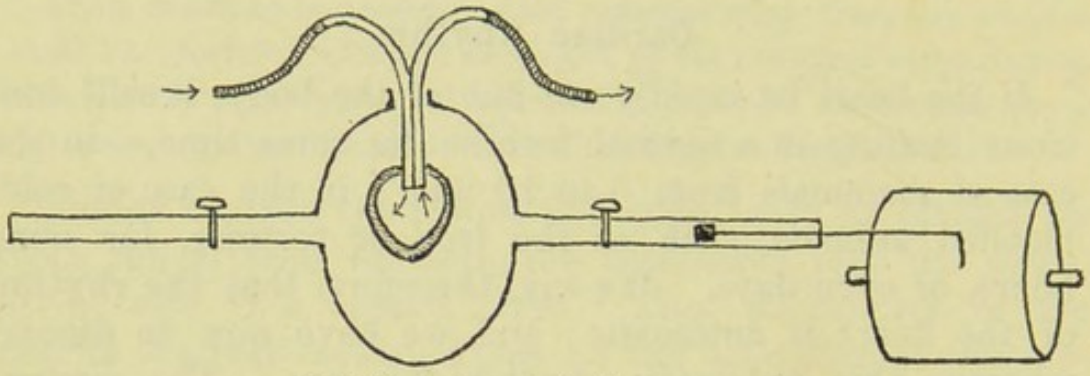
Methods of Investigation

The contractions of the frog's heart may be recorded by magnifying its movements by means of a light lever, one end of which rests upon the ventricle, while the other end is made to write upon a blackened surface—or, as in Gaskell's method, by clamping the heart in the auriculo-ventricular groove, and attaching threads from auricle and ventricle to two levers which are arranged to write one over the other. Or we may register the changes in the intraventricular pressure by allowing dilute blood or some other nutrient fluid to flow through a perfusion cannula tied into the ventricle, and attaching the exit-tube of the cannula to a small mercurial manometer.

Another way is to register the changes in volume of the heart. The ventricle is tied round a perfusion cannula,

and is inserted into an air-tight vessel containing oil. On one side of the vessel is a tube, in which a lightly moving piston is fitted, to which a writing lever is attached. Fluid is passed through the heart by the perfusion cannula at a constant pressure. The changes in volume are indicated by the movements of the piston.

FIG. 62.



Schäfer's heart plethysmograph.

The frog's heart differs anatomically in several respects from the mammalian heart. It consists of sinus venosus, two auricles, one ventricle, and bulbus arteriosus. The venous blood from the body flows into the sinus venosus by the three venæ cavæ, and thence into the right auricle. The left auricle receives the blood from the lungs. The ventricle thus receives mixed arterial and venous blood.

The muscular fibres of the heart are less highly developed

FIG. 63.

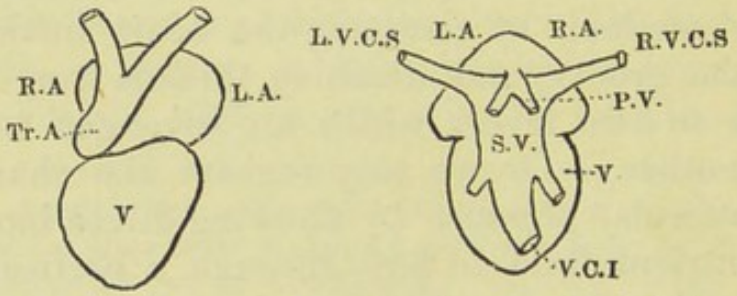


Diagram of frog's heart (after Cyon). V. Ventricle. R.A., L.A. Right and left auricles (atrium). S.V. Sinus venosus. P.V. Pulmonary veins. L.V.C.S. and R.V.C.S. Left and right superior vena cava. V.C.I. Vena cava inferior. Tr.A. Truncus arteriosus.

than those of the mammalian heart. They are spindle-shaped, and only dimly cross-striated. The cross-striation becomes more distinctly marked as we proceed from sinus to ventricle, the sinus muscle-fibre representing the most primitive condition. There is complete muscular continuity between all the cavities of the heart. The circular ring of muscle at the junctions of sinus with auricles, and of auricles with ventricles, presents only slight traces of cross-striation.

The heart is well supplied with nerve-fibres and ganglion-cells.

The two vagi enter the sinus venosus, and branch just under the pericardium. Here they become connected with a collection of nerve-cells, spoken of as Remak's ganglion.

From the sinus, the two vagi, now called septal nerves, pass down in the interauricular septum, one in front and the other behind. Near the auriculo-ventricular groove they enter two collections of ganglion-cells, called Bidder's ganglia. From these ganglia non-medullated fibres are distributed to surrounding parts of the auricle and to the whole of the ventricle. In the upper third of the ventricle occur scattered ganglion-cells attached to the nerve-fibres. These are quite absent in the lower half or two thirds.

The frog's heart in the body, or when removed from the body intact, beats regularly, the contraction starting in the sinus, then travelling to auricles, ventricle, and bulbus. If, however, the heart be removed by cutting it across the sino-auricular junction, or if the auricles be functionally separated from the sinus by a ligature round this junction (Stannius' ligature), the auricles and ventricles stop dead in an uncontracted condition (diastole) while the sinus goes on beating regularly. After the lapse of a period varying from five minutes to half an hour the detached part of the heart begins to beat, at first slowly, and then more rapidly, but never attaining the rate of the sinus. The auricles beat first, and then the ventricle.

If now the ventricle be cut away by an incision in the auriculo-ventricular groove from the auricles, the latter go on beating; while the former, after a few beats due to the excitation of the incision, stops still, and only after a considerable time begins again to contract very slowly.

On the other hand, a ventricle apex preparation (that is to say, the lower two thirds of the ventricle separated functionally from the rest of the heart) never beats again under normal circumstances. To single stimuli it responds with a single beat, not with a series of beats as the whole heart does.

If the lower third of the ventricle be separated functionally in the living frog by crushing the ring of tissue between it and the upper third, it never gives a spontaneous beat again, although, however, it is under the most normal conditions possible. There is thus a descending scale of automatic power in the different parts of the frog's heart,—from sinus, where it is highest, to lower part of ventricle, where it is apparently absent. From this fact it has been thought that the automaticity of the frog's heart is dependent on the ganglia present in it. The contraction is supposed to be started by impulses proceeding from the sinus ganglion. If this be cut off, Bidder's ganglia, or the scattered cells in the upper third of the ventricle, can take up its task of originating impulses. The muscle-cells under this hypothesis act as the servants of the ganglion-cells, just as the voluntary muscles of the cells in spinal cord and brain.

But we have evidence that the muscle-cells do not take so subordinate a *rôle* as this in the heart, and that the larger ganglia, at any rate, are of very little importance in initiating the rhythm. Remak's and Bidder's ganglia may, with care, be excised without markedly interfering with the normal rhythm or sequence of contraction. The ventricle apex may be made to contract rhythmically by slightly increasing the pressure on its interior, either by clamping the aorta in the living frog, or by supplying a

ventricle-apex preparation through a perfusion cannula with diluted blood at a pressure rather above the frog's normal blood-pressure. A strip cut from the apex of the tortoise's ventricle may be made to beat rhythmically, if it be hung in a moist chamber and stimulated at intervals with weak induction shocks. After a time the strip begins to beat of its own accord, and beats rhythmically for many hours.

It seems probable, then, that the automaticity of the heart is inherent in its *muscular* tissue, the difference in the automatic power of the various parts being dependent on their different histological characters. The lowly differentiated sinus-cell has high rhythmic power and a quick rhythm of beat, but contracts feebly. The more highly differentiated ventricle-cell has only slight rhythmic power, but beats forcibly, and is a good servant of the sinus. If all parts of the heart had equal rhythmic power or same rate of rhythm, there would be no reason why any one part of the heart more than another should initiate the beat. As it is, the beat always starts in the more frequently beating part, viz. the sinus. In some animals this difference of rhythmic power is less marked, and the contraction may start from either end of the heart. Even in the frog, the heart cavities may be made to contract with a reversed sequence, *i. e.* ventricle, auricles, sinus, by artificially stimulating the ventricle at a rate exceeding the normal sinus rhythm.

The next question is, how is the excitatory process conducted from sinus to auricle and thence to ventricle? It was formerly thought that this conduction was effected through nerves. It has, however, been shown by Gaskell in the tortoise's heart, where the nerve-trunks run apart from the auricles, from sinus to ventricle, that division of these trunks causes no alteration in the rhythm of the ventricle. If, however, the auricles be cut through, leaving the ventricles attached to the sinus by the nerve-trunks, the sequence of beats is utterly lost.

The auricle may be slit up by interdigitating cuts, by

which all nerve-trunks must infallibly be divided, and yet the wave of contraction passes from the sinus over the auricle, round the interdigitating cuts to the ventricle.

There is a distinct pause between the contractions of auricles and ventricle. This was supposed to point to the intermediation of nerves in the transmission of the excitatory process across the groove. The pause, however, is probably due to the fact that the muscle-cells forming the auriculo-ventricular ring are very slightly differentiated, and so contract and conduct slowly, *i.e.* this muscular ring presents a 'block.'

The auricle may be made to beat in two halves by merely dividing the sinus from the ventricular half, leaving them connected by a very narrow strip of auricular wall. In this way a block is produced at the cut. The sinus contracts, then the upper part of the auricle. This is followed by a distinct pause, during which the excitatory process is passing the block. The ventricular half of the auricle then contracts, followed by the ventricle and bulbus.

We may conclude that a normal contraction of the frog's heart originates in the muscular wall of the sinus, and travels as a wave from muscle-cell to muscle-cell, over the auricles and ventricle; the apparent pauses between sinus and auricles and auricles and ventricle being due to the low conducting power of the muscular tissue connecting these cavities.

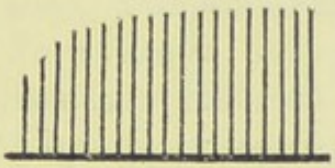
It will be seen from what we have already said that the contraction of the heart is to be looked upon as a single contraction wave, propagated from one end of the heart to the other, just as a wave of contraction passes along the sartorius (though at much quicker rate and of shorter duration) when this muscle is stimulated at one end.

In several points, however, the properties of cardiac muscle differ from those of ordinary striated muscle. Its automaticity and power of responding rhythmically to continuous stimuli have already been mentioned. The

height of contraction of a voluntary muscle is, within certain limits, proportional to the strength of stimulus. If the ventricle, rendered motionless by a Stannius' ligature, be stimulated with a single induction shock, it always responds with a maximal contraction, whether the stimulus applied be minimal or maximal. There is thus no proportionality in the heart between strength of stimulus and height of contraction. The heart, if it contracts at all, always contracts to its utmost. The height of the contraction is dependent on the condition of the muscle at the time, but not on the strength of stimulus.

If the frog's ventricle has been at rest for some time, a single contraction makes the heart more excitable and in a better condition. So if, in a Stannius' preparation, we excite the ventricle with single induction shocks once in every ten seconds, the first four or five contractions form an ascending series, each contraction being rather higher than the preceding one.

FIG. 64.



Group of pulsations showing staircase character.

Rhythm of Mammalian Heart

So far as we know, the process of contraction in the mammalian heart is essentially the same as in the frog's heart. The contraction starts in the terminations of the great veins, and travels thence over the auricles. There is then a pause of about one tenth of a second, and then the ventricle contracts, the contraction starting at the base, and travelling thence as a wave to the apex.

The only essential difference seems to lie in the comparative automaticity of the ventricles in the two cases, the mammalian ventricle possessing much more automatic

power than the frog's. If the ventricles be functionally separated from the auricles by crushing the auriculo-ventricular groove, both parts continue beating, but at different rhythms, the ventricular rhythm being as a rule much slower than that of the auricles. Conduction is probably effected, as in the frog's heart, by the intermediation of the muscular tissue. Ganglia are present in all parts of the heart, including the ventricular apex, but it is not known how far they take a part in the initiation of the normal rhythm.

Innervation of the Heart

The heart is supplied with nerves from two sources—vagi and the sympathetic. The fibres supplying the heart run a slightly different course in the frog and in the mammal, such as the dog. The sympathetic fibres to the frog's heart leave the cord by the anterior root of the third spinal nerve, pass through the ramus communicans to the corresponding splanchnic ganglion, and thence by the second ganglion, the annulus of Vieussens, and the first ganglion to the cervical sympathetic. This runs up to join the ganglion trunci vagi, and thence the fibres run down with the vagus nerve.

In the dog, the sympathetic fibres to the heart leave the spinal cord by the anterior roots of the second and third dorsal nerves, run in the rami communicantes to the stellate ganglion, and thence by the annulus of Vieussens to the inferior cervical ganglion. The cardiac branches containing these fibres run from the stellate ganglion, the annulus, the inferior cervical ganglion, and the trunk of the vagus to the heart.

The efferent fibres to the heart which run in the vagus arise in the medulla from the accessory nucleus of the spinal accessory nerve.

The effect of stimulating these two sets of nerve-fibres is the same in the frog and mammal. In the frog, since

FIG. 65.

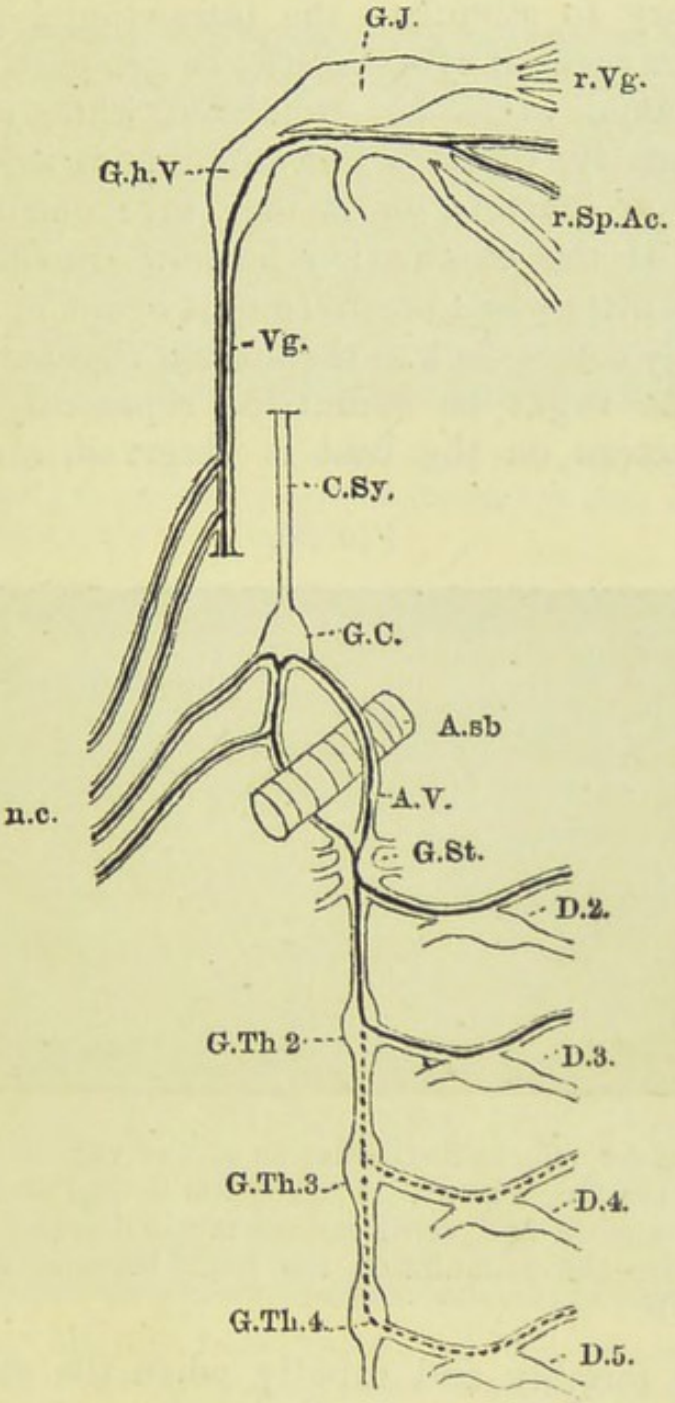
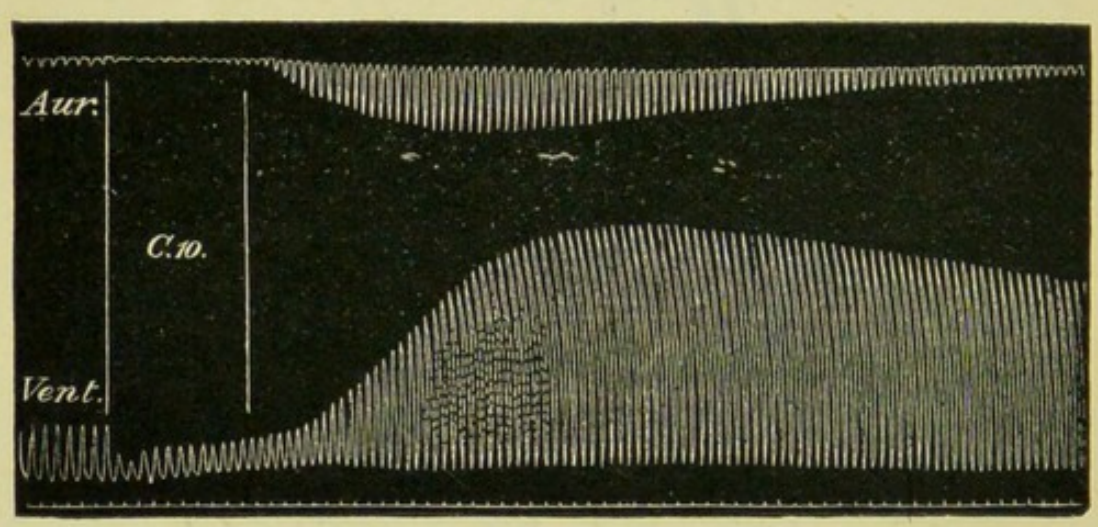


Diagram of cardiac inhibitory and accelerator fibres in the dog (from Foster). r.Vg. Roots of the vagus. r.Sp.Ac. Roots of the spinal accessory. G.J. Ganglion jugulare. G.h.V. Ganglion trunci vagi. Vg. Trunk of vagus nerve. C.sy. Cervical sympathetic. G.C. Inferior cervical ganglion. A.V. Annulus of Vieussens. A.sb. Subclavian artery. n.c. Cardiac nerves. G.St. Ganglion stellatum. D.2, D.3, D.4, D.5. Second, third, and fourth anterior dorsal spinal roots. G.Th. Ganglia of the thoracic chain.

the sympathetic fibres run down in the trunk of the vagus, it is necessary to stimulate the intra-cranial part of the vagus, or the cervical sympathetic, to get pure effects. If the intra-cranial vagus be stimulated while the heart is beating regularly, directly the stimulus is thrown in the heart stops in diastole, or it may give one beat before stopping. If the stimulation be now discontinued, the heart after a little while begins to beat again, at first slowly, and gradually comes back to the normal rhythm. In many cases, if the vagus be stimulated repeatedly, a distinct improving action on the beat is observed, *i. e.* the heart

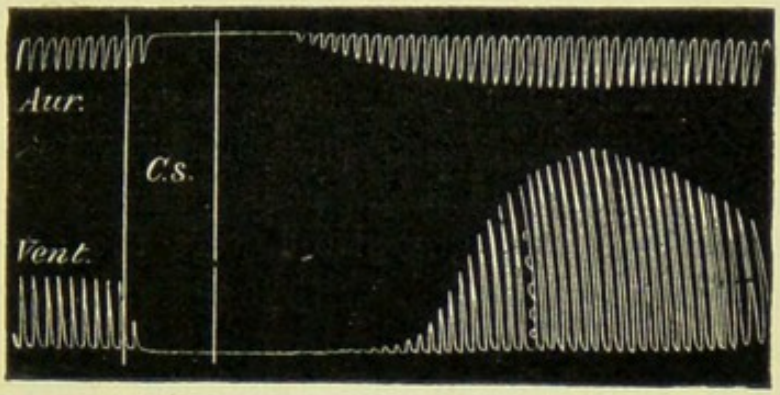
FIG. 66.



Tracing to show effect of stimulation of the vago-sympathetic nerve on the frog's heart. The rhythm is unaltered, but the beats of auricle and ventricle are much decreased in size. On ceasing the stimulation the beats become augmented. (Gaskell.)

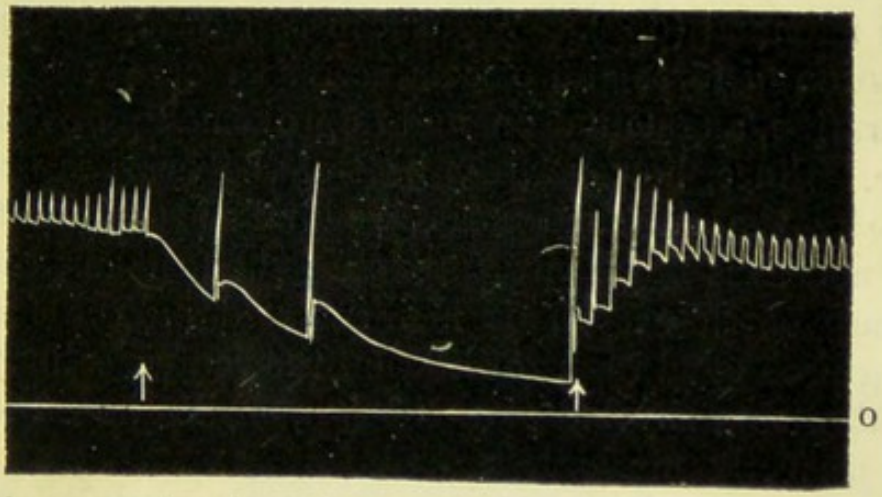
beats more forcibly and rapidly when the stimulation is discontinued than it did at the commencement of the experiment. The vagus is named the inhibitory nerve of the heart. This inhibition may, in the tortoise's heart, affect either the rhythm or the force of the ventricular contraction, the different effects being probably dependent on whether the sinus is most affected, when the beats will be slowed, or the ventricle, in which case the beat will be

FIG. 67.



A tracing similar to Fig. 66. In this case, however, the stimulation caused complete stoppage (inhibition) of both auricular and ventricular beats. (Gaskell.)

weaker. If only a weak stimulus be applied to the vagus the effect may be only to weaken or slow the beat, without causing a complete stoppage.



Blood-pressure tracing from carotid of dog (taken with Hürthle's manometer), showing effect of excitation of vagus (between the arrows). o. Abscissa line of no pressure.

Stimulation of the sympathetic cardiac nerves has exactly the reverse effect, causing increase in force or rate of the heart-beats or both results at once. They are therefore said to be augmentor and accelerator nerves.

The augmentor fibres are much less easily tired than the

vagus fibres. Hence, if the vago-sympathetic of the frog be stimulated, the first effect is inhibition due to vagus action; the vagus fibres then tiring, the effect of the stimulation of the accelerator fibres makes itself apparent, and the heart, while stimulation is still going on, commences to beat more rapidly and forcibly than it did before.

Stimulation of the vagus also lowers the conductivity of the cardiac tissue, and, with a carefully graduated stimulus, it is often possible to make a block between auricles and ventricle, so that the latter only responds to every second auricular beat. The accelerator fibres have the reverse effect. We may make an artificial block between auricles and ventricle by clamping rather tightly the auriculo-ventricular groove, so that the ventricle only beats once to every two auricular contractions. If now the accelerator nerves be stimulated the block is removed, and the ventricle beats in normal sequence to the auricles.

These two sets of fibres have exactly the same function in the mammal (dog). Vagus causes slowing of rhythm, depression of force and of conductivity; accelerators cause acceleration, augmentation, and improvement of conducting power. Since, however, the beat of the heart is normally ruled by the auricular beat, we find that the action of these nerves is much more pronounced on the auricles than on the ventricles. This is illustrated by the fact that during prolonged vagus excitation the ventricles may begin to beat with a rhythm of their own, while the auricles remain perfectly motionless.

In many animals the vagus centre in the medulla exercises a tonic or continuous inhibitory action on the heart. Thus in the dog, section of one vagus causes a slight quickening of the heart-beat (*e. g.* from 60 to 80 per minute). If now the second vagus be cut, the heart-beat is markedly quickened, and may occur 120 times in the minute. The effect of vagus section is still more marked if the vagus centre in the medulla is in a condition of increased activity, as after administration of morphia, or during asphyxia.

The accelerators are further distinguished from the vagus in the length of their latent period, which in the case of

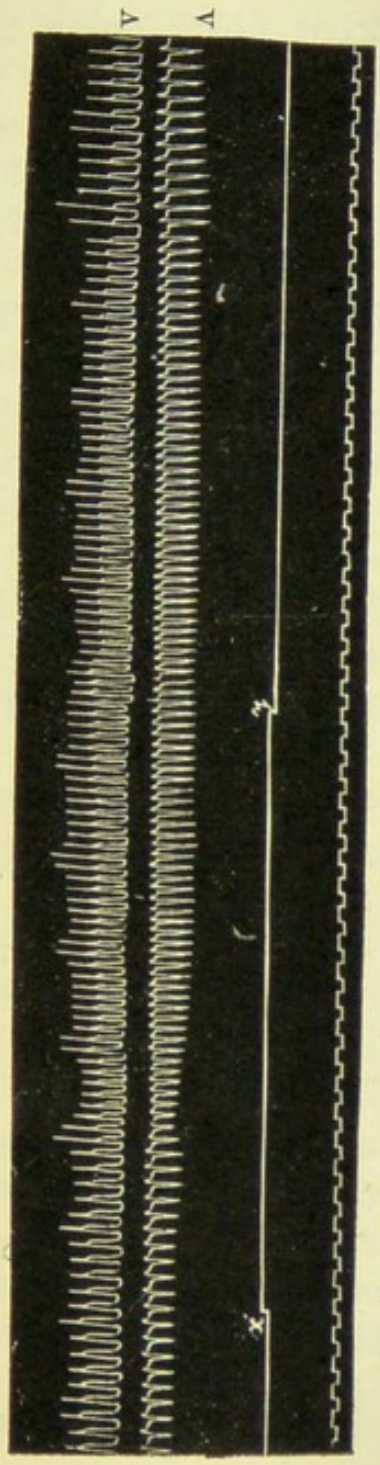


Fig. 69.

Tracings of ventricular and auricular contractions. From x to y the accelerator nerves stimulated. Lowest line = seconds.

the former is excessively long. The latent period of vagus excitation in the mammal is considerably less than a second, whereas that of the accelerators amounts to ten or even

twenty seconds. The effect of accelerator stimulation lasts for an equal length of time after the stimulation is discontinued.

Besides these efferent fibres going to the heart, there are other fibres running chiefly in the vagus which serve to carry afferent impulses from the heart to the nervous centres. Some of their terminal branches ramify over the ventricle (of the dog) immediately under the pericardium. We may investigate their functions by stimulation of the central ends of the divided nerves. They may produce one or more of four effects :

1. Pain, as evinced by the movements of an animal not fully under the influence of an anæsthetic (we should be more correct if we said that stimulation of these nerves produced reflex movement).

2. Reflex inhibition of the heart. If one vagus be cut and its central end stimulated, there is very often slowing of the heart by reflex impulses which descend the other vagus.

3 and 4. Pressor and depressor effects. Stimulation of these nerves may cause a reflex raising (pressor) or lowering (depressor) of the blood-pressure.

Cardio-inhibitory centre.—There is one little spot in the medulla, in the neighbourhood of the origin of the vagus nerves, stimulation of which causes inhibition of the heart. If this spot be destroyed, reflex inhibition of the heart can no longer be produced ; hence it is spoken of as the cardio-inhibitory centre. The afferent nerves from the abdomen and intestine seem to have very close connections with this centre, so that reflex inhibition of the heart can be easily produced in the frog by tapping a loop of intestine with the handle of a scalpel. This connection explains to some extent the depressed condition of the circulation in man in severe abdominal affections, such as peritonitis.

This centre is stimulated by digitalin and morphin, so that the heart is slowed under the influence of these drugs.

Muscarin stimulates the nerve-endings of the vagus. If

applied to the frog's heart, it causes gradual weakening and slowing of the beat, and the heart finally stops still in diastole. If a solution of atropin be now applied, the heart commences beating again. It is found that stimulation of the vagus is now absolutely ineffectual in producing inhibition. Hence we argue that atropin paralyses the terminations of the vagus in the heart. The same paralysis of the vagus is produced in the mammal if atropin be injected into the circulation.

Curare has the same paralysing influence, but only when applied in large doses.

Physostigmin has the same action as muscarin, and, as in this case, its effect is removed by the application of atropin.

Dilute alkalies (KHO, 1 in 20,000) cause the frog's heart to stand still in a tonic contraction, the tone of the heart gradually increasing till the beats are no longer visible on the tracing.

Dilute acids have the opposite effect, removing the tonic contraction produced by alkalies, and finally causing a standstill of the heart in complete relaxation.

The Work of the Heart

The work done by the heart in a given time depends on the amount of blood expelled at each beat, the number of beats occurring in the time, and the pressure against which the blood must be expelled.

Taking the average discharge of the left ventricle at each beat as 125 grammes, and the average pressure in the aorta as 150 mm. mercury (2 metres blood), the work done at each contraction will be 250 gram-metres. Allowing 80 gram-metres for the work done by the right ventricle, we find that a heart beating 72 times per minute would do 30,000 kilogram-metres of work in the twenty-four hours. This is about one fourth the work yielded by a labourer working under supervision for eight hours (Waller).

The whole of this energy is spent in driving the blood along against the resistance in the arterioles, and is converted into heat by the friction between the blood and the arterial and capillary walls.

Other things being equal, the ventricle contracts more powerfully the greater the endocardiac tension is (within limits).

Hence increased force of auricular beat, or prolonged diastole, by causing greater distension of the ventricle, causes increased force of contraction. In the same way, *if the vagi are cut*, a rise of arterial tension increases the force and rapidity of contraction. If, however, the vagi be intact, increased arterial tension causes slowing of the beat. Thus there is a regulatory means by which the heart is prevented from tiring itself out against an insuperable resistance.

The slowing of the heart is probably carried out by afferent impulses ascending the vagi from the heart to the cardio-inhibitory centre, from which inhibitory impulses are sent *down* the vagi.

Innervation of Blood-vessels

We have already mentioned that the chief resistance to the flow of blood occurs in the arterioles and capillaries. The greater part of this resistance is in the arterioles, and is dependent on the continued contraction or *tone* of their muscular walls. If the spinal cord of a dog be divided just below the medulla, artificial respiration being kept up, the blood-pressure falls from 120 to 50 mm. of mercury. This fall is not due to any action on the heart, which goes on beating well. It is due to a relaxation of all the arterioles, and also of the portal and perhaps other veins. This relaxation causes a lowering of arterial pressure in two ways. In the first place, the peripheral resistance is largely diminished, and in the second place the total capacity of the vascular system is increased. In conse-

quence of this increase in capacity, we find that section of the cord lowers the pressure, not only in the arteries but also in all the veins of the body.

This experiment shows that the tone of the vessels is dependent on the integrity of their connections with some part of the nervous system. If a section be made just above the medulla, the blood-pressure remains high. If, however, a certain part of the medulla be destroyed, the blood-pressure sinks as low as if the cervical cord were divided. Stimulation of the same part causes a great rise of blood-pressure, due to increase in peripheral resistance. We learn, then, that the continued contraction or tone of the small arteries is provided for by a small bit of the medulla, which we call the vaso-motor centre. (The lower border of this centre is about 4 mm. above the apex of the calamus scriptorius, and its upper border about 4 mm. higher. It coincides in position with the antero-lateral nucleus of Clarke.)

In this section we have to consider the means by which the vaso-motor centre is able to control the calibre of the blood-vessels, and therefore the blood-supply to various parts of the body.

In order to study the influence of the nervous system on the distribution of the blood in various parts of the body, two forms of instruments are chiefly employed, and in many cases these must be used together. They are the mercurial manometer already described, which serves for the registration of the mean blood-pressure and its variations, and the plethysmograph or oncometer. The latter is an instrument for registering variations in size of any organ or part of an animal. Fig. 70 represents diagrammatically the structure of Roy's kidney oncometer. This is a metal capsule, the two halves of which are jointed together, and are accurately fitted to one another except at (h), where a small hole is left for the exit of the kidney vessels and ureters. A delicate animal membrane (m) is attached to the rim of each half of the oncometer, the

FIG. 70.

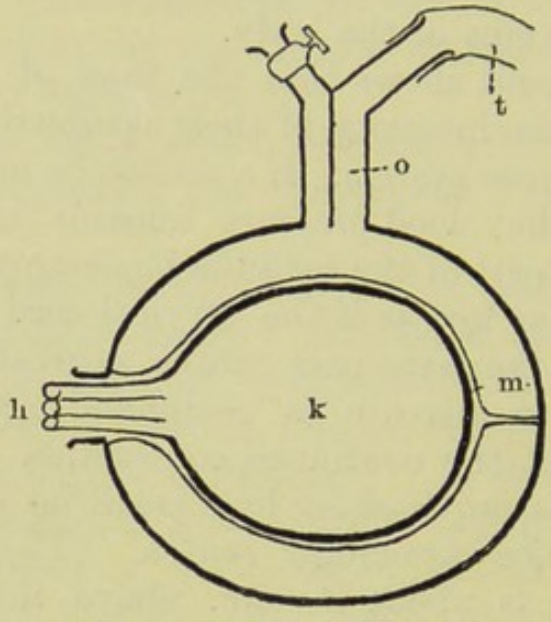


Diagram of oncometer.

space between this and the brass capsule being filled with warm oil. The kidney (k) rests inside, supported on the bed of warm oil, from which it is separated by the membrane. The tube (o) leads from the cavity between the

FIG. 71.

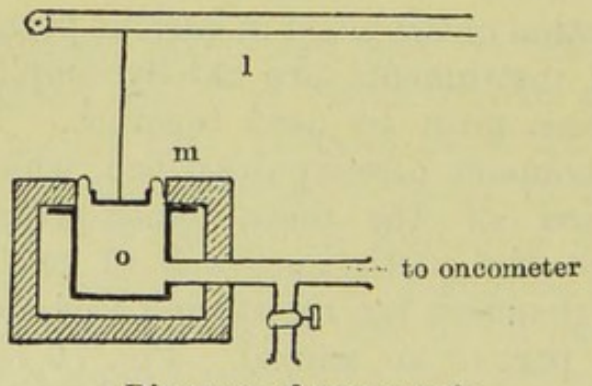


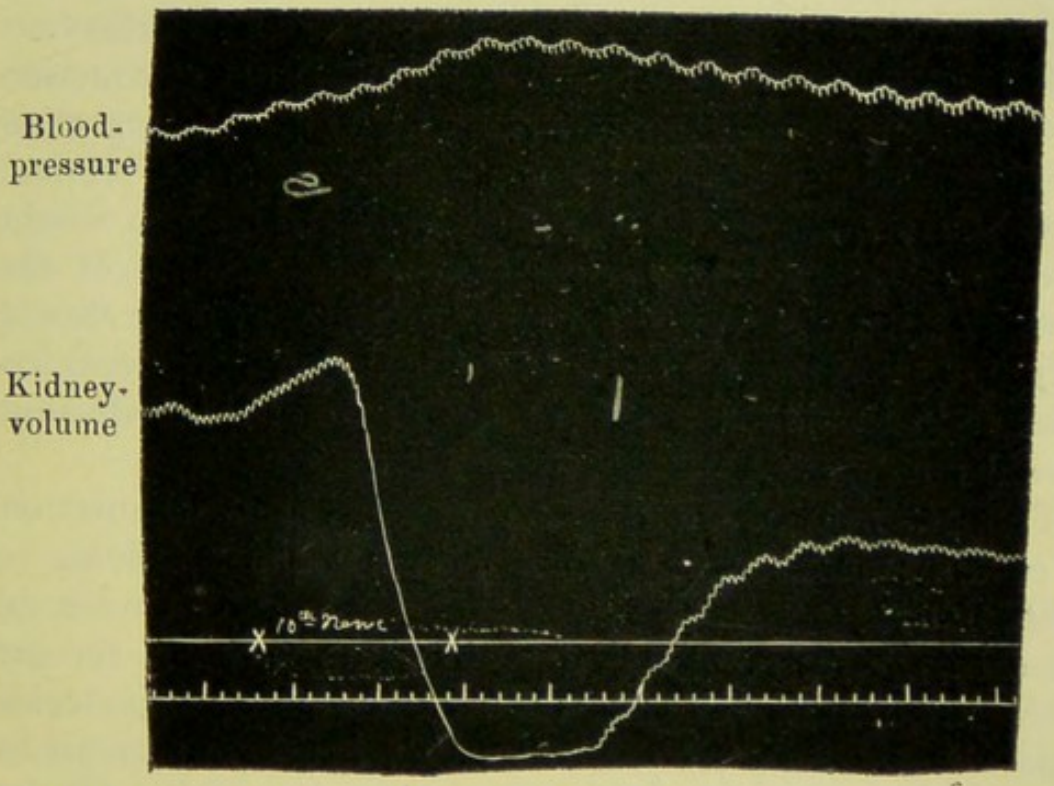
Diagram of oncograph.

brass capsule and membrane to the registering apparatus or oncograph, represented in Fig. 71. Any swelling of the kidney will drive oil out of (o) into the oncograph, and will thus raise the piston of the latter. The excursions of

the piston are recorded by the lever (l), which is arranged to write on a blackened surface. Plethysmographs for the limbs and other organs have been constructed on a similar principle.

A plethysmograph must always be used in connection with a blood-pressure manometer if we wish to investigate the active condition of the vessels of the organ under consideration. Fig. 72 will serve as an example to show the

FIG. 72.



Simultaneous tracings of carotid blood-pressure and volume of kidney. Between × and × the peripheral end of the divided 10th nerve was stimulated. Time-marking = seconds. (Bradford.)

mode in which these two forms of instruments are employed for the investigation of vascular conditions. The upper curve is the carotid blood-pressure, recorded by means of a mercurial manometer. The lower is the tracing recorded by the lever of an oncograph in connection with an oncometer, in which the kidney of the

animal is placed. At the point marked with a cross on the tracing, the peripheral end of the anterior root of the tenth dorsal nerve was stimulated. It will be seen that this stimulation is followed by a slight rise of general blood-pressure, but an enormous shrinking of the kidney-volume. The rise of blood-pressure shows us that there must be somewhere a constriction of arterioles giving rise to increased peripheral resistance, since the heart-beat is obviously unaffected. An increased blood-pressure would by itself tend to force more blood into the kidney, and so would cause an expansion of the kidney.

It is evident that there must be an active contraction of the arterioles of the kidney, emptying this organ of blood, and so causing it to diminish in size. If we had used the oncometer alone, we should have been in doubt whether the shrinking might not be due to failure of the heart's activity. Again, without the oncometer we should only have known that there was increased peripheral resistance in the blood-vessels in some part of the body, but should not have been able to localise it.

This experiment has taught us already that stimulation of certain nerves causes constriction of the arterioles in definite parts of the body. This influence of nerves on the calibre of the arterioles is still better shown in the ear of the rabbit. If this be held up to the light, the arteries and veins can be plainly seen. If now the sympathetic in the neck be divided, the ear on the same side will instantly become redder and warmer than the other, and on holding it up to the light, all the vessels will be observed to be much dilated and many small vessels will be evident that before could not be seen. On stimulating the upper end of the cut sympathetic the reverse effect is produced ; the vessels contract, and the ear becomes once more cool and pale. In the same way constriction of the vessels in the web of the frog's foot may be observed under the microscope to follow stimulation of the sciatic nerve. Similar experiments to these have shown that the

muscular walls of all the arteries in the body are under the control of the central nervous system, and that they are held in a condition of continued contraction or tone under the influence of the vaso-motor centre. Division of the spinal cord in the neck cuts off the arteries in the trunk and limbs from the vaso-motor centre, and these in consequence become dilated, and the blood-pressure falls. Division of the cord in the dorsal region similarly causes dilatation of the vessels in the lower limbs. If the animal be kept alive after this operation for some time, the vessels recover their tone, but lose it again if the spinal cord be destroyed. We see then that, although the chief vaso-motor centre lies in the medulla, there are also subsidiary centres in the cord, which are able, after a time, to take up by themselves the work of regulating the condition of the blood-vessels in parts of the body supplied by the spinal nerves. The nerves that convey impulses causing constriction of the arteries are called vaso-constrictors or vaso-motors.

Course of the Vaso-motor Nerves

All the vaso-constrictor nerves of the body leave the spinal cord by the anterior roots of the spinal nerves from the second dorsal to the second lumbar inclusively. Leaving the roots, they pass by the rami communicantes to the ganglia of the sympathetic chain lying along the front of the vertebral column. The fibres to the head and neck pass into the ganglion stellatum, from here through the ansa Vieussenii to the inferior cervical ganglia, and thence along the cervical sympathetic trunk to their destination.

Those to the limbs run in the communicating branches between the sympathetic chain and the spinal nerves, and are carried in the latter to their destination. The most important vaso-motor nerve of the body is the splanchnic nerve. The area of the vessels innervated by this nerve is so large, that section of this nerve on each side causes a large fall in the general blood-pressure. This fall is more

marked in animals such as the rabbit and other herbivora, in which the alimentary canal is proportionately very much developed, and has consequently a very large blood-supply.

It is evident that, since the arteries are in a constant condition of moderate contraction, a dilatation might be brought about by a relaxation of this tone, by an inhibition of the normal constrictor impulses proceeding to the vessels from the vaso-motor centre. We find, however, in many parts of the body, evidence of the existence of a nerve-supply to blood-vessels antagonistic in its function to the vaso-constrictors. Thus, if the chorda tympani nerve going to the submaxillary gland be cut, no change is evident in the blood-vessels of the gland. If, however, its peripheral end be stimulated, there is instantly free secretion of saliva from the gland, and all the blood-vessels are largely dilated. In consequence of this dilatation the blood rushes through the capillaries so quickly that it has no time to lose much of its oxygen ; the blood flowing from the vein is therefore bright arterial in colour, and is increased to six or eight times the previous amount. If atropin be injected into the animal, the action of the chorda tympani on the blood-vessels is unaffected, although the secretion on stimulation is abolished. The chorda tympani is therefore said to contain vaso-dilator fibres for the vessels of the submaxillary gland. Other examples of vaso-dilator (or dilatator) nerves are the lingual nerve to the blood-vessels of the tongue, and the nervi erigentes to those of the penis. It is probable that all the vessels in the body have a double nerve-supply, vaso-constrictor and vaso-dilator. The presence of the latter variety in a mixed nerve is often difficult to prove, since on ordinary faradic stimulation the constrictor effect is always more pronounced. Moreover, the dilators do not seem to conduct any tonic influences to the vessels. Hence, after section of a mixed nerve, the only effect observed is that due to the removal of the tonic constrictor influences, and the vessels in the area of distribution of the nerve are there-

fore dilated. Two methods, however, have been made use of to demonstrate the existence of vaso-dilators in a mixed nerve-trunk.

(*a*) If the sciatic nerve be cut, the vessels of the leg and foot dilate. This paralytic dilatation passes off after two or three days, and the vessels resume their normal calibre. If now the peripheral end of the sciatic nerve be stimulated, *dilatation* of the vessels is produced. It seems that the degenerative processes affect the constrictor fibres earlier than the dilator fibres, so that at a certain period after nerve-section the latter alone respond to stimulation.

(*b*) If a mixed nerve be stimulated with shocks slowly repeated at intervals of one second, instead of with the ordinary faradic current, vaso-dilator effects are often obtained, whereas stimulation of the same nerve with the faradic current produces vaso-constriction. Thus rapid stimulation of the anterior root of the tenth dorsal nerve in the dog produces shrinking of the kidney from contraction of its blood-vessels. If the same nerve be rhythmically stimulated with single shocks repeated at slow intervals, the kidney swells, showing that its vessels have dilated.

The course of the dilators differs very much from that of the constrictors. Instead of leaving the central nervous system in a particular area, and running through the sympathetic chain before proceeding to their destinations, it seems that the dilators may leave the brain or cord by any cerebro-spinal nerve. Thus the chorda tympani springs from the root of the facial nerve, the nervi erigentes from the second and third sacral nerves.

There is a striking analogy between the nerves distributed to the blood-vessels and those going to the heart—which is, indeed, only a specialised part of the general blood-tubes of the body. These nerves, according to their action on the metabolic activity of the tissues supplied, are divided by Gaskell into *anabolic* and *katabolic* nerves.

The anabolic nerves, as indicated by their name, cause a building up or regeneration of the contractile tissue.

They therefore act as inhibitory nerves, and bring about a condition of rest in the tissue. This class of nerves would include the vagus and the vaso-dilator fibres.

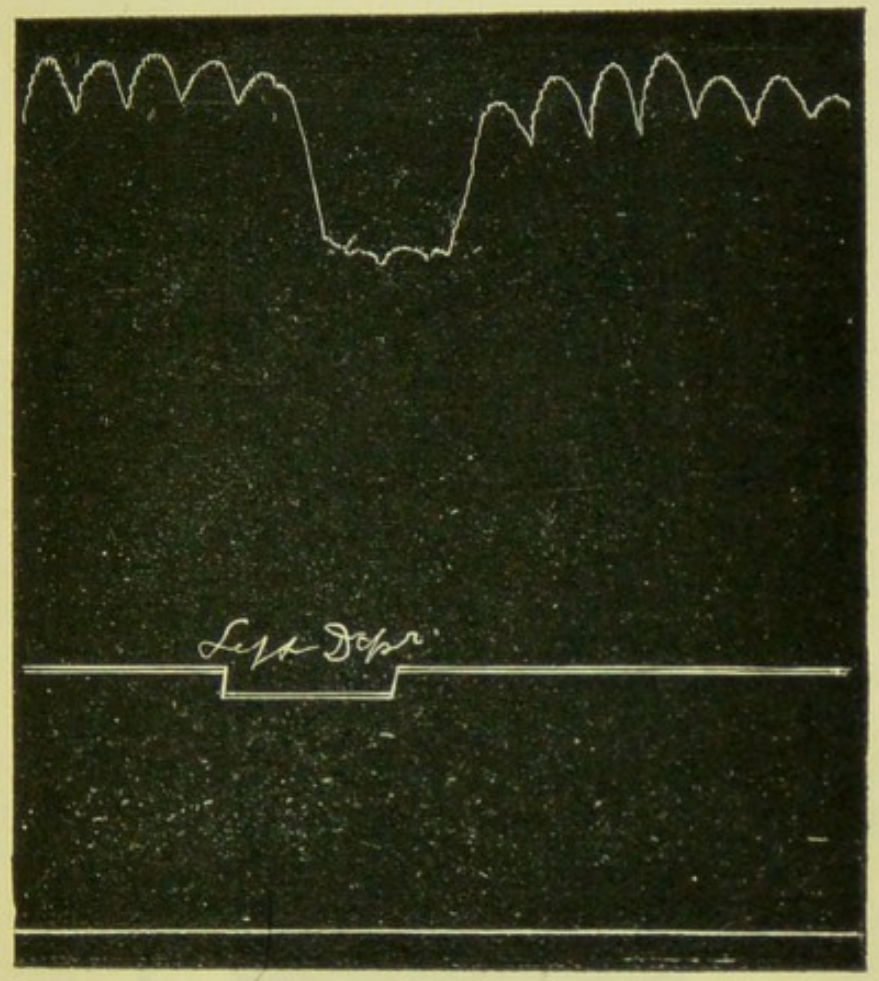
The katabolic nerves cause an increased activity of the contractile tissue, and, as was shown in treating of voluntary muscle (p. 108), active contraction is associated with and derives its energy from a disintegration or katabolism of the complex and unstable muscle molecule (inogen). An ordinary motor nerve to a muscle is therefore a katabolic nerve. This class would include the accelerator nerves to the heart and the vaso-constrictors. The course of these two sets of nerves bears out this comparison, the path taken by the accelerator nerves being identical at first with that of the vaso-constrictor fibres to the head and neck.

Life is reaction; every vital act is a reaction of the organism to changes in its environment. Hence we have not completed our view of the changes affecting the vessels until we have not only considered the means by which the nervous system acts on the vessels, but also the means by which the centres are excited to action. In fine, we must complete the reflex arc affecting the vessels by considering the afferent impulses to the vaso-motor centre.

The afferent impulses to this centre may be divided into *pressor* and *depressor*; and these names are also applied to the nerves that carry such impulses.

There is in the rabbit, cat, and horse, a small nerve in the neck that runs up from the heart to join the vagus or its superior laryngeal branch. If after section of both vagi (to prevent reflex inhibition of the heart) this nerve be cut and its central end stimulated, while the blood-pressure is being registered by means of a mercurial manometer connected with the carotid artery, a marked fall of blood-pressure is at once observed. This fall of pressure is hardly noticeable after section of the splanchnic nerves, showing that the stimulation of the depressor has affected

FIG. 73.



Blood-pressure curve from rabbit showing effect of excitation of central end of depressor nerve (mercurial manometer).

the vaso-motor centre, inhibiting the constrictor impulses that normally pass down the splanchnic nerves.

All sensory nerves are *pressor* nerves, *i. e.* stimulation of their central end causes a marked rise of blood-pressure in animals under curare and morphia. Thus a rise of the general blood-pressure follows stimulation of the central end of the cut sciatic or superior laryngeal nerves (Fig. 74). This rise of pressure is due to constriction of the arterioles, especially in the splanchnic area. The effect, however, of excitation of a pure sensory nerve is not quite so simple as at first appears. In fact, it seems to be a general rule that stimulation of the central end of a sensory nerve causes general arterial constriction with a rise of blood-

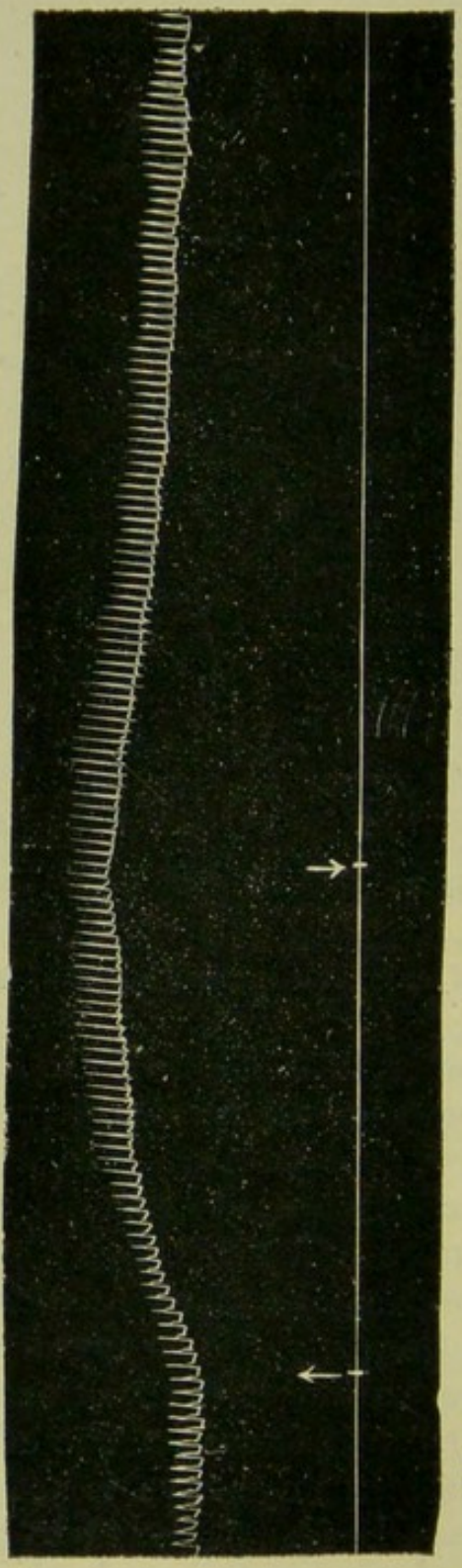


FIG. 74.

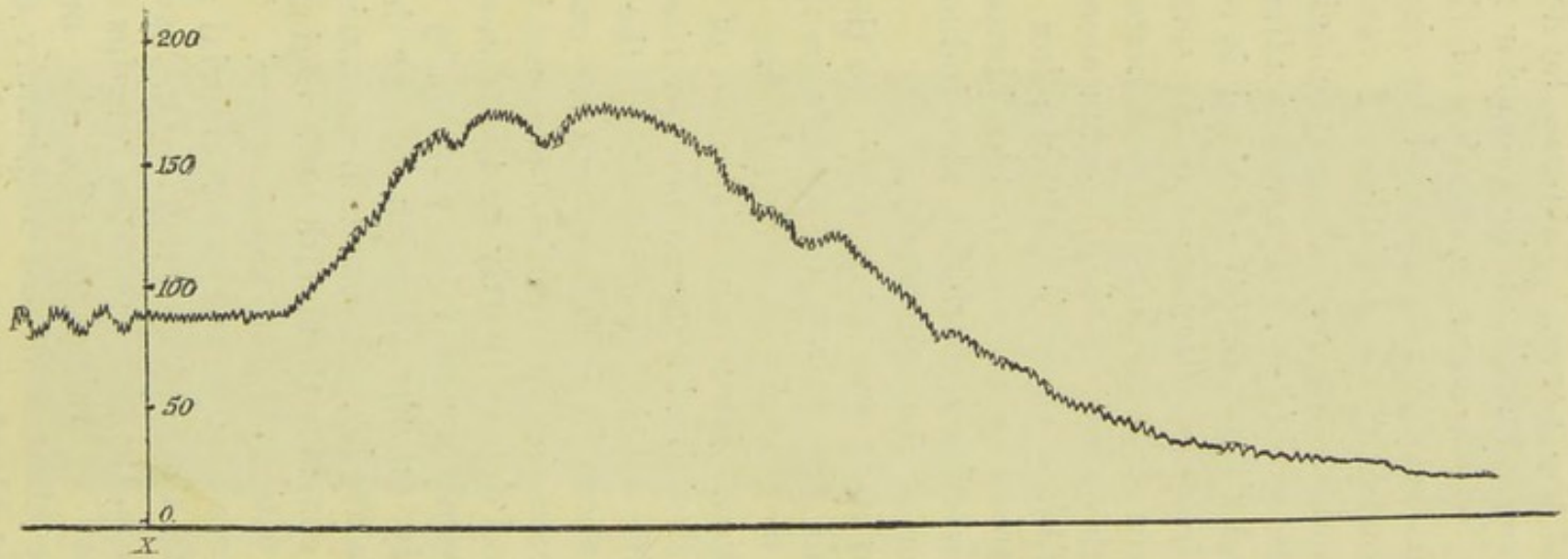
Blood-pressure curve from carotid of dog. Between the arrows the central end of a sensory nerve was stimulated (Hürthle's manometer).

pressure, and at the same time a vaso-dilation in the area of distribution of the nerve. This can be demonstrated by exciting the central ends of the posterior roots of the nerves to a limb, which causes a swelling of the limb due to dilatation of its vessels, accompanied by rise of general blood-pressure owing to constriction of vessels in the splanchnic area and elsewhere. The physiological purpose of this arrangement is obvious. Thus when a limb is injured and inflamed, and a good supply of blood is required for reparative processes, the stimulation of the sensory nerves in the injured area calls forth reflexly a dilatation of the blood-vessels in this area. This dilatation alone allows an increased flow of blood through the part; but this flow is still further increased by the rise of blood-pressure caused by the general arterial constriction also induced reflexly by the stimulation of the same nerve.

In addition to its power of response to the effects of peripheral stimuli, the vaso-motor centre in the medulla may also react to changes occurring in the blood with which it is supplied. Thus administration of digitalis or strophanthus to an animal causes a marked rise of general blood-pressure due to the constriction of the peripheral vessels, brought about by impulses from the centre.

The changes occurring in the blood-pressure in asphyxia are important, and depend partly on the abnormal stimulation of the vaso-motor and vagus centres by the venous blood, and partly on the affection of the heart itself. These phenomena are best observed in a curarised animal, and we will first consider them with both vagi cut, in order to shut out the action of the vagus centre. The blood-pressure is registered by means of a mercurial manometer in connection with the carotid artery. On leaving off the artificial respiration, the blood-pressure remains at the same height for twenty or thirty seconds, the only change noticed being the absence of the respiratory oscillations. At this point the blood-pressure suddenly rises rapidly, and in another ten seconds may reach a height twice

FIG. 75.



Curve of blood-pressure tracing during asphyxia. The tracing was taken by a manometer connected with the femoral artery of a dog under curare. Artificial respiration discontinued at *X*. Both vagi had been previously divided.

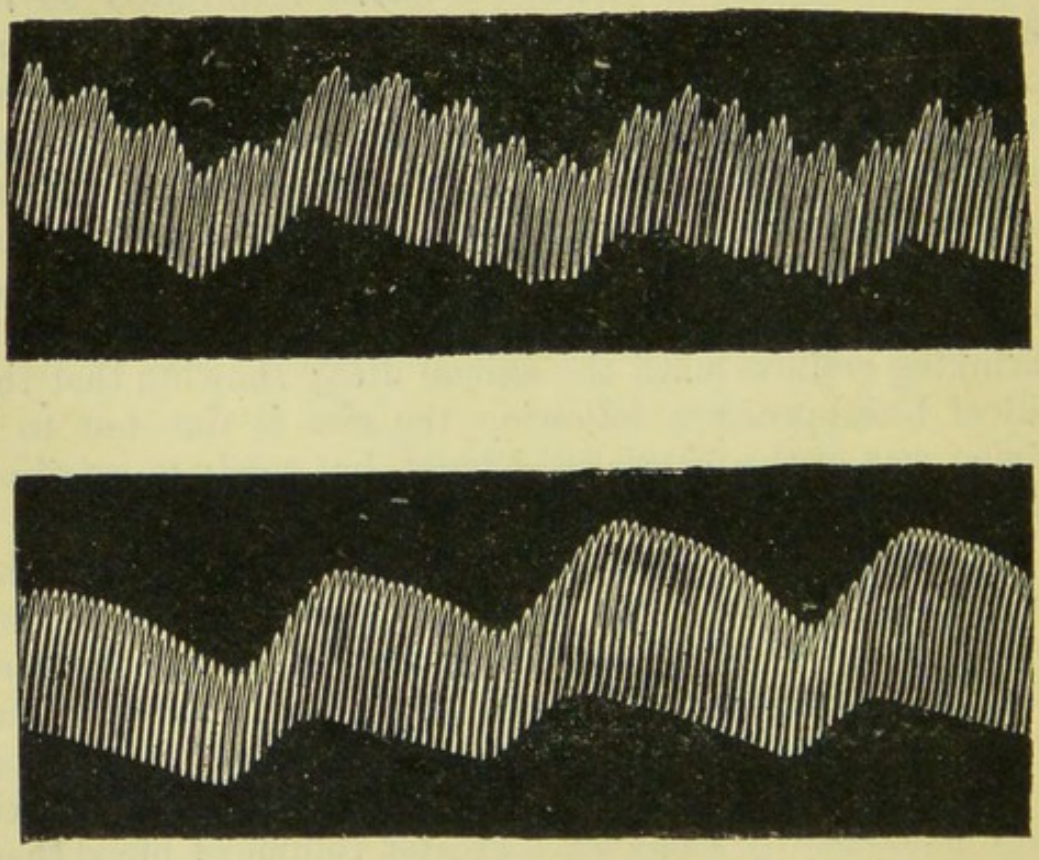
or three times as great as it was previously. The heart beats a little more forcibly in consequence of the increased cardiac tension, but its frequency is almost unaltered. The blood-pressure remains at this height for about a minute, and then gradually falls, the heart-beats becoming smaller and smaller, until the pressure has sunk to a point very little above the abscissa line (level of no pressure). This fall in pressure is due to the failure of the heart. The heart, badly supplied with oxygen, cannot overcome the enormous resistance presented by the contracted arterioles; it gets over-filled, and gradually loses the power of expelling any of its contents. If, when the blood-pressure has sunk to its lowest point, the heart be rapidly cut out of the body, it will at once begin to beat fairly forcibly, being relieved of the excessive internal tension. The vessels, however, remain constricted until the death of the animal. This is shown by two facts. If while the pressure is sinking, artificial respiration be recommenced, the heart supplied with oxygen at once begins to beat more forcibly, and the blood-pressure may rise to an even greater height than immediately after the commencement of the asphyxia. Again, if the volume of the kidney be recorded by means of the oncometer, the rise of general blood-pressure produced by asphyxia is seen to be accompanied by an enormous shrinking of the kidney, and this shrinking endures until the animal dies; showing that the fall of blood-pressure following the rise is due not to a giving way of the arterial resistance, but solely to a failure of the heart.

If in the dog, and to a less extent in other animals, the vagi be left intact, the blood-pressure tracing during asphyxia has quite another appearance. At the point of the tracing corresponding to the rapid rise in the previous experiment, there is in this case only a slight rise of pressure, but the heart begins to beat very slowly. At each beat it necessarily sends out a greater volume of blood than when it is beating more frequently, and hence the oscilla-

tions on the heart-pressure curve caused by the heart-beats become very large. This slow beat is due to the action of the vagus centre which is excited by the venous blood, and it is at once abolished by section of the two vagi. The sparing of the heart by means of this vagus action enables it to last longer, and the final fatal fall of blood-pressure due to heart failure comes on rather later than when the vagi are divided.

During the period of increased pressure, waves are often observed on the blood-pressure curve, which must arise in a slow rhythmic variation of the constrictor impulses sent out from the vaso-motor centre. These waves are known as the Traube-Hering curves, and are not to be confused with the waves on an ordinary pressure curve due to respiration, being much slower in their rhythm than the latter. They are observed not only during asphyxia, but

FIG. 76.



Blood-pressure tracings showing Traube-Hering curves.

may occur in blood-pressure tracings from normal dogs, and are frequent in dogs poisoned with morphia. Fig. 76 represents tracings obtained from a dog under the influence of morphia and curare. The upper curve, taken while artificial respiration was being carried on, shows the three forms of curves—the oscillations due to the heart-beat, next in size those due to the respiratory movements, which in their turn are superposed on the slow prolonged curves, *i.e.* the Traube-Hering curves. The lower curve is taken immediately after cessation of the artificial respiration, and shows only the heart-beats and the Traube-Hering curves.

The Capillary Circulation

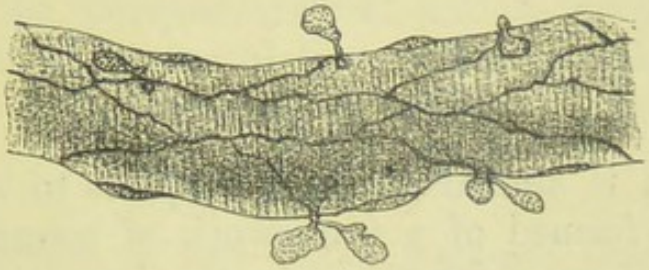
The capillaries may be regarded as the chief part of the circulation, since the whole object of the varied arrangements of the heart and arterioles is to secure an adequate flow of blood through these smallest vessels—that is, a supply of blood adequate to the needs of the tissues in which the capillaries are embedded. The transudation of lymph and the chemical interchange between the tissues and the blood take place only in the region of the capillaries and small veins. At present we have no evidence of an influence of the nervous system on the calibre of the capillaries, or on the interchange taking place between them and the surrounding tissues, although the circulation here is indirectly affected by changes induced in the calibre of the arterioles.

The condition of the endothelial wall of the capillaries and its influence on the blood-stream seem to be chiefly dependent on the nutrition of the surrounding tissues. This is well exemplified in the series of phenomena classed under the head of inflammation. By inflammation we understand those processes wherein the organism reacts to a destructive lesion of its tissues; and these processes in the higher animals are connected with marked vascular

changes, which can be well studied on the tongue of the frog. If this be spread out and arranged for microscopical observation, a beautiful picture of the normal circulation of the blood through the arterioles, capillaries, and veins is afforded. As a destructive lesion to call forth inflammatory changes, a small piece of the tongue may be cut off, or the tongue may be painted with a very weak solution of croton oil. The following series of phenomena are then observed. At first the injury is followed by a dilatation of all the vessels, consequent upon dilatation of the arterioles, and the blood rushes through the capillaries, and many vessels make their appearance which were before invisible. After a time, the vessels still remaining dilated, the stream of blood becomes slower, and it is then seen that in the small veins there are two layers: a layer next the vessel wall, in which large numbers of leucocytes are present, and which remains almost stationary; and an inner layer of slowly moving red corpuscles. Since this slowing of the circulation is unattended by any narrowing of the calibre of the vessels, it must evidently be due to an increased friction between the blood-plasma and its contents and the capillary wall. It has been explained by saying that the layer of endothelium is more adhesive. In the capillaries the endothelium is also thickly covered with leucocytes, but here the red corpuscles are mixed with the leucocytes, and there is not such a division into two layers as in the veins. Very soon, at one or two spots, it will be observed that a leucocyte is squeezing itself or being squeezed through the capillary wall, so that half of it lies inside, half of it outside the vessels, and the emigration speedily becomes complete. This emigration of white blood-corpuscles increases in extent, and at the end of seven or eight hours the tissues in the immediate neighbourhood of the small veins and capillaries are infiltrated with masses of leucocytes. At the same time the amount of lymph that transudes through the vessel walls is largely increased, so that it cannot be carried off quickly enough

by the lymphatics, and remains in the interstices of the tissues, causing a swelling or *œdema*.

FIG. 77.



Emigration of leucocytes through capillary wall. (Arnold.)

The true significance of this process of inflammation has been pointed out in recent years by Metchnikoff. This observer has shown that all the vascular phenomena of inflammation are directed towards furthering the emigration of leucocytes, and that these leucocytes, or *phagocytes*, have the power of devouring the irritant body if it be a micro-organism, or of removing the tissues killed by the lesion, and so clear the ground for a regeneration of the tissue. Such a condition of phagocytosis—that is, a collection of wandering cells to devour and remove disintegrated tissues, foreign bodies, or micro-organisms—has been shown to occur in all animals, even in those destitute of a vascular system. The animals with such a system have the advantage over the lower animals, in that the circulating blood is always bringing up fresh relays of leucocytes to vanquish and destroy the offending body. In many cases the chemical or microbic influence destroying the tissues is too powerful for the leucocytes to overcome; they also are destroyed, and the dead leucocytes collect in the tissues and form pus. If the leucocytes are successful in removing the irritant body, they disappear, perhaps wandering back into the blood-stream, and the lost tissue is replaced by regeneration of the surrounding tissues. The foregoing is a dogmatic account of a subject which is now very much

under discussion, but it may serve to draw attention to the physiological importance of the leucocytes, and the relationship of the endothelial wall to the tissues on the one hand and to the blood-stream on the other.

The Spleen

This organ is similar in many respects to a lymphatic gland. It is formed of a framework of connective tissue and unstriated muscular fibres, in the interstices of which is contained the *splenic pulp*. This consists of a fine fibrillar network, on the fibrils of which lie endothelial cells. The meshes contain the cells of the splenic pulp, which are fairly large polygonal cells and leucocytes. Just as in a lymphatic gland the cellular elements of the tissues are bathed by the lymph which flows through the gland, so in the spleen the walls of the capillaries become discontinuous, and the blood is poured out into the interstices of the tissue. The spleen is, therefore, the only tissue in the body where the blood comes in actual contact with the tissue-elements themselves. The blood from the splenic pulp is collected into large venous sinuses, which run along the trabeculæ to the hilus, where they unite to form the splenic vein. The arteries to the spleen are beset in their course along the trabeculæ with small nodules of lymphoid tissue, which are known as the Malpighian follicles.

It is evident that the blood must meet with considerable resistance in passing through the close meshwork of the splenic pulp. To ensure a constant circulation through the gland, we find that the muscular tissue of the capsule and trabeculæ has the property of rhythmic contraction. If the spleen be enclosed in a plethysmograph, or splenic oncometer, and its volume be recorded by connecting this with the oncograph, it will be seen that it is subject to a series of large, slow variations, each contraction and ex-

pansion lasting about a minute, and recurring with great regularity. The heart-beats are not seen on this tracing, and the respiratory undulations, if present at all, are only slight. The contractile power of the spleen is under the control of the nervous system, and a rapid contraction may be induced by stimulation of the splanchnic nerves.

Functions of the Spleen

The structure of this organ suggests that the splenic cells must exercise a constant influence on the blood which surrounds them, and that this influence is not purely of a chemical nature. We have seen that in the liver and kidney, which exercise so powerful an effect on the composition of the blood passing through them, the proper cells of these organs are separated from the blood-stream by the capillary wall. Microscopic examination of the cells of the splenic pulp shows us that these are full of particles of brown pigment or fragments of red corpuscles. In many cases of infectious disease, such as recurrent fever, the splenic cells are observed towards the end of the attack to be full of the organism—spirillum—which is the cause of the disease. In fact, these cells are so arranged that they can take up solid particles held in suspension in the blood-plasma. We must, indeed, look upon the spleen as the great blood-filter, purifying the blood in its passage by taking up particles of foreign matter and effete red corpuscles. The same process of phagocytosis, which has just been described under inflammation, is in the spleen a normal occurrence.

A *rôle* has also been assigned to the spleen in the formation of red blood-corpuscles, but the evidence is not sufficient to determine whether such a process occurs normally.

Chemical analysis of the spleen reveals the presence of a large number of what are called extractives, such as succinic, formic, butyric, and lactic acids, inosit, leucin, xanthin,

hypoxanthin, and uric acid. There is also a proteid allied to alkali-albumen, combined with iron, as well as several pigments probably derived from the hæmoglobin of the red corpuscles destroyed by the cells of the splenic pulp. The fact that in cases where the spleen is pathologically enlarged, as in leucocythæmia, the uric acid in the urine is largely increased, points to a connection between the spleen and the formation of uric acid in the body. The numerous extractives which are formed probably owe their origin to the destructive changes effected on the effete constituents of the blood by the agency of the splenic pulp cells.

Movement of Lymph

In the frog the circulation of lymph is maintained by rhythmically contracting muscular sacs, which are placed in the course of the main lymph-channels, and pump the lymph into the veins. In the higher animals and in man the onward flow of lymph is effected entirely by the pressure at which it is secreted from the capillaries into the interstices of the tissues. In the smaller lymph-radicles the pressure of lymph may attain 8 to 10 mm. soda solution. In the thoracic duct, at the point where it opens into the great veins of the neck, the pressure is obviously the same as in these veins, that is to say, from −4 to 0 mm. Hg., the negative pressure being occasioned by the aspiration of the thorax. This difference of pressure is sufficient to cause a certain amount of flow. It must be remembered, however, that under normal circumstances no lymph at all flows from a resting limb. The only part of the body which gives a continuous stream of lymph during rest is the alimentary canal, the lymph in which is poured out into the lacteals, and thence makes its way through the thoracic duct. Movement, active or passive, of the limbs at once causes a flow

of lymph from them. Since the lymphatics are all provided with valves, the effect of external pressure on them is to cause the lymph to flow in that direction only, *i. e.* towards the thoracic duct and great veins. Hence we may look upon muscular exertion as the greatest factor in the circulation of lymph. The flow of lymph from the commencement of the thoracic duct in the abdominal cavity to the main part of it in the thoracic cavity is materially aided by the respiratory movements; since, with every inspiration, the lacteals and abdominal part of the duct are subjected to a positive pressure, and the intra-thoracic part of the duct to a negative pressure, so that lymph is continually being sucked into the latter.

CHAPTER VII

DIGESTION

We have already mentioned that the cells derived from the hypoblast of the embryo, and lining the inner surface of the tube from which the body is formed, are alimentary in function, *i. e.* they have the office of taking up the various foodstuffs and converting them into a form suitable for assimilation by the other tissues of the body. In some of the lower animals the cells lining the alimentary canal devour the food particles in the same manner that the amœba does, secreting around them, after ingestion, a fluid which seems to dissolve them. In the higher Vertebrates this process is simplified, in that the cells lining the canal are differentiated into those that secrete a fluid capable of dissolving foodstuffs, and those which have the duty of absorbing the foodstuffs that have been rendered soluble by the action of the digestive fluids. The secreting cells are collected together in depressions or outgrowths of the epithelial lining of the alimentary canal to form glands; and we find that the secretions in different parts of the canal have different properties, some being adapted to rendering soluble the starchy constituents of food, while the action of others is limited to proteids.

During the time that the food is in the mouth it is acted upon by the mixed secretions of the parotid, submaxillary, and sublingual salivary glands. And here we find the chief digestive action consists in the conversion of insoluble starch into soluble dextrins and sugar.

In the stomach the food is acted on by the gastric juice, the secretion of a number of simple tubular glands with

which the mucous membrane is thickly set. Its chief action is on the proteids, hydrating these and converting them into albumoses and peptones. In the duodenum the food is acted on by the pancreatic juice and the bile, the secretion of the liver. The former has a digestive influence on all three classes of foodstuffs, converting starch into sugar, proteids into peptones, and splitting up neutral fats with the formation of neutral glycerin and free fatty acids. In the small and large intestine the mucous membrane is thickly set with a number of simple tubular glands, which are called Lieberkühn's follicles. These secrete an alkaline juice, which has only slight digestive powers. It contains an invert ferment which converts cane-sugar into lævulose and dextrose, and maltose into dextrose.

FERMENTS.—All the digestive juices are said to owe their power to the presence in them of certain ferments; and we may take the opportunity of saying a few words with regard to ferment action in general. Ferments enter or are said to enter into most of the physiological processes of the body. To a ferment has been ascribed a prominent part in the coagulation of the blood; and we shall meet with them later on in considering the functions of the liver and kidney. But it is in digestion that these bodies play the most important part. In all the changes that are effected by their agency there is the conversion of a body of high potential energy into one with less potential energy; and this conversion is in most cases associated with hydrolysis, *i. e.* the original body is combined with one or more molecules of water to form the new substance of lower potential energy.

In inquiring into the nature of ferments we are met at the outset with the difficulty that probably no one has ever prepared a pure ferment; so that we can only study their properties by studying those of the fluids or precipitates presumed to contain a ferment from the fact that they can give rise to certain changes in other substances.

First, as to the conditions of their activity. A ferment such as diastase can convert an indefinite amount of starch into sugar, provided that the product of its activity (*i. e.* the sugar) be not allowed to accumulate in too large a quantity. So by increasing the strength of a ferment solution we do not increase the amount of substance it is able to transform, but merely the rapidity of its action.

A ferment is only active within certain limits of temperature; and for each ferment there is a certain optimum temperature at which its activity is greatest. This, for the ferments met with in the body, is between 40° and 45° C. For diastase and malt ferment it is between 60° and 65° C. At a temperature of 0° the activity of all ferments that occur in warm-blooded animals is indefinitely checked, although it has been shown that the pepsin or gastric ferment of fishes still preserves some power at this temperature. At 65° C. all ferments met with in the body are destroyed, and do not recover on cooling.

They are soluble in distilled water, and precipitated from their solutions by alcohol. The digestive ferments are precipitated by saturation of their solutions with ammonium sulphate. This method has been used for obtaining them in a state approaching purity, and they have been found to have the general composition of proteids. The amount that can be collected, however, is so small that it is impossible to make an accurate study of their properties, and even then we do not know whether the substance we have represents the pure ferment, or is merely a proteid to which the ferment is intimately adherent.

A ferment is, therefore, a body which can effect changes in a surrounding fluid of certain bodies of high potential energy into bodies of more stable composition with an evolution of kinetic energy in the form of heat, without itself being used up in the process.

The nature of ferment action may be better conceived if we compare it with certain changes that have long been

known in organic chemistry, and are spoken of as katalytic changes. Thus nitrogen trichloride may be made to explode by contact with various substances, such as phosphorus or oil. In its explosion it splits up into free nitrogen and chlorine—molecules which are more stable, and have therefore less potential energy than those of the original nitrogen trichloride. In the manufacture of sulphuric acid, nitric oxide is used as a carrier of oxygen from the atmosphere to the sulphur dioxide produced by the burning of sulphur. Thus :

$$\underset{\text{Nitric oxide.}}{2NO} + O = \underset{\text{Nitrogen trioxide.}}{N_2O_3}$$

$$\underset{\text{Sulphur dioxide.}}{SO_2} + N_2O_3 + H_2O = \underset{\text{Sulphuric acid.}}{H_2SO_4} + \underset{\text{Nitric oxide.}}{2NO}$$

In this case we have at the end of the reaction the same amount of nitric oxide that we started with ; and it would be theoretically possible, by using a small quantity of nitric oxide as oxygen-carrier, to convert an indefinite amount of sulphur dioxide into sulphuric acid. Since in this reaction we know the exact chemical processes that go on, the word katalysis is not used. On the other hand, we employ this word in speaking of the splitting up of hydrogen peroxide by means of spongy platinum into water and oxygen :

$$\underset{\text{Hydrogen peroxide.}}{2H_2O_2} = 2H_2O + O_2$$

But the difference is probably merely one of degree. The substance which acts katalytically exercises an attraction on one of the atoms in the unstable molecule, which is sufficient to give the impetus to its decomposition, although not leading to an actual combination of the two, as in the case of the nitric oxide quoted above. So we may suppose that the invert ferment, for instance, combines with a molecule of water, and passes it on to the cane-sugar ; or it may be that it merely exercises an attraction on some of

the constituents of the cane-sugar molecule, so increasing its tendency to break up and unite with the surrounding molecules of water, with the evolution of heat and the production of the more stable bodies, lævulose and dextrose.

The ferments which play so important a part in the digestive functions belong to the class of *unorganised* ferments. The term ferment has been applied to another class of bodies, which are distinguished as the *organised* ferments. These are living organisms which have the power of inducing definite changes in the media in which they live. This faculty is intimately bound up with the life of these organisms. Destruction of this by the action of small amounts of chloroform, or by subjecting them for some time to the action of absolute alcohol, irrevocably destroys their fermentative properties. With the organised as with the unorganised ferments there is a change of the affected substance from a condition of high to one of lower potential energy. The changes induced, however, are often much more than a mere hydrolysis. The yeast fungus, for instance, converts sugar into alcohol. In this process the change represents the metabolism of the organism itself. Just as we take in carbohydrates and proteids and change them in our bodies to CO_2 and urea, so the yeast fungus takes up sugar and converts it into CO_2 and alcohol, so that these bodies are the excreta of this organism. It is evident, then, that our conception of the action of ferments as developed above must be confined to that of unorganised ferments. The action of the organised ferments stands in the same category as the metabolic processes of the higher animals, and has no more real claim than these to the title of *fermentative*.

The Digestive Juices and their Secretion

The digestive juices are formed by the agency of glands. These are recesses or branching tubules lined with a continuation of the general alimentary epithelium. This secre-

tory epithelium is separated by a basement membrane from the surrounding connective tissue, in which ramify blood-vessels, lymphatics, and nerves. The secretory cells are bathed by the lymph that exudes from the capillaries; and from this lymph they select the substances necessary for their nourishment, and form therefrom the special ingredients of their secretion which they turn out into the lumen of the gland tubule. This process is an act of vital selection by the cell, and is not a mere filtration or transudation of certain constituents of lymph through the epithelial membrane.

Saliva

The saliva is a mixture of the secretions of the submaxillary, sublingual, parotid, and small mucous and serous glands of the buccal cavity. It has a low specific gravity, 1002 to 1009; it is slightly alkaline, and slimy from the presence of mucin. On microscopic examination it is seen to contain epithelial scales and 'salivary corpuscles' —small round cells with granular contents, which are probably leucocytes escaped from the tonsils. It consists of—

Water.

Salts, especially potassium and sodium chlorides.

Traces of albumen.

Mucin.

A diastatic ferment (ptyalin).

Occasional traces of potassium sulphocyanide.

Gases, especially carbon dioxide, with traces of oxygen and nitrogen.

In twenty-four hours the amount of saliva secreted varies from one half to two litres. The greater part is reabsorbed in the alimentary canal.

Functions

Saliva chiefly serves to moisten food-stuffs, and so aid in mastication and deglutition. This is indeed in carnivora its sole function. In herbivora and man it exercises a

digestive action on starch by virtue of the ptyalin it contains. If some saliva be added to some boiled starch in a test-tube, and the mixture be kept at 35° C. for some time, the starch is gradully converted into a mixture of maltose and dextrin. The stages of the process are as follows :

1. Starch, opalescent solution, blue with iodine.
2. Soluble starch, clear solution, blue with iodine.
3. A mixture of dextrins, erythro- and achroodextrin. The former with iodine gives a mahogany-red colour.
4. Maltose and achroodextrin, the erythrodextrin being converted into maltose, while some of the achroodextrin remains unaffected. The liquid now reduces Fehling's solution by means of the maltose it contains, and gives no coloration with iodine. Addition of large excess of absolute alcohol gives a white precipitate of achroodextrin. This ferment action is dependent on temperature, is most active at about 40° C., and is finally abolished at about 60° C. It can only take place in a neutral or slightly alkaline medium, the ferment being destroyed in the presence of acid.

Salivary glands.—These are divided into two classes, serous and mucous glands, which differ from one another in the characters of their secretion and in their histological features.

The mucous glands have larger acini, which are lined with large clear cells. Between these cells and the basement membrane are seen small cells which stain deeply, denoted from their shape crescentic or demilune cells. The secretion is thick and viscid from the presence of mucin.

Serous glands have smaller tubular acini which are lined with polyhedral granular cells. Their secretion is watery and consists chiefly of water, salts, and ptyalin, with a trace of albumen and globulin.

The parotid in man and in the dog is a pure serous gland. The submaxillary in the dog is a pure mucous gland, but in man it is a mixed mucous and serous gland.

Changes accompanying Activity

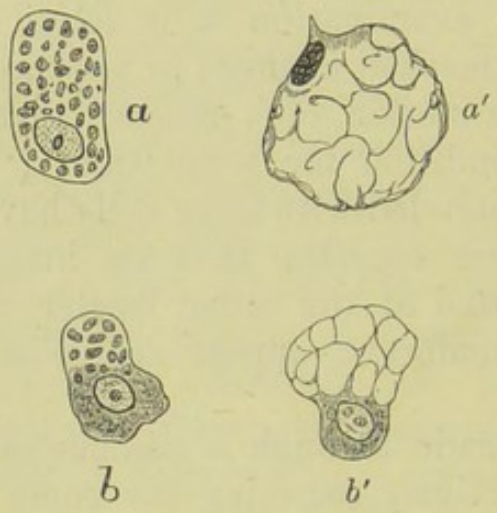
The salivary glands may be made to secrete by administration of pilocarpin or by stimulation of their nerves. On histological examination it is found that activity is associated with marked changes in appearance of the cells. If we examine a section of a mucous gland that has been in a resting condition for some time ('resting gland'), the acini are distended with large cells having clear hyaline contents, so close together that no lumen can be seen. The nuclei situated at the outer border of the cells, near the basement membrane, appear shrivelled, with irregular margins.

In a section made through a discharged gland (*i. e.* one that has been actively secreting for some time), the acini and the cells are smaller, the lumen quite distinct, and the nuclei round and swollen. The whole section appears darker from the fact that the cells have taken up the staining fluid more readily. The difference between the sections depends chiefly on the fact that, in the sections of the resting gland, the cells are distended with mucin, which does not take up the staining agent, and gives the cells their clear hyaline appearance. When secretion occurs, the mucin is discharged into the lumen, so that the cells shrink and consist more largely of protoplasm. In this process some of the cells themselves may be destroyed, their place being taken by the demilune cells.

If, instead of examining sections of hardened glands, we examine fresh glands teased in normal saline fluid, or fixed with osmic acid vapour, the appearance presented is quite different. The cells of the resting gland are not clear and hyaline, but are full of coarse granules. When secretion occurs these granules disappear. If to a fresh specimen of resting gland any of the ordinary hardening agents (such as spirit or Müller's fluid) be added, the granules are seen to swell up and fuse together to form a hyaline mass distend-

ing the cell. In fact, the ordinary picture of the hardened resting gland is reproduced (Fig. 78).

FIG. 78.



Mucous cells from a fresh submaxillary gland of dog (Langley). *a*. Mucous cell examined fresh from a resting gland. *a'*. The same cell treated with weak alcohol. *b* and *b'*. Cells from a discharged gland before and after treatment with weak alcohol.

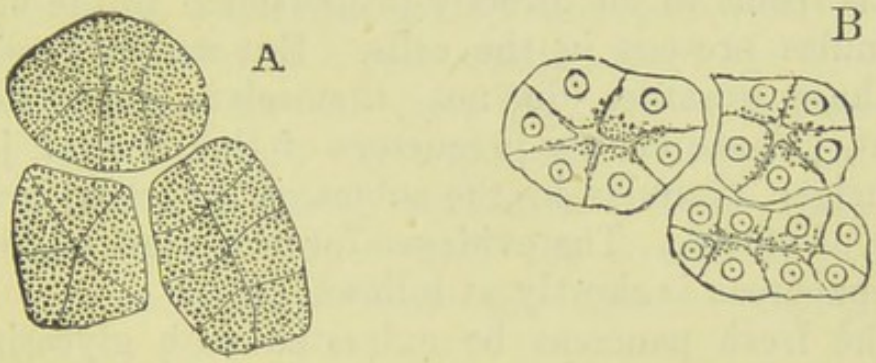
We see then that the resting gland in a normal condition does not contain mucin, but contains a precursor of mucin—*mucigen*, which appears in the form of granules. As these are turned out of the cell they undergo some change, perhaps associated with imbibition of water, and are transformed into mucin.

A similar change occurs in the serous glands when secretion takes place. The cells of the resting parotid gland, examined in normal saline fluid, are swollen and full of fine granules. With activity these granules are discharged, and the cells shrink and become clearer (Fig. 79).

In the pancreas of the rabbit, which is very similar in structure to a serous salivary gland, the changes coincident

with secretion can be observed in the living animal, since here the gland is spread out between the layers of the

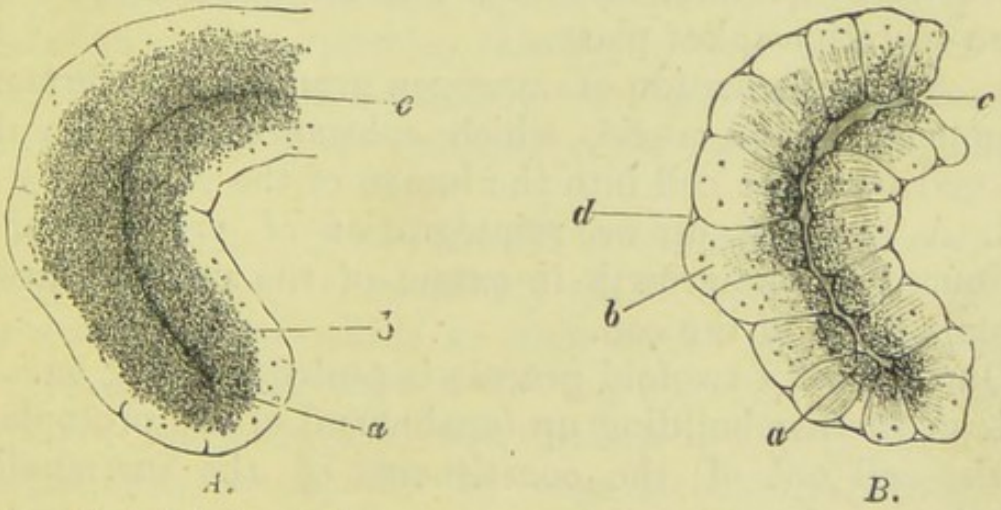
FIG. 79.



Acini of a serous salivary gland. A. Resting condition. B. Discharged condition.

mesentery, so that individual acini may be examined under high powers. When the resting gland is observed in this way, each acinus is seen to be composed of two zones, an outer clear zone and an inner granular zone. The out-

FIG. 80.



A terminal lobule of the pancreas of the rabbit. *A*. In resting condition. *B*. After active secretion.

lines of the cells cannot be distinguished (Fig. 80). When secretion is excited by the injection of pilocarpin or other means, the inner zone clears up, the granules being dis-

charged into the lumen; the homogeneous outer zone becomes wider, while the nuclei and borders of the individual cells can be clearly made out.

The amount of ferment to be extracted from the pancreas seems to be directly proportional to the number of granules present in the cells. But we have evidence that these granules do not themselves represent the ferment, but are merely precursors of the ferment, just as the mucigen granules in the submaxillary gland are precursors of mucin. The evidence for this view in the case of the pancreas is shortly as follows.

If the fresh pancreas be extracted with glycerin, the extract has little or no ferment action. If, however, it be allowed to stand at the ordinary temperature of the air for twenty-four hours, or be treated with dilute acetic acid and then placed under glycerin, an extract is formed, containing all the active properties of the pancreatic juice. During standing, or in the treatment with acid, the granules give rise to the ferment. These precursors of ferments are spoken of as *zymogens*.

We see, therefore, that two changes occur in the cell when secretion takes place.

1. A transformation of zymogen granules into ferment, of mucigen into mucin, which substances are then discharged from the cell into the lumen of the gland.

2. A building up or reintegration of protoplasm, as evidenced by the growth in extent of the stainable protoplasmic parts of the cell.

During rest a twofold process is probably going on.

1. A further building up (anabolism) of the protoplasm of the cell out of the constituents of the surrounding lymph.

2. A katabolism or breaking down of the cell-protoplasm, with the formation of zymogen granules, which are stored up in the cell till the economy requires that they should be converted into ferment and discharged into the lumen.

Active secretion is associated in the living body with—

1. Increased blood-supply. If secretion be excited in the submaxillary gland by stimulation of the chorda tympani nerve, a cannula having been previously inserted into the distal end of a vein coming from the gland, the amount of blood flowing from the vein is increased five or six times. Before excitation the blood drops slowly from the cannula; during excitation it runs freely, has a bright arterial red colour, and the stream may present pulsations, transmitted from the arteries through the capillaries.

2. Evolution of heat.

3. Increased production of CO_2. The venous blood, however, appears bright red, since this increased production is more than compensated by the increased flow of blood through the gland.

4. Electrical changes.

It might be thought that the secretion was a result of the larger flow of blood through the gland, and indeed of the raised pressure in the capillaries, consequent upon the dilatation of the arterioles causing an increased transudation. The following facts, however, show that secretion is an active process of the epithelial cells, and is not dependent on filtration.

1. If manometers be inserted in the carotid artery, and in the duct of the submaxillary gland, the pressure of the secretion may be double as high as the blood-pressure in the carotid, so that fluid is flowing from the blood-vessels at a low pressure into the duct at a high pressure—a process not explicable by any mechanical theory of filtration.

2. If atropin be administered, stimulation of the chorda tympani nerve produces no secretion in the submaxillary gland, although dilatation of the blood-vessels takes place as usual.

3. Some secretion may be caused by stimulating the

chorda tympani nerve in a head recently severed from the body.

Nerve-supply

The salivary glands have a double nerve-supply, from the sympathetic and from the cranial nerves. The submaxillary gland receives its sympathetic fibres from branches of the cervical sympathetic which ramify on the

FIG. 81.

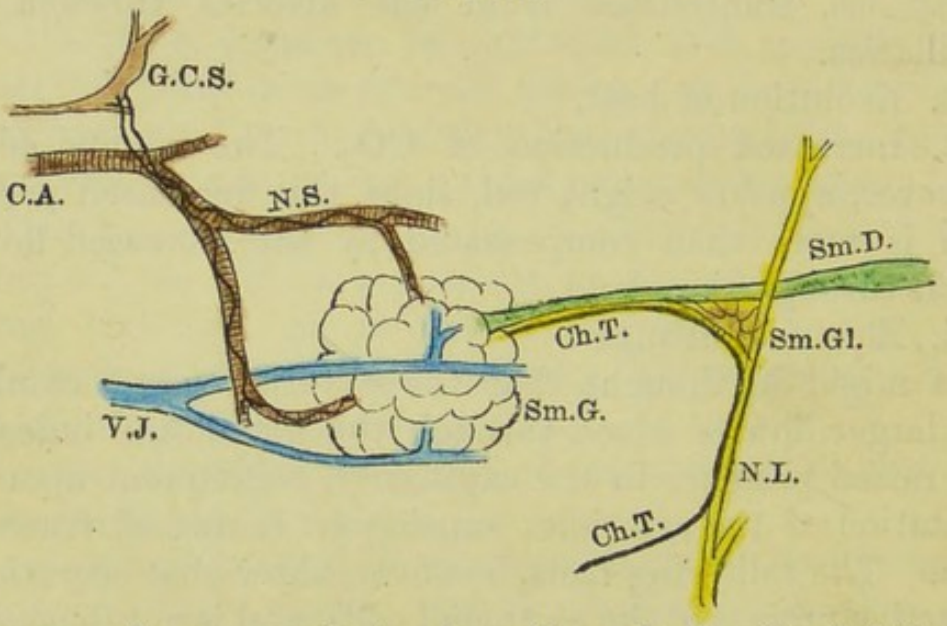


Diagram of nerve-supply to submaxillary gland. Sm.G. Submaxillary gland. N.L. Lingual nerve. Ch.T. Chorda tympani. Sm.Gl. Submaxillary ganglion. Sm.D. Wharton's duct. V.J. Jugular vein. C.A. Carotid artery. G.C.S. Superior cervical ganglion. N.S. Sympathetic fibres ramifying on facial artery. (After Foster.)

facial artery, and its cranial fibres from the chorda tympani nerve. These fibres run for a short time with the lingual nerve, and then leave it as a slender nerve which, reaching Wharton's duct (duct of submaxillary gland), runs along this to the gland. The fibres are connected in the hilus of the gland with nerve-cells. A small collection of nerve-cells—the submaxillary ganglion—is found in the triangle between the chorda tympani nerve, lingual nerve and duct.

With the cells of this ganglion are connected fibres of the chorda tympani going to supply the sublingual gland (Langley).

Different effects are obtained according as the chorda tympani or the sympathetic fibres are stimulated. Stimulation of the chorda tympani in the dog gives rise to an active dilatation of the vessels of the gland, and a copious watery secretion containing only a small amount of mucin and formed elements.

Stimulation of the sympathetic causes constriction of the vessels, and a scanty flow of very thick viscid saliva, rich in mucin and formed elements. The changes that occur in the cells are much more marked under sympathetic than under chorda stimulation. In consequence of the differences in the action of these two sets of nerve-fibres, they have been supposed to have two distinct functions.

The chorda fibres are vaso-dilatator and secreto-motor of water ; the sympathetic fibres are vaso-constrictor and secreto-motor of organic matter. The latter have been also denoted trophic, because of the marked change in the cells that is caused by their stimulation. They might well be called the katabolic fibres of the gland.

The *parotid gland* has also a double nerve-supply : fibres from the cervical sympathetic, and cerebro-spinal fibres running in the auriculo-temporal branch of the fifth nerve, but originating probably from the glosso-pharyngeal and running through the tympanic branch of this nerve (nerve of Jacobson). Stimulation of the cerebro-spinal fibres produces in the rabbit and dog a copious flow of limpid saliva of low specific gravity. Stimulation of the sympathetic causes in the rabbit a scanty flow of saliva free from mucin, but containing more proteids and ferment than the cerebro-spinal secretion. In the dog stimulation of the sympathetic causes no secretion, although the changes, that we have already described as accompanying activity, take place in the cells.

Reflex secretion.—The secretion of saliva is normally brought about reflexly by stimulation of the branches of the fifth and glosso-pharyngeal nerves distributed to the mucous membrane of the mouth and tongue, the stimulus being furnished by the presence of food in the mouth, by acids, or by the masticatory movements.

The centre for the secretion of saliva is located in the medulla, since from this part of the central nervous system arise both the afferent and efferent nerves by which the secretion is regulated. The peripheral nerve-cells, such as the collection that goes by the name of the submaxillary ganglion, cannot act as a reflex centre, and probably their sole function is to preside over the nutrition of the nerve-fibres distributed to the glands.

Gastric Juice

Gastric juice is the secretion of the glands lining the mucous membrane of the stomach. Of these, two varieties are distinguished. At the cardiac end of the stomach the glands are simple tubules, with short necks or ducts. The secreting part of the tubule is lined with a single layer of small granular cubical cells (chief cells); between these and the basement-membrane are a number of larger oval cells—parietal or oxyntic cells—which stain differently from the central cells.

In the pyloric region the glands consist of tubules which are branched at the end, and have a comparatively long neck or duct. In this region we find only chief cells, no oxyntic cells being present. The necks of all the glands are lined with columnar epithelium, similar to that covering the free surface of the mucous membrane.

Gastric juice may be obtained by making a gastric fistula, *i. e.* an opening communicating from stomach to exterior, and then putting in a clean sponge. This by its mechanical irritation causes a secretion of gastric juice, which may be collected on the sponge. Obtained in this

way, it is a clear, colourless, acid liquid, with a specific gravity varying from 1001 to 1010. Its chief constituents are two ferments, pepsin and rennet ferment; and free hydrochloric acid. It also contains salts, and a large amount of water, which constitutes about 95 per cent. of its bulk.

The hydrochloric acid is shown to exist in a free condition from the fact that on elementary analysis the amount of chlorine present is more than sufficient to saturate the bases. As a test for the presence of free hydrochloric acid, an alcoholic solution of tropæolin is often used, which becomes lilac in the presence of this acid.

Functions

The chief action of gastric juice is on proteids, which it converts into albumoses and peptones. This action is easily studied if we take some washed fibrin and put it in ·2 per cent. hydrochloric acid. In this acid the fibrin swells up and becomes transparent, but does not dissolve, even though kept at 40° for some time. If now to the swollen-up mass we add some gastric juice, or a few drops of glycerin-extract of gastric mucous membrane, the fibrin is speedily dissolved and a clear solution results. Neutralisation of the fluid with alkali throws down nearly the whole of the proteid present as acid albumen. If, however, the action be long continued, the neutralisation precipitate becomes less and less, and the fluid contains chiefly albumoses with a little peptone. These may be shown to be present by the following tests.

Nitric acid gives a precipitate which dissolves on heating and reappears on cooling.

Caustic potash and a trace of copper sulphate give a pink colour, which turns to violet on the addition of more copper sulphate—biuret reaction.

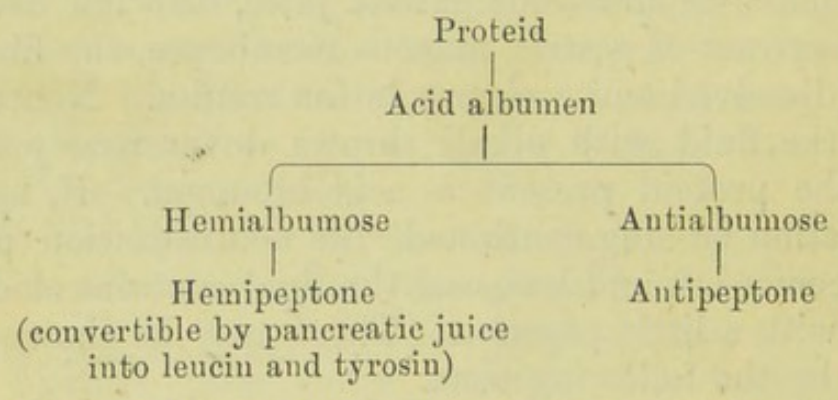
Saturation with ammonium sulphate gives a copious precipitate of albumoses. If this be filtered off, the filtrate

contains a small amount of peptone. To produce any large quantity of peptone the gastric juice must act for a considerable length of time.

The stages in the action of gastric juice on proteids are therefore—

Coagulable proteid.
Syntonin or acid albumen.
Albumoses.
Peptones.

In the second chapter we have mentioned three different varieties of albumoses, which may be separated by their various solubilities and precipitability by neutral salts. All three varieties are generally to be found in an ordinary gastric digestion mixture. Another classification of albumoses has been suggested, founded on the fact that two different kinds of peptone may be obtained from them —*hemipeptone*, which may be converted by pancreatic juice into leucin and tyrosin; and *antipeptone*, which is not further affected by this juice. Using this classification, the action of the gastric juice upon proteids may be represented by the following scheme :



Gastric juice acts in the same way on insoluble coagulated proteids, dissolving these and converting them into syntonin, albumoses, and peptone.

Gelatin is converted by gastric juice into bodies known as gelatin peptones, and in this conversion loses the power of forming a jelly when cold.

Collagen, the constituent of the connective tissues, from

which gelatin is obtained on prolonged boiling, is also digested by gastric juice, giving rise to the same end-products as gelatin.

In this way the connective tissue binding together the fat-cells of adipose tissue is broken up and dissolved, and the fat is set free in a liquid form, ready to be acted on by the pancreatic juice.

Another important function of the gastric juice depends on the fact that dilute hydrochloric acid acts as an antiseptic. Meat and fibrin may be kept for several days in gastric juice without undergoing decomposition. If, however, the acid be neutralised, decomposition sets in rapidly on exposure to air, and at the end of twenty-four hours the mixture has a fœtid odour, and is found to be swarming with bacteria. This action is of great importance in the normal life of the individual. The microbes which have been shown to be the causes of typhoid and cholera are destroyed by gastric juice. Hence there is little likelihood of contracting these diseases unless the secretion of gastric juice be insufficient, or the acid neutralised by the presence of alkalies or rendered inert by too much dilution.

On starches and fats gastric juice has no action. Ingestion of large amounts of cane-sugar gives rise to a free secretion of mucus on the surface of the gastric mucous membrane, and this mucus is said to contain an invert ferment which has the power of converting cane-sugar into dextrose and lævulose.

Action on milk.—Milk, which is the sole diet of the infant, is in itself a whole food, and contains representatives of all five classes of foodstuffs—proteids, fats, carbohydrates, salts, and water (Chap. X). The chief proteid of milk—caseinogen—is a body allied to alkali albumen, but presenting important differences from it. From the gastric mucous membrane, especially in young animals, a ferment may be extracted known as rennet ferment. On adding a few drops of rennet solution to milk, and warm-

ing the mixture to about 40° C., it sets into a solid mass, so that the vessel may be inverted without spilling the contents. On allowing the clot to stand it shrinks, enclosing in its meshes the greater part of the fat-globules of milk, so that the clot floats in an almost transparent fluid (curds and whey). This clotting depends on a change induced in the caseinogen of the milk under the action of the ferment.

Pure caseinogen may be prepared in the following way. Milk is saturated with magnesium sulphate; the casein is precipitated, and carries down with it the greater part of the fat. The precipitate is dissolved in water, the fat filtered off, and then excess of acetic acid added, which produces a flocculent precipitate of caseinogen. This is collected in a filter and washed repeatedly with distilled water. If it be dissolved in lime-water a clear colourless solution is formed. If rennet be added, and the mixture allowed to stand at 40° C., a clear colourless clot of casein is produced. This act of clotting, just as the clotting of blood, is intimately dependent on the presence of lime. If the precipitate of caseinogen be washed till all lime salts are removed, addition of rennet causes no clotting; but the mixture clots at once on addition of calcium phosphate or chloride.

Thus in clotting of milk two processes are concerned:

1. A conversion of caseinogen into some other body, which may be called soluble casein.

2. A combination of this soluble casein with a lime salt to form insoluble casein, which is precipitated in a gelatinous form.

These facts are well shown by the following experiment of Ringer. Two test-tubes are taken, *a* and *b*, containing a solution of pure caseinogen free from lime. To *a* rennet ferment is added, and to *b* a solution of calcium chloride; and the two tubes are kept at 40° C. for some time. No visible reaction takes place. If *a* be now boiled, so as to destroy the rennet ferment present, and on cooling a few

drops of calcium chloride be added, clotting occurs. In this experiment the rennet ferment has evidently produced some change in the caseinogen although no clotting was produced, since the boiled fluid only needs the addition of lime salt to make it clot. The fact that *b* did not clot shows that lime salts are without effect on a solution of caseinogen which has not been previously exposed to the action of rennet ferment.*

Circumstances affecting activity of gastric juice.—Gastric juice is most active at about 40° C. At 0° its action is indefinitely suspended. If boiled the ferment is destroyed. The action goes on most rapidly when the percentage of HCl is ·2 per cent.; larger amounts of acid hinder its action. Neutralisation stops the action altogether; and if the juice be rendered slightly alkaline and be kept at the temperature of the body for some time, its activity is permanently destroyed. Its action is also hindered if the products of its activity be allowed to accumulate to a large extent. In the stomach this is guarded against by the continual absorption of the albumoses and peptones by the gastric mucous membrane which is constantly going on.

The Secretion of Gastric Juice

The functions of the two different kinds of gastric glands have been determined by cutting out a portion of the cardiac or pyloric parts of the stomach, and sewing its

* The student must be careful to distinguish between the curdling of milk by rennet and its curdling by addition of acid, or when it becomes sour in consequence of the development in it of lactic acid. In the former case the curdling is a true clotting, and is due to the conversion of the soluble caseinogen into the insoluble casein, just as when fibrinogen is converted into fibrin. When acid is added to milk the caseinogen is merely precipitated, just as fibrinogen is precipitated by saturation with common salt. And this precipitate can be dissolved up again as caseinogen and made to clot, *i. e.* can be converted into casein by the agency of rennet ferment.

edges to the margins of the abdominal wound. The gap in the stomach wall thus produced is closed by suturing the edges together, so that the final result of the operation is that the stomach is rather smaller, and there is a little cul-de-sac consisting of either cardiac or pyloric mucous membrane communicating with the exterior. Secretion may be excited by mechanical irritation of this mucous membrane by the introduction of a sponge or some food, and the juice may be collected. It is then found that a cardiac cul-de-sac contains free HCl and pepsin, and so has the power of digesting proteids. A pyloric cul-de-sac, on the other hand, yields a secretion which is neutral or slightly alkaline, but which is shown to contain pepsin from the fact that, on adding HCl to it till its percentage is ·2 per cent., the juice is able to digest proteids. We see, then, that both cardiac and pyloric glands yield pepsin, but only the cardiac glands yield free hydrochloric acid. Since in both sets of glands the central cells are the same, it is concluded that these cells give rise to the pepsin, while the large oval parietal cells in the cardiac end form the free hydrochloric acid.

Coincident with activity, changes take place in the central cells analogous to those which we studied in the case of salivary glands. The central cells of the glands from a fasting stomach (*i. e.* of an animal that has not taken food for eighteen hours) are swollen and filled with granules. When secretion occurs two zones can be distinguished, an outer protoplasmic zone, free from granules, and an inner granular zone, which becomes less and less marked as secretion proceeds. These granules consist of a zymogen, *pepsinogen*. If the fresh mucous membrane be extracted with glycerin, much less ferment is obtained than if the extraction be performed after treatment of the mucous membrane with dilute acid. The pepsinogen is further distinguished from the pepsin by the fact that it is only slowly affected by a solution of sodium carbonate, which very rapidly destroys pepsin.

The secretion of gastric juice may be excited by direct stimulation of the mucous membrane by the presence of food, &c., in the stomach. We have evidence that a copious flow of gastric juice may be excited through nervous channels either reflexly through the mouth, or in consequence of events occurring in the brain. This reflex secretion is well shown in the following experiment:— The œsophagus of a dog is divided in the neck, and the two ends stitched to the wound so that they open exteriorly. At the same time a gastric fistula is made. The dog is fed and kept in good condition by the introduction of milk into the lower end of the œsophagus, or by the direct introduction of food into the stomach. When the animal has quite recovered, he is starved for nine hours, and is then allowed to eat meat. The dog eats greedily, and, since the food cannot reach the stomach, but tumbles out by the opening of the œsophagus in the neck, will go on eating for a very long time. Directly the dog begins to eat, a copious secretion of gastric juice is obtained, as much as 300 c.c. of pure gastric juice being poured out in one hour, clear and colourless like water. The same effect may be produced by simply showing the dog a piece of meat, and it is stated that the flow ceases as soon as the dog realises that he is not intended to have the meat. Pawlow, to whom we owe the above experiment, has shown that the efferent nerve in the reflex, that is to say, the secretory nerve to the stomach, is the vagus. If proper precautions be observed, stimulation of the vagus causes invariably a secretion of gastric juice.

Pancreatic Juice

The liver and pancreas pour their secretions into the duodenum by means of a common opening.

The pancreatic juice obtained from a recently established fistula is a clear, viscid, alkaline fluid, of a specific gravity

1030. It contains a considerable proportion of proteid, chiefly globulin, so that it becomes solid on boiling. Its other constituents are—

Various ferments;

Salts, especially sodium carbonate; and

Water, about 90 per cent.

If a permanent fistula be made, the secretion after a time alters in character, becoming poorer in proteids and more watery (specific gravity 1010).

An artificial juice may be prepared in the following way. The pancreas is chopped up, treated with a saturated solution of salicylic acid, and then extracted with 1 per cent. solution of sodium carbonate. A potent extract may also be made by treating the minced gland after the action of the acid with strong glycerin. The glycerin extract of the fresh gland has little or no action, since the pancreas contains only a precursor of the ferment—a zymogen, which has to be converted into the ferment trypsin by the action of the acid, or by allowing the pancreas to stand after death.

The histological changes that occur during secretion have been already described (p. 213).

Secretion is normally excited by the taking of food, and appears to be a reflex act starting from the gastric mucous membrane. If care be taken to keep the animal under absolutely physiological conditions (*i. e.* free from pain or fright, and unpoisoned by anæsthetics), stimulation of the peripheral end of the vagus causes a copious secretion of pancreatic juice. The secretion may also be excited by an injection of pilocarpin.

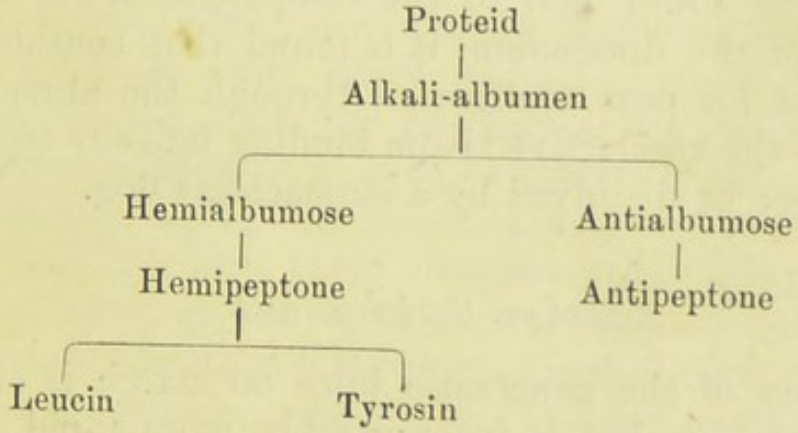
Functions.

The pancreatic juice has a threefold action on proteids, carbohydrates, and fats, and is therefore the main digestive fluid of the body. It is said to contain three ferments: trypsin, a proteolytic ferment; amylopsin, an amylolytic

or starch-digesting ferment; and steapsin, a ferment acting on fats. All attempts to separate these three ferments in a pure form have hitherto failed.

Action on Proteids

Proteids are converted by this juice into albumoses and peptones, as in the case of the gastric juice. Trypsin, however, is only active in an alkaline medium, and is destroyed in the presence of an acid. The first product of its action is therefore not acid- but alkali-albumen. Another important difference of this ferment from pepsin lies in the fact that it carries on the process of decomposition still further, splitting up part of the peptone into two amido-acids—leucin (amido-caproic acid) and tyrosin (oxy-phenyl-amido-propionic acid). So the action of this juice on proteid may be represented in the following schema:



If fresh fibrin be digested with this juice it does not swell up, but is gradually eroded and dissolved at the edges. Its action is much more potent than that of gastric juice. If equal amounts of proteid be digested for twenty-four hours in gastric and pancreatic juices, the pancreatic mixture is found at the end of that time to contain much more peptone than does the gastric mixture, in which the greater part of the proteid is still in the form of albumoses.

Since the bacteria of putrefaction thrive readily in a slightly alkaline solution of proteid, such as pancreatic juice, care must be taken in all experiments with this juice

to prevent putrefaction. To this end thymol or 'formalin' may be mixed with the solution. If this precaution be omitted, the mixture at the end of twenty-four hours has a foul odour, and is found to be swarming with bacteria under the agency of which the proteids are further split up, with the formation of many amido-acids, free fatty acids, and aromatic bodies such as phenol, indol, and skatol. To the presence of the last two bodies is due the horrible fæcal odour of a pancreatic digestion mixture which has been allowed to stand without the addition of an antiseptic.

Gelatin is affected by pancreatic juice in the same way as by gastric juice, being converted into gelatin-peptones, which do not gelatinise on cooling. This juice, however, is unable to dissolve collagen, the chief constituent of the connective tissues. Hence if the stomach of a dog be cut out, and the lower end of the œsophagus sewn to the upper end of the duodenum, it is found that considerable quantities of fat pass undigested through the alimentary canal, since the connective tissue binding fat-cells together can no longer be dissolved by a stomachless dog.

Action on Carbohydrates

The action of the pancreatic juice on starch is similar to that of ptyalin, but is incomparably more rapid. The stages of conversion are the same as in the case of ptyalin, the end-products being achroodextrin and maltose. If the action be long continued, the process of hydrolysis may go on to the formation of dextrose, but the amount of this body formed is in all cases very slight.

Action on Fats

Fresh pancreatic juice contains a ferment which has a hydrolytic action on neutral fats, splitting them up into glycerin and a free fatty acid, thus :

$$C_3H_5(C_{16}H_{31}O_2)_3 + 3H_2O = C_3H_5(OH)_3 + 3HC_{16}H_{31}O_2.$$

Tripalmitin (neutral fat). Glycerin. Palmitic acid.

This decomposition, however, takes place in the presence of the alkaline salts of the pancreatic juice and the alkaline bile. The free fatty acid formed by the ferment action combines with the alkali present, displacing the CO_2, to form a soap. The presence of soap in the solution enables it to hold all the rest of the neutral fat in suspension. Thus if a drop of rancid oil (*i. e.* one containing free acid) be allowed to drop on to the surface of a 1 per cent. solution of sodium carbonate, the acid at the exterior of the drop unites with the alkali to form a soap, which is immediately dissolved. This chemical change and solution going on at the surface of the drop sets up diffusion currents in the surrounding fluid, which carry off little particles of the neutral fat. These immediately become coated with a layer of soap, which prevents them running together again. So we see a white cloud appearing round the drop of rancid oil, and under the microscope the cloud is observed to consist of innumerable tiny droplets of fat suspended in the alkaline liquid. A single shake causes the whole drop to break up into these droplets, the milky fluid thus formed being spoken of as an *emulsion*. In this way the pancreatic juice has the power of emulsifying neutral fats.

This fat-splitting action may go on in a neutral or slightly acid medium, and so is not subject to such restrictions as are the proteolytic or amylolytic functions of the pancreatic juice.

This juice also contains a ferment similar to rennet, which has the property of curdling milk. It is probably of no physiological importance.

The Bile

The bile is the product of secretion of the liver. This organ differs in structure from all other glands of the body,

the cells being so numerous and pressed together around the capillary meshwork that their primitive arrangement as secreting tubules is no longer to be made out in the adult liver.

The liver has a double blood-supply: the portal vein, which supplies a rich capillary anastomosis round every liver-cell, and carries venous blood from the alimentary canal; and the hepatic artery, which carries oxygenated arterial blood, and supplies chiefly the connective tissue surrounding the bile-ducts and blood-vessels in the divisions between the lobules, known as Glisson's capsule.

The secretion of bile is a continuous process, but it does not flow directly into the intestine, being stored up during fasting in the gall-bladder, whence it is discharged by the contraction of this viscus when the acid chyme passes the orifice of the common bile-duct.

The discharge of bile into the intestine is greatest about three to five hours, and again about thirteen hours, after the ingestion of food.

Bile as obtained from the gall-bladder is dark brown or greenish in colour. It is alkaline and slimy from the presence of mucin. Its specific gravity varies from 1010 to 1040. The following table represents the average composition of human bile taken from the gall-bladder:

100 parts contain—	
Water	85 parts.
Bile salts	10 ,,
Fats, lecithin, and cholesterin . .	1 part.
Mucus and pigment . . .	3 parts.
Inorganic salts . . about	1 part.

Besides these constituents, bile contains gases, especially carbon dioxide, and traces of soaps.

If the bile be collected as it is secreted by the liver, by inserting a cannula in the hepatic duct, it is found to contain a larger percentage of water and little or no mucin.

It is evident, therefore, that during its stay in the gall-bladder the bile loses its water, and acquires mucin, which is secreted by the mucous membrane of the gall-bladder.*

The bile salts are two in number,—*glycocholate* and *taurocholate of soda.*

The relative amounts of the two salts vary in different animals, the taurocholate being most abundant in carnivora, and the glycocholate in herbivora. In human bile, glycocholate forms nearly the whole of the bile salts present.

The bile salts may be extracted in the following way :— Bile is mixed into a paste with animal charcoal, and the mixture dried, pounded up, and extracted with absolute alcohol and filtered. On adding ether to the alcoholic filtrate, and allowing it to stand, a crystalline precipitate is produced, consisting of the two bile salts. These have a bitter taste, and are easily soluble in water. Their presence in a fluid may be shown by *Pettenkofer's reaction.*

Addition of a drop of cane-sugar solution and excess of concentrated sulphuric acid to a solution of bile salts gives a purple colour. This colour may be interfered with by the dark brown colour produced by the charring of the sugar with the sulphuric acid. Either of the following ways may be adopted to obtain a good purple reaction :—

A. The bile and sugar are shaken up in a test-tube until the upper part of the tube is filled with froth. If the concentrated sulphuric acid be now poured down the side of the tube, the froth is stained a purple colour where it comes in contact with the acid.

B. A porcelain capsule is rinsed out successively with solutions of bile salts, cane-sugar, and dilute sulphuric acid (25 per cent.). On warming the capsule gently over a flame, water is driven off from the thin film of dilute acid, and the concentrated acid thus produced acts on the thin film of sugar and bile salts, causing a brilliant purple colour of the whole of the inner surface of the capsule.

Glycocholic acid is a conjugated acid, which on hydro-

* It is probable that the greater part of the substance occurring in bile, and precipitated by acetic acid, and generally known as mucin, is really a nucleo-albumen.

lysis splits up into glycin (amido-acetic acid) and cholalic acid ($C_{25}H_{40}O_5$).

Taurocholic acid is also a conjugated acid, which can be split up into taurin, an amido-acid containing a large proportion of oxidised sulphur (amido-isethionic acid), and cholalic acid.

The mucin and nucleo-albumen present may be precipitated by acetic acid. The precipitate is soluble in dilute alkalies.

The bile-pigments are *bilirubin* (brown) and *biliverdin* (green). The colour of the bile depends on the relative amounts of these two pigments present. Biliverdin ($C_{16}H_{18}N_2O_4$) may be obtained on oxidation of bilirubin ($C_{16}H_{18}N_2O_3$).

The presence of bile-pigments may be proved by *Gmelin's test.* A drop of bile on a white plate is treated with a drop of yellow nitric acid. Where the two drops come in contact a play of colours is produced, due to the formation of various oxidation-products of bilirubin. These colours occur in the following order—brown, green, blue, red, yellow. The end-product of the reaction which gives the yellow colour is known as *choletelin.*

The cholesterin present is probably kept in solution by the bile salts. Under abnormal conditions, cholesterin may be precipitated and may form concretions in the gall-bladder (gall-stones). More rarely we meet with gall-stones consisting of the bile-pigments in combination with alkaline earths.

Actions of Bile

Bile contains small quantities of an amylolytic ferment which has a feeble digestive action on starch. If added to a mixture of starch and pancreatic juice, it materially hastens the action of the latter.

On adding bile to an acid solution of albumoses and peptones, such as the products of gastric digestion which come through the pylorus into the first part of the duo-

denum, a precipitate is produced, consisting of glycocholic acid, syntonin, and albumoses.

One function of the bile, then, is to neutralise the gastric juice and prepare the way for pancreatic secretion.

The alkaline salts of the bile can combine with the fatty acids set free by the pancreatic juice to form soaps, and so aid in the digestion and emulsification of fats. Bile is also supposed to assist in the absorption of fats by virtue of the bile salts it contains. Oil will not run through a filter moistened with water, but will do so if it be moistened with a solution of bile salts. The presence of bile salts lowers the surface-tension between the oil and the water, so that in the intestine the droplets of fat are able to come into intimate contact with the absorbing surface of the epithelium.

The presence of bile in the intestine excites contractions of the muscular walls, and so acts as a natural purgative. In the same way the muscular fibres of the absorbent villi are stimulated by the presence of bile, and contract, forcing the contents of the villus into the subjacent lacteal.

Bile is often spoken of as an antiseptic, but this statement must be qualified. The free bile acids, especially taurocholic acid, have a pronounced antiseptic action. The action is, however, lost when the acids are combined with alkalies, as in the bile itself, which decomposes extremely readily.

A theory of the mechanism of fat absorption, which has been put forward by Altmann, deserves mention here, since it seems to afford an explanation of many phenomena not easily explicable by the ordinary emulsification theory. According to Altmann, fats are not absorbed at all in a particulate form, but in solution, as free fatty acids or soaps. The process is as follows:—The neutral fat is split up by the pancreatic juice into free fatty acid and glycerin. This decomposition may amount to 11 or 12 per cent. of the total fat. The free fatty acid thus produced is dissolved by the solution of bile acids, and in this form is absorbed by the epithelial cells of the intestinal

villi. In the cells a process of synthesis takes place, and free acid is combined again with glycerin to form a neutral fat, which makes its appearance as small granules or spheres in the protoplasm of the cell. When the fatty acid thus produced is absorbed, the fat-splitting ferment of the pancreatic juice, which is most potent in a slightly acid medium, causes a further decomposition of the neutral fat, and this process goes on until the whole of the fat has been absorbed as free fatty acids and glycerin. This theory harmonises well with the following facts:—Extirpation of the pancreas or obstruction of the bile-duct checks the digestion and absorption of fat. After extirpation of the pancreas, fats are not absorbed even if administered to the animal in the form of a fine emulsion containing neutral fat suspended in a solution of soap. If, however, to this emulsion chopped-up pancreas be added, a large proportion of the fat is absorbed. If fatty acids are administered to a man they are absorbed, but appear in the chyle as neutral fat, showing that a synthesis of the fatty acid and glycerin has taken place on the passage of the fatty acid through the epithelial layer from the intestine to the lacteal. In the same way soaps administered with the food appear in the chyle as neutral fats.

The Origin and Fate of the Biliary Constituents

The bile is to be regarded partly as a secretion, having an important function in the digestion of fats, and partly as an excretion—a means by which the effete colouring matter of the blood is got rid of.

The bile salts are formed by the liver, as is shown by the fact that after extirpation of the liver in frogs or birds, no accumulation of these salts takes place in the body. If, however, the bile-ducts be ligatured, bile salts are found in the blood and in the urine. The glycin and taurin are probably derived from proteid disintegration, but we know nothing concerning the precursors of cholalic acid. In the intestine the bile salts play their part in the digestion of fats, and are then for the most part re-absorbed, passing along the portal vessels to the liver, where they are again secreted, so that they can exert their functions over and over again. A certain amount is split

up in the intestine into the amido-acids and cholalic acid, the former being reabsorbed, and the latter being excreted with the fæces.

The bile-pigments are the products of disintegration of the hæmoglobin of the blood. They play no further part in the body, and are excreted with the fæces in a slightly altered form. It was long debated whether they were formed by the liver, or whether some might not be formed in the blood itself or in the other tissues from the disintegrated red corpuscles. It is found that, after blood has been extravasated into the tissues, the hæmoglobin undergoes certain modifications, and is converted into the body named hæmatoidin. Now hæmatoidin is isomeric and probably identical with bilirubin, and this fact was looked upon as furnishing strong evidence for the hæmatogenous origin of bile-pigments. Experiment has shown, however, that when blood-corpuscles are broken up in the circulation (a process which is normally taking place on a small scale) no bile-pigment is formed except by the agency of the liver. A great breaking-up of blood-corpuscles and setting free of hæmoglobin may be caused in animals by the inhalation of arseniuretted hydrogen. If the liver be present, this disintegration of blood-corpuscles causes a greatly increased formation of bile-pigment, which is eliminated with the bile, or partly reabsorbed by the lymphatics from the biliary passages, giving rise to jaundice. If in a goose the liver be shut out from the circulation or extirpated, and arseniuretted hydrogen administered, not a trace of bile-pigment is produced.

The cholesterin of the bile is sometimes looked upon as a product of nerve-disintegration, since this substance is found abundantly in the central nervous system; but we have no evidence for or against this view.

Bile is secreted at a very low pressure—1½ cm. Hg. If the pressure in the bile-ducts rises above this point, as may easily happen when the flow is obstructed in consequence of inflammatory thickening of the mucous membrane, or

by the presence of a gall-stone, or even by a very viscid bile, the bile is reabsorbed by the lymphatics and reaches the blood, and nearly all the tissues of the body are stained yellow by the pigments, giving rise to jaundice. This pressure, however, is higher than the pressure in the portal vein, which is only about 1 cm. Hg.; for we must remember that the blood in the portal vein has already passed through a system of capillaries, so that its pressure is extremely low. The fact that the pressure in the bile-ducts may exceed that in the portal vein shows that the secretion of water is not effected by a mere process of filtration.

Succus Entericus, or Intestinal Juice

The secretion of the tubular glands (Lieberkühn's follicles), which beset the mucous membrane of the intestine, may be obtained in a pure condition in the following way. An opening is made into the abdomen of an animal, a piece of the small intestine five or six inches long is separated from the rest, its attachment to the mesentery with its blood-vessels and nerves being left intact. The two ends of the remaining piece of intestine are sutured together, so that the animal is left with a continuous but shortened alimentary canal. One end of the excised piece is closed by sutures, and the margins of the other end sewn to the margins of the abdominal wound. An intestinal fistula is thus produced, from which the juice may be collected free from contamination by the other digestive juices. Intestinal juice obtained in this way is a clear, limpid fluid, with a specific gravity of 1010, containing a trace of proteid, and salts, of which sodium carbonate is the most abundant. In consequence of the presence of this salt it has a strong alkaline reaction.

Actions

On proteids, fats, and starch, succus entericus has no action. It, however, contains an invert ferment, by the agency of which cane-sugar is converted into dextrose and lævulose, and maltose is converted into dextrose. Its alkaline reaction is probably important in neutralising the free acids, lactic, butyric, &c., produced by the action of putrefactive micro-organisms on the foodstuffs.

The secretion may be excited by mechanical irritation. The following experiment is supposed to show the influence of the intestinal nerves on the secretion. The abdomen being opened, the small intestine is ligatured in four places, so as to shut off three equal lengths of bowel; all the nerves going to the middle segment are divided and the abdomen closed. At the end of two or three hours the wound is opened, and it is found that the middle segment is distended with fluid, whereas the other two segments, which have their nerves intact, are comparatively empty. This secretion has been regarded as analogous to the paralytic secretion of saliva which continues for some weeks after section of all the nerves going to the submaxillary gland. We do not know, however, how far this phenomenon is to be ascribed to vascular changes taking place in the loop of intestine, in consequence of the section of its nerves.

Absorption of Foodstuffs

We must now consider the ways in which the foodstuffs, that have been digested and rendered soluble in the alimentary canal, pass into the circulation to be distributed to all the cells of the body. There are two main paths of absorption—the blood-vessels and lymphatics. The blood-vessels form a dense capillary anastomosis immediately under the epithelial layer covering the inner surface of the mucous membrane. In order to increase the absorb-

ing surface, the mucous membrane of the small intestine is thrown into transverse folds—the valvulæ conniventes, which are thickly covered with finger-like elevations or villi. The body of a villus is made up of a reticular tissue composed of branching cells, the meshes of which may contain leucocytes of various forms. In the centre of the villus is a wide lymphatic vessel, the lacteal. The endothelial cells forming the wall of the lacteal are continuous with the branched cells of the reticular tissue, but there is no free communication between the spaces of this tissue and the beginning of the lymphatic. Below, the cavity of the lacteal is continued into the plexus of lymphatics lying in the submucosa. The intestinal surface of the villus is covered with a single layer of columnar epithelial cells, which have a hyaline border presenting delicate vertical striation, apparently due to the presence in the border of a number of cilia-like processes. The capillary network lies outside the lacteal immediately under the epithelium. The blood-vessels pour their contents into the radicles of the portal vein, which carry them thence to the liver. The lymphatics in the submucosa join to form larger trunks, which run between the two layers of the mesentery to a collection of lymphatic glands at the back of the peritoneal cavity. The lymph, after flowing through these glands, is collected into a large vessel—the receptaculum chyli, from which it is carried in the thoracic duct to be discharged into the blood-stream at the junction of the left jugular and subclavian veins.

During fasting the lymph contained in these vessels is exactly similar to that contained in any other part of the body. If a cannula be inserted in the thoracic duct of a fasting dog, and the animal be then given a meal rich in fat, it is found that the amount of lymph flowing from the cannula is the same as before, but the lymph has changed its appearance, being now white like milk. On microscopic examination this milky appearance is found to be due to the presence of small fatty globules similar

to those in milk, and of a number of very fine particles—much finer than any of the globules met with in milk, and which may exhibit Brownian movement. These constitute the molecular basis of the chyle. If the abdomen of the animal be opened, the course of the lymphatics along the mesentery is evident from the milky character of their contents. It is on account of this milky appearance during digestion that the name of lacteal has been given to the lymphatics of the alimentary canal; and chyle is simply lymph with fatty globules, and molecular basis.

Since the whole of the chyle is poured by the thoracic duct into the blood, the plasma or serum of the latter, obtained after a meal containing fat, is also found to present a milky appearance, in consequence of the presence of fat globules derived from the chyle. If, however, the thoracic duct be ligatured, a fatty meal is not followed by any increase in the amount of fat in the blood.

It is apparent, then, that the greater part of the fat is absorbed by the chyle, and 60 per cent. of the absorbed fat can be obtained from the chyle through a cannula placed in the thoracic duct. Comparative analyses of portal and carotid blood during digestion show that the amounts of fat contained in the two are the same; hence it is concluded that no fat is absorbed through the intermediation of the blood-vessels. It has not yet been found possible to trace the mechanism of absorption of the proportion of fat which does not enter the blood by way of the lacteals. It is possible that it may be utilised or built up into more complex compounds in the tissues of the intestinal mucous membrane.

We must now inquire how the fat gets into the lacteals. If sections be made of the villus during the digestion of fat, and stained with osmic acid, the epithelial cells are seen to be full of black fatty granules of various sizes. These granules are also to be observed in the spaces surrounding the central lacteal.* The lacteal itself is full of

* Many of the leucocytes also present black granules, but these are

lymph with fat globules, but the latter are here much more minute, and correspond to the molecular basis of the chyle.

We must conclude that the fat is taken up by the epithelial cells covering the villus, passing through their striated border. These extrude the fat granules on the other side into the spaces of the reticular tissue. From these spaces they are either taken up by the cells forming the boundary of the lacteal, and passed on by them in a very finely divided condition into the chyle as the molecular basis, or they are forcibly pressed through the wall of the central lacteal by the contractions of the muscular tissue of the villus.

The other constituents of the foodstuffs seem to be absorbed chiefly, if not completely, by the blood-vessels. Blood normally contains a small amount of dextrose (·1 to ·2 per cent.), and the proportion of sugar in the lymph is the same as in the blood. After a meal rich in carbohydrates, the proportion of sugar in the chyle flowing from the thoracic duct is the same as that in the blood from the carotid artery ; but it is found that there is slightly more sugar in the blood from the portal vein than in that from the hepatic vein or carotid artery. It is inferred, therefore, that the blood in the capillaries of the intestinal wall takes up sugar in the form of dextrose and carries it to the liver. Here the excess of sugar is taken up by the hepatic cells, and converted by them into the colloid carbohydrate, glycogen, which is deposited in the substance of the cell. In this way the liver acts as a storehouse of carbohydrate material, and prevents the sugar in a rich carbohydrate meal from escaping into the general circulation. This function is important, since it is found that if the amount of sugar in the blood be raised above the normal, the excess is immediately excreted by the kidney ; so that without such an economical organ as the liver the greater part of a carbohydrate meal would at once be wasted.

supposed not to be of a fatty nature, since they are not dissolved on treating the section with ether.

We have seen above (p. 210) that the end-product of the action of the salivary and pancreatic ferments on starch is a mixture of maltose and achroodextrin. In the blood of the portal vein, however, we find only dextrose ; and it appears that the dextrin and maltose must undergo some further change before reaching the blood. We know for certain that the succus entericus contains a ferment which can convert maltose into dextrose ; but it is possible also that the epithelial cells lining the intestine are able to effect a transformation of both dextrin and maltose into dextrose. It must be remembered, too, that normal blood-plasma, serum, and lymph contain a ferment which quickly converts boiled starch, glycogen, dextrin, or maltose into dextrose. At any rate, under normal circumstances, no dextrin or maltose is to be found in the blood of the portal vein or in the chyle, although these substances are absorbed from the intestine.

Proteids are for the most part converted into peptones and albumoses before absorption. This absorption takes place by means of the blood-vessels. Thus a large proteid meal is as readily absorbed in a dog whose thoracic duct is ligatured as in a normal dog. A large proteid meal always gives rise to a large increase in the amount of urea excreted in the urine, and this increase is found also in a dog whose thoracic duct has been ligatured, showing that the proteid has been absorbed and distributed through the whole system.

If, however, we analyse the blood of the portal vein during active proteid digestion, not a trace of peptone is found. Injection of even small quantities of albumoses or peptone into the portal vein or any part of the blood-stream gives rise at once to peptonuria, and the greater part of the peptone injected reappears in the urine, from which it can be collected. Thus it is evidently impossible that the proteids can reach the blood-stream in the form of peptone ; and the following experiments show that peptone is regenerated into coagulable proteid in its passage through the epithelial cells of the alimentary canal.

A piece of the mucous membrane of the stomach during active proteid digestion is excised and divided into two pieces. One piece (A) is thrown at once into boiling water, and the other piece (B) is allowed to remain for three hours in a warm moist chamber at 40° C., and is then plunged into boiling water. On analysing the two pieces a large amount of peptone is found in A, whereas in B the merest trace or none is present. During the stay in the warm chamber, all the peptone in B has been converted into something else, probably coagulable proteid. That this action depends on the vital activity of the epithelial cells, and not on unorganised ferments present in the cells, is shown by the fact that plunging the membrane into water at 60° C. is as efficacious in stopping the action as when water at 100° C. is used. At 60° C. all living cells in the body are destroyed, but not unorganised ferments.

The following experiment leads to the same conclusions: —A loop of a dog's intestine is excised, its contents washed out with a normal saline fluid, 1 grm. of peptone placed in it, and the ends ligatured. Dilute defibrinated blood is now passed through the vessels supplying the loop for two or three hours in order to keep it alive. At the end of this time, on cutting open the loop, all the peptone is found to have disappeared, and on analysis of the blood that has passed through the vessels of the loop, no peptone can be found, showing that peptone has been converted into a coagulable proteid in its passage through the absorbing epithelium. It is not necessary that the proteid should be all peptonised before being taken up by the epithelial cells. It has been shown that proteid, such as egg albumen or acid albumen, may be absorbed by an isolated loop of bowel, or by the lower end of the large intestine, which has been washed free from any trace of proteolytic ferment that may have been carried down to it from the pancreatic juice. Peptonisation, however, helps the work of the epithelial cells, and materially hastens the process of absorption.

Salts and water are also taken up chiefly by the blood-vessels. The processes of diffusion and osmosis are often looked upon as playing a great part in the absorption of these substances. The fact, however, that the relatively slightly diffusible sugar is taken up much more rapidly than the diffusible salt potassium iodide, and similar facts, show that even here the selective activity of the living epithelial cell also functionates. No doubt the cell makes use of the physical processes of diffusion and osmosis, but it can absorb substances in direct defiance of those laws when by doing so it is rendering a common service to the organism.

Summary of the Changes undergone by the Food in the Alimentary Canal

In the mouth the food is broken up into small particles by mastication, and moistened with alkaline saliva, in order to fit it for deglutition. A small part of the starch is converted into dextrin or maltose.

On reaching the stomach the action of the saliva may go on for fifteen or twenty minutes. At the end of this time the secretion of gastric juice, excited by the presence of food and of alkaline saliva in the stomach, is sufficiently abundant to neutralise and render acid all the gastric contents, and so stop the action of the ptyalin. Under the action of the gastric juice the greater part of the proteids is dissolved, converted into syntonin, albumoses, or peptones, and the connective tissues are dissolved, setting free the fat, which floats about in a free state. At the same time some of the salts, water, and sugar which have been swallowed, and the peptones formed from the food, are being absorbed by the gastric mucous membrane. For the first two or three hours after ingestion of food the pylorus is firmly closed. At the end of this time it relaxes at intervals to allow the passage of the fluid parts of the gastric contents, which are spoken of at this period

as chyme. The passage of food through the pylorus goes on for seven or eight hours after the ingestion of food, and towards the end of this time larger lumps of undigested material are allowed to pass on into the duodenum.

In the duodenum the chyme comes in contact with the alkaline pancreatic juice and bile. The latter causes a precipitate in the chyme, consisting of bile acids, syntonin, and albumoses. This precipitate is dissolved later on by the further operation of these juices. Here the remaining digestive processes take place, the undigested proteids being dissolved, and the acid albumen and albumoses resulting from gastric digestion being converted into peptone and partially into leucin and tyrosin. Starches are changed into maltose and dextrin, and, under the further agency of the intestinal juice, into dextrose. The fats are partially split up and emulsified.

Throughout the whole of the small intestine active secretion and absorption are taking place, so that the amount of water in the intestinal contents in the lower part of the small intestine is about the same as in the upper part. The contents of the lower part acquire a distinct fæcal odour, from the indol and skatol produced by the action of putrefactive bacteria on the proteids of the food. In the large intestine the processes of absorption predominate over those of secretion; hence that part of the intestinal contents which has not been absorbed becomes less and less watery, and acquires the character of fæces, in which form it is periodically expelled from the body.

The fæces consist mainly of the indigestible residue of the food, or of substances which have been taken in too large quantities to be digested, and contain—

(*a*) Cellulose, woody fibre, elastic tissue, keratin, and remains of muscle-fibres, starch-grains, and fat.

They also contain—

(*b*) The unabsorbable part of the digestive juices, such as mucin, altered cholalic acid, bile-pigments, cholesterin.

(*c*) Indol and skatol, various forms of bacteria, and disintegrated epithelial cells from the intestinal mucous membrane.

Muscular Mechanisms of Digestion

Mastication

By movements of the lower against the upper jaw, the food is crushed between the teeth and reduced to a finely subdivided condition to fit it for the action of the various digestive fluids. The lumps of food are continually pushed between the teeth by movements of the tongue, cheek, and lips. The whole act is voluntary, although it is associated with and rendered easier by the saliva which is poured out into the mouth at the same time, and the secretion of which is excited reflexly.

The nerves supplying the muscles engaged in mastication are the fifth nerve (to jaw muscles), facial, and hypoglossal.

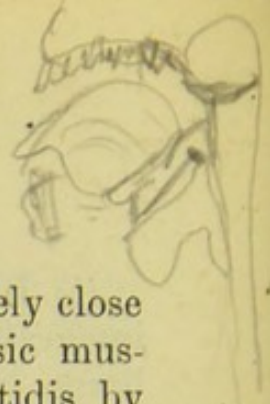
Deglutition

When the food is sufficiently subdivided, it is gathered by movements of the tongue against the hard palate into a bolus which rests on the dorsal surface of the tongue, whence it is propelled through the fauces into the œsophagus.

The movements of deglutition may be divided into three stages.

In the first stage the bolus is carried by the tongue through the isthmus faucium. This act is voluntary. As soon as the bolus has passed the isthmus, it is in a region common to the food and respiratory processes.

Here, by a series of rapid reflex movements, constituting the second stage, it is sent on into the beginning of the œsophagus. The movements are as follows :—The levator palati draws the soft palate upwards and backwards,



which with the contracted palato-pharyngei entirely close the nasal cavities. At the same time the intrinsic muscles of the larynx contract, closing the rima glottidis by approximating the vocal cords, while the entire larynx is drawn up behind the hyoid bone by the thyro-hyoid muscle, and the superior opening of the larynx is closed by the approximation of the arytænoid cartilages to the base of the tongue and the epiglottis. Then by the contraction of stylo-pharyngei and palato-pharyngei the upper part of the pharynx is drawn like a glove on a finger over the bolus of food, which is grasped by the superior constrictor, and passed on from this to the middle and inferior constrictors of the pharynx.

The third or œsophageal stage is slow and entirely involuntary. The bolus is forced down the œsophagus by a peristaltic wave of contraction passing down the muscular walls of this viscus.

The propagation of this contraction from one segment of the œsophagus to the next is a reflex act. Section of the vagus branches to the œsophagus arrest the wave, although it is not checked by section or ligature of the œsophagus itself. A peristaltic contraction is not necessary in most cases to secure the carrying of food to the stomach. If a series of acts of deglutition be made at intervals of a second, no peristaltic wave of contraction takes place till after the last mouthful has been swallowed. It seems that each act of deglutition inhibits the third stage of the preceding one, so that the food slides easily through a relaxed œsophagus.

The cardiac end of the stomach is normally contracted, but relaxes in the last stage of deglutition.

Nervous Mechanism of Deglutition

Deglutition is a complex reflex act, which is started by impulses from the mucous membrane of the fauces or upper part of the larynx. These travel up to the medulla

through branches of the fifth nerve and the superior laryngeal branches of the vagus.

Stimulation of the central end of the glosso-pharyngeal nerve checks any movements of deglutition that are in progress, and may excite vomiting.

The efferent channels are the hypoglossal nerve (to the tongue), the facial (to the myo-hyoid), the glosso-pharyngeal, vagus, and spinal accessory (to the muscles of the soft palate, pharynx, and œsophagus).

Movements of the Stomach and Intestines

The movements of the stomach are caused by slow peristaltic contractions of its muscular coats of unstriated fibre. They become very active about fifteen minutes after the ingestion of food, and more energetic still towards the end of gastric digestion. At first their sole action is to move the food about, keeping up a continuous current in the mass of food along the greater curvature from cardia to pylorus, and in the centre from pyloric to cardiac end, so that all parts of the food are brought in contact with the mucous membrane and gastric juice. Towards the end of gastric digestion, the wave of contraction as it reaches the pyloric end becomes intensified, and drives the more or less digested chyme through the pyloric orifice. The movements of the intestines are typically peristaltic, and consist of an annular wave of constriction passing along the whole length of the intestine from above downwards. Stimulation of the intestine at any point causes a double wave, passing upwards and downwards along the intestine from the excited point. The propagation of the contraction is independent of any extrinsic nerves. It is not known what part the plexus of nerves between the two layers of the muscular coat (Auerbach's plexus) plays in the propagation of the excitatory process.

Influence of Nerves

Stimulation of the peripheral end of the splanchnic, while peristaltic movements are going on, causes a constriction of the intestinal blood-vessels, and inhibits the intestinal contractions. If, while the intestines are quiescent, the peripheral end of the vagus be excited, movements are provoked; but this effect is only produced if the intestines contain some food. If the intestines are empty, as after long fasting, they are perfectly quiescent, and no movement can be excited by simple excitation of the vagus.

Section of the splanchnics either does not affect the movements, or renders them more active in consequence of the vascular engorgement produced. Energetic peristaltic movements are excited if the blood be made venous by asphyxia, or if the supply of oxygenated blood to the intestines be lowered in consequence of heart failure. Thus involuntary evacuations are a frequent result of fainting fits.

Defæcation

The residue of the undigested food and other matters forming the fæces are driven on by the peristaltic contractions of the large intestine, until they reach the sigmoid flexure. Here their progress is checked for a time by a circular band of muscle—the superior sphincter, which does not carry on the peristaltic wave. The mass of fæces accumulates in the sigmoid flexure, and is added to after each meal.

The anus is closed by two distinct muscles—the external sphincter, a thin sheet of striated muscle; and the internal sphincter, a thick ring of unstriated muscle surrounding the last three inches of the rectum, and about half an inch thick. The internal sphincter is normally in a condition of tonic contraction. This contraction, however, is not usually needed to keep back the fæces, since any that

have escaped past the sigmoid flexure are retained in the upper part of the rectum by a transverse fold of mucous membrane. They are also kept back by the acute angle that the last part of the rectum makes with the preceding part, and by the contractions of the perinæal muscles which maintain this curvature and empty the lower part of the bowel.

Defæcation is normally started by a voluntary act, although it may take place involuntarily, as is shown by the fact that it occurs in a dog whose spinal cord has been divided in the dorsal region.

The steps of normal defæcation are as follows:—The glottis being closed, a forcible expiratory effort of the abdominal muscles is made. The perinæal muscles being relaxed at the same time, the lower part of the rectum is straightened, and a portion of the contents of the sigmoid flexure is forced down into the lower part of the rectum. The presence of a foreign body in the lower part of the rectum irritates the mucous membrane, and excites reflexly the rest of the act. Strong peristaltic contractions take place along the whole of the descending colon (sigmoid flexure and rectum), while both sphincters are relaxed, thus forcing out the contents of the bowel. The last section of the rectum at the close of the act is emptied by a forcible contraction of the levator ani and the other perinæal muscles.

The carrying out of this reflex act is dependent on the integrity of a certain part of the lumbar spinal cord. If this 'centre' be destroyed, the tonic contraction of the sphincter muscles disappears. This centre may be either excited to increased action, or be inhibited by peripheral stimulation of various nerves, or by emotion, such as fear. Application of warmth to the region of the anus causes reflex relaxation of the sphincter; application of cold increases its tonic contraction.

Vomiting

Vomiting is a reflex act which lies on the borderland beween physiological and pathological processes. It is at any rate the normal reaction of the stomach to an irritant. The act of vomiting is generally preceded by a feeling of nausea, copious salivation, and retching. Retching is a violent inspiration while the glottis is kept firmly closed, so that air is drawn into the œsophagus and distends it. This stage is followed by contraction of the fibres radiating from the cardiac end of the œsophagus, which opens and allows gas to escape. The head being bent forward and the mouth widely opened, so as to straighten the œsophagus as much as possible, and the glottis kept closed, a forcible contraction of the abdominal muscles occurs, attended by contraction of the muscular wall of the stomach itself, which forces out its contents.

Vomiting can be accomplished by contraction of the stomach alone, or of the abdominal muscles alone; for it may be excited in an animal by injection of apomorphin even after its stomach has been replaced by a bladder, or its abdominal muscles and diaphragm paralysed by section of the intercostal and phrenic nerves. Vomiting may be excited reflexly by irritation of the palate, fauces, stomach, peritoneum, or, indeed, of any abdominal organ. It may also be excited from the brain, in consequence of emotions or evil smells. The co-ordination of the movements of vomiting is dependent on a centre in the medulla—'vomiting centre'—not far from the respiratory centre. The various emetics may cause vomiting, either reflexly by irritation of the stomach (mustard, salt water, zinc sulphate), or directly by their action on the centre, *e. g.* apomorphin.

CHAPTER VIII

RESPIRATION

THE processes of external respiration, namely, the taking up of oxygen and the giving off of CO_2—the product of the union of the oxygen with the carbon of the foodstuffs,—are effected in the lungs, which are built up in the following way. The trachea or windpipe, a wide tube about $4\frac{1}{2}$ inches long, divides below into two main branches—bronchi; and these subdivide again and again, becoming gradually smaller. The terminal ramifications or bronchioles open into rather wider parts—the infundibula, the walls of which are beset with a number of minute cavities, the alveoli. The larger tubes are kept patent by rings or plates of cartilage in their wall. The smaller tubes have no cartilage, their walls being composed of fibrous and elastic tissue and a coating of unstriated muscular fibres, which are able by their contraction to occlude the passage. The whole system of tubes is lined with a layer of epithelium—ciliated columnar in the trachea, bronchi, and bronchioles, and cubical over the parts of the infundibulum not occupied by air-cells.

The alveoli are the special respiratory parts of the lung. Their walls are composed of connective tissue containing a large number of elastic fibres, and are covered internally by a single layer of extremely thin, large, flattened cells. The alveoli are closely packed together, so that in a section of the lung an alveolus is seen to be in contact with others on all sides. Immediately below the squamous epithelium ramify blood-capillaries derived from the pul-

monary artery. These form a close network, and the blood in them is in close proximity to air on all sides, being separated from the air in the alveoli only by the thin endothelial cells of the capillary wall and the flattened cells lining the alveoli.

The lungs in their development grow out from the front part of the alimentary canal into the front part of the body-cavity on each side—the pleural cavity. The surrounding body-walls become strengthened by the formation of the ribs, so that the lungs are suspended in a bony cage-work, the thorax. Their outer surface is covered with a special membrane, the *pleura*, which is reflected to the wall of the thorax from the roots of the lungs, and completely lines the cavity in which they lie. The surface of the pleura facing the pleural cavity is lined with a continuous layer of flattened endothelial cells, and is kept constantly moist by the secretion of lymph into the cavity. Thus, being only attached to the thorax where the bronchi and great vessels enter, the lungs are able to glide easily over the inner surface of the thorax, with which under normal circumstances they are in intimate contact.

A constant renewal of the air in the lungs is secured by movements of the thorax, which constitute normal breathing. With inspiration the cavity of the thorax is enlarged, and the lungs swell up to fill the increased space. The capacity of the air-passages of the lungs being thus increased, air is sucked in through the trachea. The movement of inspiration is followed by that of expiration, which causes diminution of the capacity of the thorax and expulsion of air.

The expiration follows immediately upon inspiration. At the end of expiration there is normally a slight pause. The number of respirations in the adult is about 17 or 18 a minute. This is, however, much affected by various conditions of the body, and also by the age of the individual. Thus a new-born child breathes about 44 times a minute, a child of five about 26 times, a man of twenty-

five about 16, and of fifty about 18. The frequency is increased by any muscular effort, so that even standing up increases the number of respirations compared with a person lying down. These movements are much affected by psychical activity ; they are to a certain extent under the control of the will, although, as we shall see later, they can occur in an animal deprived of its brain, and we know they are normally carried out without any special act of volition. We can breathe fast or slow at pleasure, and can even cease breathing for some time. It is impossible, however, to prolong this respiratory standstill for more than a minute ; the need of breathing becomes imperative, and against our will we are forced to breathe.

With every inspiration the cavity of the thorax is enlarged in all dimensions, from above downwards by the contraction of the diaphragm, and in its transverse diameters by the movements of the ribs.

The diaphragm is a sheet of muscle separating the cavity of the chest from that of the abdomen. This sheet, which is tendinous at the centre, is arched, the convex side protruding up into the thorax, forming thus a dome-like boundary of the peritoneal cavity. With every contraction the tendinous centre is drawn down, so that the dome becomes flatter and the cavity of the thorax is enlarged. In this contraction the diaphragm presses on the contents of the abdomen, so that we see a swelling up of the abdomen with each inspiratory movement.

The enlargement in the other diameters is effected by an elevation of the ribs. Each pair of corresponding ribs, which are articulated behind with the spinal column and in front with the sternum, forms a ring, directed obliquely from behind downwards and forwards. With each inspiratory movement the ribs are raised, the obliquity becomes less, and the horizontal distance between sternum and spinal column is therefore increased. Moreover the ribs from the first to the seventh increase in length from above downwards, so that when they are raised, the sixth

rib, for instance, occupies the situation previously taken by the fifth, and the transverse diameters of the thorax at this height are increased. With each inspiration there is a rotation of the ribs. In the expiratory condition they are so situated that their outer surfaces are directed not only outwards, but also downwards. As they are raised by the inspiratory movements, they rotate on an axis directed through the fore and hind ends of the rib, so that their outer surfaces are turned directly outwards. In this way a certain enlargement of the thoracic cavity is produced. As the thorax is raised there is always some stretching of the rib cartilages.

In expiration the processes are reversed, and the cavity of the thorax is diminished in all these dimensions.

The movements of the thorax are effected by means of muscles. Inspiration is performed by the following muscles :

The diaphragm, which is the most important, and almost suffices alone to carry out quiet respiration.

The external intercostal muscles, which shorten and so raise the ribs.

The levatores costarum and serratus posticus superior.

These muscles are the only ones normally engaged in carrying out inspiration. When, in consequence of muscular exertions, or from any other cause, the inspiratory efforts become more forcible, a large number of accessory muscles are brought into play. These are—

The scaleni,
Sterno-mastoid,
Trapezius,
Pectoral muscles,
Rhomboids, and
The serratus anticus major.

Normal expiration is chiefly effected passively. When the inspiratory muscles cease to contract, the lungs, which were stretched by the previous inspiration, contract by virtue of the elastic tissue they contain, and the thorax itself

sinks by its own weight, and by the elastic reaction of the stretched costal cartilages. Probably under normal circumstances the internal intercostal muscles also contract with each expiration.

In forced expiration a large number of muscles may take part—such as the serratus posticus inferior, and the muscles forming the wall of the abdomen, *i. e.* the rectus, obliquus, and transversus abdominis muscles.

As the lungs expand with each inspiration, their position changes somewhat in relation to the thoracic wall. The roots, the hinder borders, and the apices of the lungs remain nearly stationary. The front parts move downwards and inwards, so that their inner borders in front approach one another. By percussing the chest, it may be easily made out that the resonant area, corresponding to the parts where the lungs are in contact with the thoracic walls, increases with each inspiration, and diminishes with each expiration.

Even at the end of expiration the lungs are in a stretched condition. This is shown by the fact that if in an animal or in the corpse an opening be made into the pleural cavity, air rushes into the opening and the lungs collapse, driving a certain amount of air out through the trachea. Since, then, the lungs are always tending to collapse, it is evident that they must exert a pull on the thoracic wall. This pull of the lungs gives rise to a *negative pressure* in the pleural cavity. If we connect a mercurial manometer with the pleural cavity, we find this pull of the lungs amounts in the corpse to 6 mm. of mercury. If the lungs are fully distended, as after full inspiration, the elastic forces are more brought into play, and the negative pressure in the pleura may amount to 30 mm. Since the lungs are always tending to collapse, it is apparent that respiration becomes impossible directly free openings are made into the pleural cavities on both sides. With each inspiratory movement air rushes in through these openings, so that the thoracic movements can no longer exert any

influence on the volume of the lungs. The negative pressure in the thorax is diminished by any factor decreasing the elasticity of the lung tissue. Thus in an old man, where the elastic tissue is degenerated and the alveoli are enlarged, giving rise to the condition known as emphysema, the lungs may collapse only slightly or not at all on opening the chest. The lungs do not collapse on making an opening in the chest of a new-born mammal; but this is owing to the fact that the lungs completely fill the thorax in the expiratory position, and it is only later that with the growth of the ribs the thorax gets, so to speak, too large for the lungs, which are therefore stretched to fill it.

The force exerted by the inspiratory muscles is nearly all spent in overcoming the elastic resistance of the lungs and costal cartilages. A free access of air is provided for by contractions of certain accessory muscles of respiration. With each inspiration the glottis is widened by abduction of the vocal cords. When the glottis is observed by means of the laryngoscope, a rhythmical separation and approximation of the vocal cords are observed, synchronous respectively with inspiration and expiration. When inspiration is laboured, the alæ nasi are dilated by the action of the dilatator nasi. This movement of the nostril, which is constant in many animals, becomes very prominent in children suffering from any respiratory trouble.

If a manometer be connected with one of the nostrils, so as to register the pressure in the air-cavities, it is found that there is a negative pressure of − 1 mm. Hg. with inspiration, and a positive pressure of 2 or 3 mm. with expiration. With forced inspiration the negative pressure may amount to − 57 mm. Hg., and with forced expiration there may be a positive pressure of + 87 mm.

Under no circumstances can we by forced expiration empty the lungs of air. At the end of the most forcible expiration, if the pleura were perforated, the lungs would collapse and drive more air through the trachea. When breathing quietly a man takes in and gives out at each

breath about 500 c.c. of air. This amount is known as the *tidal air*. By means of a forcible inspiratory effort it is possible to take in about 1500 c.c. more (*complemental air*). At the end of a normal expiration a forcible contraction of the expiratory muscles will drive out about 1500 c.c. more (*supplemental air*). These three amounts together constitute the 'vital capacity' of an individual. This total may be determined by means of the instrument known as the spirometer, which is merely a small gas meter with a gauge, by which the amount of air in it can be at once read off. The person to be tested fills his lungs as full as possible, and then expires to the utmost into the spirometer. The air left in the lungs after the most vigorous expiration (*residual air*) amounts to about 2000 c.c.

Of the 500 c.c. of tidal air taken in at each inspiration, only a certain part reaches the alveoli, part being required to fill the air-tubes, trachea, bronchi, and bronchioles which lead to the air-cells. The volume of the air-tubes has been reckoned to amount to 140 c.c., so that of the 500 c.c. about 360 c.c. reach the alveoli. For the same reason the expired air represents the air from the alveoli (360 c.c.) diluted with 140 c.c. of air which has remained in the air-tubes and undergone very little change, other than the elevation of temperature and saturation with aqueous vapour. We have, therefore, to allow for this air contained in the so-called 'dead space' of the lungs when we seek to arrive at the composition of alveolar air from an analysis of expired air.

Nervous Mechanism of Respiration

We thus see that for the normal carrying out of respiration a complicated series of co-ordinated movements is necessary. And this is not all. The respiratory movements must be adjusted in rhythm and strength to the varying

needs of the organism. When the animal is performing active work, when the muscles of the body are contracting vigorously and producing large quantities of carbon dioxide, the respiratory movements must be also quickened and deepened in order to provide for the due aëration of the blood, and the discharge of the excess of carbon dioxide produced.

This co-ordination of the activities of the respiratory muscles and their adaptation to the varying needs of the organism are brought about through the agency of the nervous system, and in particular by a circumscribed space situated in the medulla oblongata.

If a section be made just above the pons dividing the brain from the lower parts of the central nervous system, it will be observed that the respiratory movements go on normally.

If another section be made at the lower border of the medulla, the diaphragm and ribs will be motionless, but respiratory movements may be still observed to take place in the facial muscles and larynx. These experiments show that the part of the nervous system presiding over the movements of respiration is situated somewhere between the two sections. This 'centre' can be localised still more exactly. Injury to a small portion of the medulla in the immediate neighbourhood of the nuclei of the vagus nerves, and just below the vaso-motor centre, causes total cessation of respiratory movements and death of the animal. Hence this part of the nervous system was called by Flourens, its discoverer, the *nœud vital*.

In new-born animals a few abortive attempts at respiration are sometimes observed even after destruction of this centre; and it is therefore supposed that there are subsidiary centres in the cord controlled and regulated by the centre in the medulla. Their independent activity, however, is very slight, and is not observed at all in older animals.

The question now arises whether the activity of this centre in the medulla may be regarded as automatic or reflex; that is to say, do the rhythmic discharges pro-

ceeding from it depend merely on local changes taking place in the centre, induced perhaps by changes in the surrounding lymph or blood, or on a rhythmic or continuous excitation of the centre by stimulation of some afferent nerve? There is no doubt that the centre may act automatically. If the vagus nerves be cut and the spinal cord divided just below the medulla, respiratory movements of the alæ nasi are seen to continue and to grow more pronounced as the blood becomes venous in consequence of the cutting off of the chief respiratory muscles from the medullary centre.

If, the nervous centres being intact, the supply of oxygen to the centre be interfered with by ligature of the carotid and vertebral arteries, or by extensive loss of blood, the respiratory movements increase in strength and frequency. And this occurs even when the vagus nerves—the sensory nerves from the lungs—are cut. This increased respiration, due to deficient oxygenation of the centre, is spoken of as *dyspnœa*.

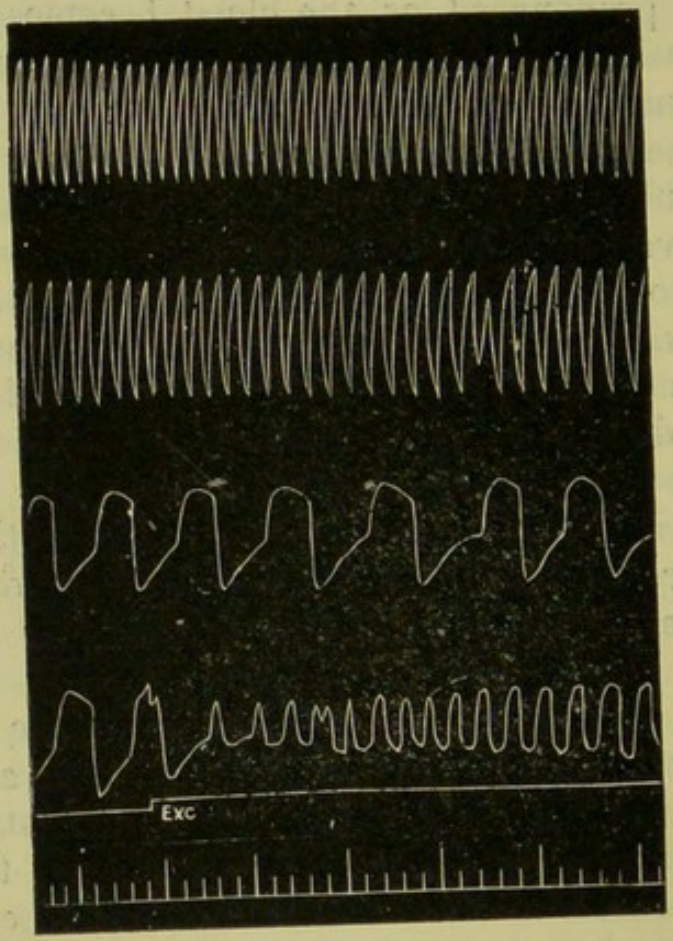
Dyspnœa may also be produced by increasing the activity of the centre, and therefore its demand for oxygen, by warming the blood in the carotid arteries on its way to the brain.

Although, however, the centre has thus the power of automatic activity, we have reason to believe that this power is never exerted under normal circumstances, but that, when the animal is breathing quietly, the whole respiratory process is a series of reflex actions, each inspiration exciting, by means of afferent fibres in the vagus, a change in the centre which causes it to send out expiratory impulses, and each expiration bringing about in the same way the following inspiration.

In studying the nervous mechanism of respiration, it is necessary to have some accurate method of recording the respiratory movements. They may be registered by means of a tambour applied to the chest, communicating with another tambour provided with a lever, which is

arranged to write on a blackened surface; or a side tube to a cannula in the trachea may be connected with the registering tambour. In the first case, movements of the thorax are registered; in the second, changes of intra-pulmonary pressure. These methods are obviously useless when it is wished to study the effects of artificial distension or collapse of the lungs. In this instance we may use the ingenious method described by Head. In the rabbit a slip of the diaphragm on

FIG. 82.



Tracings of respiratory movements.—A. Normal. B. After division of one vagus. C. After section of both vagi. D. Both vagi cut. The central end of one vagus stimulated with weak induced current at Exc.
Lower line = time-marking, indicating seconds. (From Waller.)

either side of the ensiform cartilage is so disposed that the end of it may be freed and attached by a thread to a lever without injury to its blood- or nerve-supply. It is found that this slip contracts synchro-

nously with the rest of the diaphragm, so that it serves as a sample of the diaphragm, the contractions of which may be recorded uninfluenced by passive movements of the chest-wall or artificial increase of intra-pulmonary pressure.

If, while the respiratory movements are being recorded in one of the aforementioned ways, both vagi be divided,* a marked change in the respiratory rhythm is at once seen (Fig. 82). The respiratory movements become less frequent and are increased in amplitude. If now the central end of one of the vagi be stimulated with an interrupted current, the respiration may be quickened (as in the experiment represented here), or, as is more commonly the case, the inspiratory movements are increased at the expense of the expiratory, so that finally a condition of inspiratory standstill is produced, and the slip of the diaphragm enters into prolonged contraction.

With a very weak stimulus it is sometimes possible to produce augmentation of the *expiratory* movements. This effect, however, may be more strikingly brought about by stimulation of the central end of the superior laryngeal nerve. Excitation of this nerve produces first an inhibition of inspiration, so that the respiratory muscles come to a standstill in the position of expiration, and then a forcible contraction of the expiratory muscles takes place. This illustration of the presence of expiratory fibres in the superior laryngeal nerve is not confined to laboratory experience, but is constantly occurring in everyday life. The superior laryngeal nerve supplies sensory fibres to the mucous membrane of the glottis, and we know that

* The division of the vagi is best effected by putting them on a hooked copper wire, of which the upper end is inserted in a freezing mixture. In this way complete functional division of the nerves is obtained without any excitation. If the nerves be cut, a certain amount of stimulation takes place in consequence of the closure of the demarcation current produced by the cross-section.

the slightest irritation of these fibres—the presence of a crumb or a particle of mucus—causes forcible expiratory spasms, with spasmodic closure of the glottis, which we term a cough.*

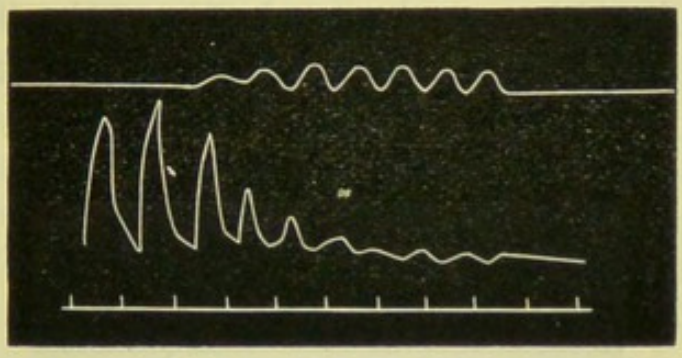
So we see that the vagus nerve contains two kinds of afferent fibres, or at any rate afferent fibres with two distinct functions. Stimulation of the one kind stops inspiration and produces expiration; stimulation of the other stops expiration and produces inspiration.

Since section of both vagi causes slowing of respiration, it is evident that, under normal circumstances, impulses must travel up the vagi from the lungs, which exert an augmentory influence on the respiratory centre and quicken respiration. The respiratory movements cause an alternate distension and contraction of the lungs, and it has long been thought that it is these changes in the volume of the lungs which start the accelerating impulses that travel up the vagus nerves. To test the truth of this hypothesis it is necessary to study the two phases of respiration separately; that is, to see first the result on the respiratory impulses of repeated distension of the lungs, and secondly of a sudden collapse or a contraction caused by sucking air out of the lungs. The first mode of experiment, when air is driven repeatedly into the lungs, is spoken of as *positive* ventilation; and the second, when air is sucked repeatedly out of the lungs, as *negative* ventilation. In these experiments it is advantageous to employ Head's method of registering the diaphragmatic movements. If, in a rabbit breathing quietly, air be repeatedly blown into the lungs, the inspiratory movements, as evidenced by the contraction of the diaphragm, are gradually knocked

* It must not be imagined, however, that the fibres of the superior laryngeal nerves are concerned in the reflex maintenance of the normal respiratory rhythm. They are cited here merely because the result of their stimulation resembles that which would be caused by stimulation of the analogous expiratory fibres which run in the trunk of the vagus from the *lungs* to the respiratory centre.

down, till finally the animal is in a condition in which no inspiratory movements whatever are made (Fig. 83), or the diaphragmatic standstill may be followed by a strong

FIG. 83.

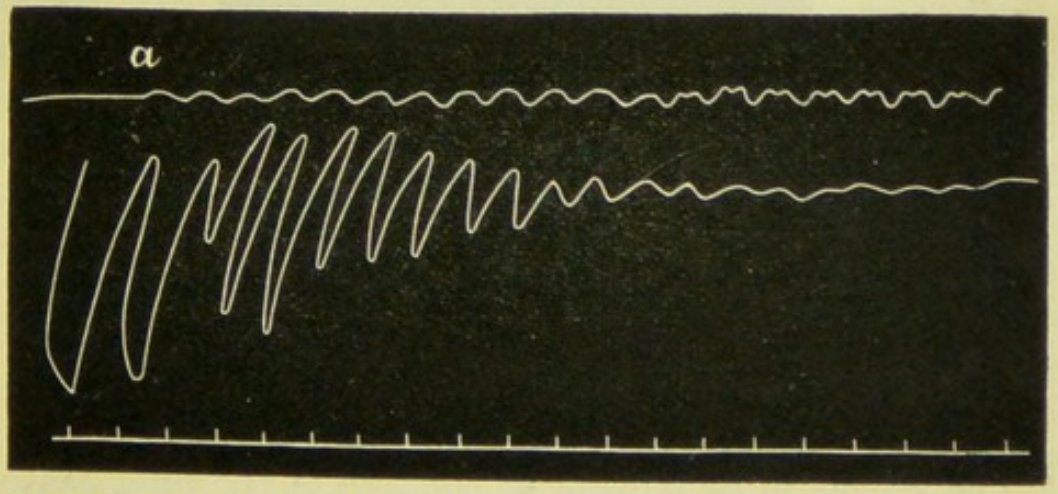


Positive ventilation (Head). Under the influence of positive ventilation, the inspiratory contractions of the diaphragm become less and less till they disappear completely.

contraction of the expiratory muscles. Thus distension of the lungs has the same effect as stimulation of the superior laryngeal nerve in stopping inspiration and producing expiration.

If, on the other hand, air be sucked out of the lungs at

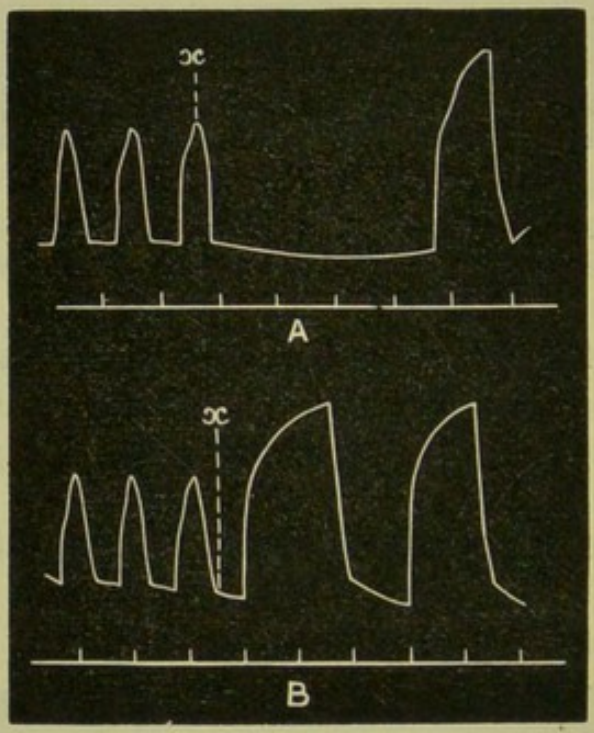
FIG. 84.



Negative ventilation (Head). At *a* negative ventilation was commenced. The expiratory relaxation of the diaphragm is seen to become more and more incomplete, until it finally enters into continued contraction.

regular intervals (negative ventilation), the movements of the diaphragm are amplified, and it does not relax completely between each individual respiration. The relaxation becomes more and more incomplete, until finally the diaphragm enters into a condition of continued contraction, which may last for several seconds (Fig. 84). Thus collapse of the lung inhibits expiration and augments inspiration.

Fig. 85.



Effects of distension—collapse of lung. Both curves are described by a lever attached to a slip of the diaphragm of a rabbit. A contraction of the diaphragm (inspiration) raises the lever; during relaxation of the diaphragm the lever falls.
In A, the trachea is closed at x, the height of inspiration; a pause follows, during which the lever gradually sinks until an inspiration (a very powerful one) sets in.
In B, the trachea is closed at the end of expiration, x; there follow powerful inspirations. (From Foster.)

The effects of distension or collapse of the lung may be still more readily shown by simply closing the trachea at the end of inspiration or of expiration. The results of such an experiment are shown in Fig. 85.

These experiments throw complete light on the quickening action of the vagus on respiration. Normal respiration is a series of reflex acts. Each inspiratory movement causes an expansion of the lung, which in its turn stimulates the vagus nerve-endings, inhibiting the movement which has given rise to the stimulus, and causing the ensuing expiratory movement. The collapse of the lung attending expiration acts like the negative ventilation in the experiment above-mentioned in stimulating the inspiratory nerve-endings of the vagus, and the impulse thus produced acting on the medullary centre checks the expiratory and hurries on the inspiratory movement. In this way, under normal circumstances, the activity of the respiratory centre is brought into play, not by the venosity of the surrounding blood, but reflexly through the agency of the vagi.

The important part played by the vagi in the regulation of normal respiration is shown still more strikingly if the respiratory centre in the medulla be separated from the higher parts of the brain before the section of the vagi is carried out. Separation of the medulla from the higher parts of the brain, as by a section just behind the corpora quadrageminа, has practically no influence on the respiratory rhythm. If, now, both vagi be divided, the normal respiratory movements cease entirely, being replaced by a series of inspiratory spasms, each of which lasts several seconds, and is followed by a pause of half to one minute duration. These spasms are inadequate for the proper oxygenation of the blood. They become gradually less and less frequent, and the animal dies in about half an hour of asphyxia. We must conclude, therefore, that the respiratory centre with the help of the vagi is able to carry out normal respiratory movements. If both vagi are cut, these impulses arrive at the centre from the higher parts of the brain regulating its activity, and enabling it to carry out modified but sufficient respiratory movements. Removed from both these sources of afferent impulses, the centre only dis-

charges a series of spasms, which are totally inadequate for the removal of the blood gases, so that the animal dies.

We may summarise these results as follows:

Respiratory centre with vagi—normal respiration.

Respiratory centre with brain—modified respiration.

Respiratory centre alone—inadequate spasmodic contractions of respiratory muscles, and death of animal.

Apnœa.—If positive and negative ventilation be used together, so that air is blown into and sucked out of the lungs at a rate quicker than the animal's respiratory rhythm, both inspiratory and expiratory processes are inhibited, and a standstill of respiration ensues. This condition is called apnœa. It is shown to be chiefly reflex in origin by the fact that an apnœic cause may be observed after artificial respiration for a short time with inert gases, such as hydrogen or nitrogen. The pause, however, does not last so long as when air or oxygen is employed, since in the former case the blood becomes so venous that the stimulation of the centre thereby produced overcomes the effects of reflex excitation, and a violent respiratory movement ensues.

Asphyxia.—This term is applied to those phenomena which occur in animals whose respiratory centre is deprived of oxygen. This deprivation may be effected in various ways, by ligature or plugging of the trachea, or by opening both pleural cavities so that the respiratory movements no longer dilate the lungs, or by ligature of the vessels going to the brain, or extreme artificial anæmia through bleeding. The phenomena may be divided into three stages.

1. In the first stage the respiratory movements are increased in rhythm and amplitude. Gradually the expiratory movements become increased out of all proportion to the inspiratory, and this stage merges into—

2, which consists of expiratory convulsions, in which almost every muscle in the body is involved.

3. At the end of the second minute the expiratory con-

vulsions cease almost suddenly, and give way to slow, deep inspirations. With each inspiratory spasm the animal stretches himself out and opens his mouth widely, as if gasping for breath. The whole stage is one of exhaustion. The pupils are widely dilated and the animal is perfectly insensitive, being unaffected by the strongest sensory stimulation. The pauses between each inspiration become longer and longer, till at the end of four or five minutes the animal takes his last breath.

Chemistry of Respiration

The respiratory movements, with their complicated nervous mechanism, are but means to an end. They enable the blood to take up oxygen and give off carbon dioxide on its way through the lungs, so that the blood reaches the tissue elements prepared to supply them with oxygen and to take up carbon dioxide, the product of their destructive metabolism. We have now to study the conditions that regulate gaseous interchange in the lungs and in the tissues.

As we should expect, analysis shows marked differences in the constitution of inspired and expired air. Inspired air—that is to say, ordinary atmospheric air—consists of a mixture of oxygen and nitrogen, with a very small trace of carbon dioxide gas. Its composition is—

Oxygen	20·96 vols. per cent.
Nitrogen	79 „ „
Carbon dioxide . . .	·04 vol. „

It also contains a variable amount of watery vapour, but is very rarely saturated with it. Its temperature of course varies with the season of the year.

The chief change that occurs in respired air is a decrease of the oxygen, and a corresponding increase of carbon dioxide. Its average composition in man is—

Oxygen	16·6 vols. per cent.
Nitrogen	79 „ „
Carbon dioxide . . .	4·4 „ „

It is, moreover, nearly saturated with watery vapour, which on a cold day condenses in a cloud of steam with every expiration. Its temperature, which is very slowly affected by that of the external air, is a little below the normal body temperature (about 36° C.). If the inspired air is above the body temperature, the expired air is found to be cooled down to the temperature of the body. If the inspired and expired air be carefully measured in a dry condition at the same temperature, it will be found that the volume of expired air is about $\frac{1}{50}$ less than that of the inspired. The conversion of oxygen into carbon dioxide would not of course cause any change in the volume of the gas ; for one molecule of oxygen (O_2) would, on combining with carbon, give rise to one molecule of carbon dioxide (CO_2), which at the same temperature and pressure would occupy exactly the same volume. But it must be remembered that carbon is not the only element which leaves the body in an oxidised condition. Fats, for example, contain a number of unoxidised atoms of hydrogen, which in the metabolic processes of the body are fully oxidised to be excreted as water. A certain amount of oxygen, too, is used up in the oxidation of the nitrogenous elements of food, which are excreted chiefly as urea. Hence we should expect to find this apparent loss of oxygen greater in carnivora, whose food consists mainly of proteids and fats, than in herbivora, which feed principally on carbohydrates. This, indeed, is found to be the case.

The quotient $\frac{CO_2 \text{ expired}}{O_2 \text{ inspired}}$ is known as the *respiratory co-efficient.* From what has been said, it is evident that it can never be greater than one, if the observation be extended over a fairly long period, and that it is less in carnivora than in herbivora. It must be remembered,

however, that, under the influence of muscular exertion, the amount of carbon dioxide may be temporarily so largely increased as to exceed the quantity of inspired oxygen.

As was shown on p. 257, only a certain percentage of the 500 c.c. of tidal air reaches the alveoli, 100 to 140 c.c. being required to fill the trachea and bronchial tubes. Hence the alveolar air must contain more carbon dioxide and less oxygen than the tracheal air ; and it is found that, if we take the air from the alveoli instead of that expired through the mouth or nose, the differences between it and the inspired air are much more pronounced.

Respiratory Changes in the Blood

From 100 volumes of either venous or arterial blood we can, by means of the mercurial pump, remove about sixty volumes of gas. The composition of this gas varies considerably in venous, but not so much in arterial blood.

The average composition of the gases of dog's blood is given in the following table :

From 100 vols.	May be obtained		
	Of oxygen.	Of carbon dioxide.	Of nitrogen.
Of arterial blood	20 vols.	40 vols.	1 to 2 vols.
Of venous blood	8 to 12 vols	46 „	„ „

Measured at 760 mm. and 0° C.

Thus the analyses of expired air and of the gases of the blood show clearly that the latter, in its passage through the lungs, takes up oxygen and gives off carbon dioxide. In the tissues the reverse process takes place, so that the venous blood returns to the lungs deprived of a portion of its oxygen, and loaded with CO_2. In studying the mechanism by which this gaseous interchange takes place, it will be convenient to treat the two gases separately, since their

behaviour in the blood and tissues seems to be largely independent of each other.

The oxygen in the blood is nearly entirely taken up by the hæmoglobin of the red blood-corpuscles. The serum or plasma of the blood cannot take up more oxygen than the same bulk of water—less than 1 per cent. at the ordinary atmospheric pressure and temperature. On the other hand, if from a given specimen of blood we extract the hæmoglobin and dissolve this in water, we find that the pure hæmoglobin is able to take up as much oxygen as the original blood on being exposed to or shaken with pure oxygen or air.

What is the condition of the oxygen in the blood? Is it simply dissolved, or does it enter into chemical combination with the hæmoglobin?

It is well known that, when a gas is dissolved by a liquid, the amount of gas taken up by the liquid varies directly as the pressure of the gas. Thus if one hundred volumes of water at 0° C. would dissolve four volumes of oxygen at a pressure of one atmosphere, it would dissolve eight volumes at a pressure of two atmospheres. At a pressure of three atmospheres the amount dissolved would be twelve volumes. If the liquid be removed from an atmosphere of oxygen at a pressure of two atmospheres to an atmosphere at a pressure of one, oxygen will be given off by the water until equilibrium is established between it and the surrounding medium; the water will then only contain four volumes per cent. At a pressure of half an atmosphere the amount dissolved will be two volumes. In this case it makes no difference to the amount of oxygen dissolved, whether the oxygen is alone or whether it be mixed with some other gas. Thus the amount dissolved will be the same, whether the water be exposed to pure oxygen at a pressure of 380 mm. Hg., or to a mixture of equal volumes of oxygen and nitrogen at a pressure of 760 mm. Hg. In each case the *partial pressure* or *tension* of the oxygen is the same, and therefore the same amount is dissolved.

When equilibrium is established between a gas and a liquid, so that no gas is being taken up or given off by the liquid, the tension of the gas dissolved in the fluid is equal to that in the gaseous medium. On this fact is based the method of determining the tension of a gas dissolved in liquid. The liquid is brought into contact with gaseous mixtures containing various proportions of the gas in question. It is found that the liquid gives off gas to some of these mixtures, and from others takes up gas. By making various experiments a gaseous mixture will be found with which the liquid is in equilibrium. If we know beforehand the amount of gas in this gaseous mixture we know its tension, and therefore the tension of the gas in the liquid.

One grm. of crystallised hæmoglobin can absorb about 1·5 c.c. of oxygen. If a solution of this oxyhæmoglobin be subjected in an air-pump to gradually diminishing pressure at the temperature of the body, it will be found that very little oxygen is given off until the partial pressure of the oxygen is diminished to about 60 mm. Hg. At this point a large evolution of gas takes place, so that the hæmoglobin contains very little oxygen. The same observation may be made in a reverse direction. If a solution of reduced hæmoglobin be exposed to gradually increasing pressures of oxygen, it will be found that the greatest absorption takes place between 40 and 60 mm. Hg. After this point the oxygen is very slowly absorbed, and the further absorption goes on in proportion to the partial pressure of oxygen.

Since, then, there is no direct proportion between the partial pressure of the oxygen and the amount absorbed, it is evident that the oxygen combines with hæmoglobin to form an unstable chemical compound, and that this is not a mere question of solution. This is further proved by the fact that we can displace the oxygen (O_2) from the oxyhæmoglobin by equivalent amounts of CO or NO.

A knowledge of these facts makes it easy to understand

how the oxygen is taken up by the blood as it circulates round the pulmonary alveoli. Arterial blood, such as that which fills the pulmonary vein and the systemic arteries, is very nearly saturated with oxygen, and will only take up about 1 per cent. more on shaking it with air at the body temperature. Venous blood requires 8 to 12 volumes per cent. of oxygen to saturate it; but we have already mentioned above that, at a tension of 60 mm. oxygen, the blood becomes nearly saturated. The tension of oxygen in the alveoli is considerably above this. In the trachea the tension of oxygen is about $\frac{1}{6}$ of an atmosphere (since the air here contains 16 volumes per cent.), and the tension in the alveoli will be only a little lower than this. If we take the oxygen tension in the alveoli at $\frac{1}{7}$ of an atmosphere,* it will still be something over 100 mm. Hence the venous blood brought to the alveoli by the pulmonary artery will, on there coming into intimate contact with the atmosphere, take up oxygen from it to saturation, or to a point not far removed from it.

The blood, thus laden with oxygen, travels to the left side of the heart, and from there is sent through the arteries to all parts of the body. It must be remembered that neither in the lungs nor in the tissues does the hæmoglobin come in actual contact with the source of the oxygen, nor with the cells which it is to supply. In both cases the interchange is effected through the intermediation of the plasma, and, in the tissues, of the lymph as well. Since the tissue-elements are constantly using up oxygen, which they build up into their living protoplasm, they absorb any oxygen that is present in the surrounding lymph. There is, in consequence, a descending scale of oxygen tensions from red blood-corpuscle through plasma, vessel-wall, lymph, and tissue-element. The cell draws from the lymph, the lymph from the plasma, so that the oxygen tension in the plasma sinks. This has the same effect as if we put the

* The oxygen tension in the alveoli has been reckoned as about 12·6 per cent. to 13·5 per cent. of an atmosphere.

red corpuscles in a mercury pump and lowered the pressure of gas. The immediate result is a giving off of oxygen, which is taken up by the plasma, to be in turn passed on to the lymph and the tissue-cell.

Under normal circumstances a blood-corpuscle never stays long enough in the proximity of the tissues to lose its whole store of oxygen. If, however, the further supply of oxygen to the blood be prevented, as in asphyxia, the last traces of oxygen disappear from the blood. The enormous avidity of the tissues for oxygen is shown by the following experiment (Ehrlich). If a saturated solution of methylene blue be injected into the circulation of a living animal and the animal killed ten minutes later, it is found on first opening the body that most of the organs present their natural colour, although the blood is a dark blue colour. On exposure to the atmosphere all the organs acquire a vivid blue colour. The avidity of the tissues for oxygen has been so great that they have been able to decompose the methylene-blue molecule, forming a colourless reduction-product, which on exposure to the air takes up oxygen again and re-forms methylene blue. If then the tissues are able to tear away the oxygen from a comparatively stable body like methylene blue, it is easy to understand their power of reducing oxyhæmoglobin, which is so unstable that it is decomposed by simple physical means such as exposure to a vacuum.

It was long debated whether the chief processes of oxidation take place in the blood or in the tissues. Our experiences with muscle would alone serve to convince us that in some tissues, at any rate, processes of oxidation take place, and the methylene-blue experiment shows that these processes of oxidation are intense in all the chief organs of the body. It has been found, moreover, that it is possible to keep a frog alive after substituting normal saline solution for his blood if he be placed in absolutely pure oxygen, and that in this case, indeed, the metabolism of the animal goes on as actively as before. As the frog

has no blood, it is evident that his metabolic processes, consisting of the taking up of oxygen and the giving out of carbon dioxide, must have their seat in the tissues.

The relations of carbon dioxide in the blood and the manner of its excretion through the lungs are rather more complicated and obscure than in the case of oxygen. If a given volume of blood be divided into plasma or serum and corpuscles, it will be found that the larger proportion of the carbon dioxide in the whole blood is contained in the serum, although a certain amount is also present in the corpuscles. When extracting gases from serum by means of the mercurial pump, it is found that about 5 per cent. of the carbon dioxide present is fixed*—that is to say, is only liberated after the addition of some weak acid, such as phosphoric or tartaric acid. If, however, we use whole blood for the experiment, it is found that the entire amount of CO_2 is given off. This is shown by the fact that, after extracting with the pump as much CO_2 as possible, no further amount can be obtained on addition of phosphoric acid. It is obvious that the red corpuscles act the part of a weak acid, and we can, in fact, in the first experiment use fresh red corpuscles instead of phosphoric acid to drive off the last trace of CO_2.

From 100 volumes of venous blood we can extract about 50 volumes of CO_2. The question now arises: Is this gas in a condition of solution or in chemical combination with the plasma? The answer is easy to give. At the temperature of the body 100 volumes of plasma would take up 50 volumes of CO_2 at 760 mm. Hg. pressure, *i. e.* if we may consider the solubility of the gas in plasma equal to

* It must not be thought that these 5 volumes per cent. represent the whole of the CO_2 that is chemically combined. The fact that a part of the gas is given off on exposure to a vacuum, and a part left in solution, shows merely either that one part is in a state of looser chemical combination than the other, or that the phosphates in the serum only suffice to take up part of the soda liberated by the decomposition of the sodium carbonate.

its solubility in water. It is apparent, then, that if CO_2 in the plasma exists in a state of solution, its tension will be 760 mm. Hg., that is to say, one atmosphere. Now the CO_2 tension in venous blood may be determined by the method indicated above (p. 271), and is found to be equal to only 5 per cent. of an atmosphere. This merely means that when the venous blood is brought into an atmosphere containing 5 per cent. CO_2, the relative proportions of CO_2 in the liquid and the gas remain the same. We see, then, that only $\frac{1}{20}$ part of 50 volumes can be absorbed, since the CO_2 tension is only $\frac{1}{20}$ of an atmosphere; and must conclude that of the 50 volumes $\frac{50}{20} = 2\frac{1}{2}$ volumes are in simple solution, and the remaining $47\frac{1}{2}$ volumes in chemical combination.

On analysing the ash of the serum, we find that it contains sufficient sodium present to combine with all the CO_2, besides that which is necessary to satisfy the fixed acids, hydrochloric and phosphoric. The presence of phosphates in the serum is probably of great importance for the regulation of the tension of the CO_2. If the two acids, carbonic and phosphoric, are present together in a solution containing soda, the salts formed depend on the relative masses of the two acids. If the carbonic acid is in excess, sodium carbonate is formed, together with monosodium phosphate (NaH_2PO_4). If, however, the carbonic acid be removed, or its 'mass influence' diminished by allowing it to escape freely into a vacuum, the phosphoric acid gains the upper hand and takes the lion's share of the sodium, disodium phosphate (Na_2HPO_4) being formed. In this way, as soon as the amount of free carbon dioxide decreases, however little, the amount of the CO_2 in combination also diminishes, and, moreover, to a very considerable extent. Thus in the serum, where these two salts are present, an alteration of eight volumes per cent. in its CO_2 gives rise to a change of tension of only 2·6 per cent. of an atmosphere.

This struggle between the CO_2 and the phosphoric acid for the possession of the sodium is constantly going on. In the tissues, where the CO_2 tension is high, the mass

influence of this acid predominates, and a large amount of it is taken up into the blood, where it forms sodium bicarbonate. It is difficult to be certain of the tension of the carbon dioxide in the cells themselves. In urine it is 9 per cent., and in bile 7 per cent. It may be estimated in the tissues of the intestinal wall by injecting air into a ligatured loop of intestine, and analysing the air after two or three hours. The air is then found to contain 79 per cent. CO_2. Thus the tension is much higher in the tissues than even in the venous blood, and there must be a continual flow of CO_2 from tissues to lymph, and from them to the blood-plasma.

We have seen above that the taking up of oxygen by the blood in the lungs can be explained on purely physical grounds, since the tension of oxygen in the alveoli is sufficient to cause almost complete saturation of the hæmoglobin. Our experimental data, however, do not yet suffice to show that the physical conditions at work account for the giving off of CO_2 to the air in the alveoli. In order that this might happen by a mere process of gaseous diffusion, the following conditions must be present.

The tension of the CO_2 in the pulmonary alveoli must always be less than that in the blood. If this be so, the blood in its passage through the pulmonary capillaries will give off CO_2 to the alveolar air, and the CO_2 tension in the blood will be diminished. But it is evident that this discharge of CO_2 can never go on to such an extent that the CO_2 tension in the blood should fall below that in the alveolar air; for if this were the case there would be at once a retrograde movement of the CO_2, which would then pass from the alveolar air back to the blood. We thus see that the CO_2 tension in the blood of the pulmonary vein can never be less than that of the alveolar air.

Experimental researches so far have not proved the existence of these necessary conditions, although the difficulty is often avoided by comparing the tension of venous

blood with that of the alveolar air. The accompanying table represents approximately the tensions of CO_2 in the blood and in the air of different localities.

Arterial blood	2·8 per cent.	From dog.
Venous „	5·4 „	
In air of alveoli	3·56 „	
In expired air	2·8 „	

In this table, by simply comparing the tensions of CO_2 in the venous blood and alveolar air respectively, we might say that the CO_2 had passed from a region of high to a region of low tension, in accordance with the known laws of diffusion. But the figures given for arterial blood at once show that this gaseous change has gone on beyond the establishment of equilibrium, and that in fact the CO_2 has passed from a medium where its tension is low to a medium where its tension is higher. We must therefore seek for some other explanation of the manner in which CO_2 is given off in the lungs.

I have already mentioned that part of the CO_2 in the blood is in combination with the red blood-corpuscles. A solution of hæmoglobin is also found to have a power of combining with CO_2 to form a loose chemical compound. It is thought by some that this carbon dioxide hæmoglobin acts as a carrier of CO_2 between the plasma and the alveolar air, and that under the influence of the oxygen of the alveolar air the CO_2 is expelled from the corpuscles, causing a sudden rise of CO_2 tension in the plasma, and therefore a discharge of this gas into the alveoli. There are many difficulties, however, in the way of this hypothesis, and it seems that here, as in so many other cases, we may have to give up a mechanical in favour of a vitalistic explanation, and ascribe the interchange of gases in the lungs to a secretory activity on the part of the pulmonary epithelium. This view is favoured by the fact that in some cases the oxygen tension in the arterial blood rises above that in the alveolar air, so that here there has been

a movement of both the gases concerned from a region of lower to a region of higher tension.

The parallelism of these phenomena with those of secretion cannot fail to be recognised. The secreting cells of the kidney take up urea from the blood, which only contains at any time about ·02 per cent. of this substance, and excrete it into the renal tubule, into a medium—the urine, —containing about 2 per cent.

We cannot, arguing from these analogies, refuse to accord the possibility of a similar power to the pulmonary epithelium. According to Bohr, the evolution of CO_2, and perhaps to some extent the taking up of oxygen in the lungs, are effected by the selective power of the epithelial cells, which excrete the CO_2 into the alveolar air, just as the kidney-cells excrete urea. We cannot, however, regard this question as definitely settled. It is still possible that future researches may show the relationship between the gaseous tensions in blood and alveolar air, which was given on the previous page, to be erroneous, and that the giving off of CO_2 as well as the taking up of oxygen by the blood may be found to be effected by ordinary processes of diffusion.

Changes in Composition of Air breathed

The oxygen tension of the air can be considerably reduced without causing inconvenience. Since, however, oxyhæmoglobin is dissociated at a tension of 300 mm. air (about 60 mm. O_2), we should expect that a similar dissociation would take place in the blood of an animal exposed to this pressure ; and this is found to be the case. An animal becomes dyspnœic and dies of asphyxia if it be confined in an air-tight chamber, and the pressure of the air gradually reduced to 300 mm. The experience obtained in balloon and mountain ascents is in complete harmony with the result of this experiment. Dyspnœa does not begin till a height of 5000 metres is reached, which corresponds to a mercurial pressure of 400 mm. Hg.

It is interesting, however, to note that the extreme dyspnœa with which mountaineers are attacked at a height of about 5000 metres passes off after some time, and then they may pursue their way another 1000 metres higher without any discomfort (Whymper). This power of quick adaptation to lowered atmospheric pressure seems to point to other agencies at work besides mere physical diffusion in providing for the due oxygenation of the blood.

If the oxygen in the air supplied to an animal be reduced to 3 per cent., it rapidly dies of asphyxia with convulsions. Excess of carbon dioxide also proves fatal, but in a different manner. If an animal be placed in an atmosphere containing 6 per cent. of CO_2, it gradually becomes narcotised and dies without convulsions. CO_2 is therefore looked upon as a narcotic poison.

Gases such as hydrogen, nitrogen, and methane (CH_4) are termed indifferent gases. They may be respired if mixed with 20 per cent. of oxygen, and either of the other gases may be used instead of nitrogen to dilute the oxygen that we breathe, without harm or inconvenience.

Carbon monoxide is rapidly poisonous by its action on the red corpuscles. It combines with hæmoglobin, forming CO hæmoglobin, a compound which is much more stable than oxyhæmoglobin. The blood is therefore deprived of its oxygen carrier, and the animal dies of asphyxia.

Other gases which have special poisonous properties are hydrocyanic acid, sulphuretted hydrogen, phosphuretted hydrogen (PH_3), arseniuretted hydrogen, &c.

Irrespirable gases are those which are so irritating that they produce spasm of the glottis. Such are ammonia, chlorine, sulphur dioxide, nitric oxide, and many others.

Ventilation

A point of practical importance is the securing to each individual of sufficient fresh air, so that he may always have a plentiful supply of oxygen, and may be relieved of

his waste products. It is found that a dwelling-room becomes unpleasant and stuffy when the percentage amount of CO_2 has reached 0·1 per cent. This stuffiness is supposed to be due to organic exhalations from the skin, lungs, and alimentary canal, some of which have a poisonous effect, giving rise to headache and sleepiness. Since these cannot be measured, it is taken as a cardinal rule in ventilation that the amount of CO_2 should never rise above ·1 per cent. An adult man gives off about ·6 cubic feet of CO_2 every hour. Hence in that time he raises the amount of CO_2 in 1000 cubit feet of air to ·1 per cent. He must therefore be supplied with 2000 cubic feet of air per hour in order to keep the amount of CO_2 down to ·07 per cent.

(Ordinary air contains ·04 per cent. CO_2, therefore 2000 cubic feet would contain ·8 cubic foot CO_2, which with the ·6 cubic foot given off by the man would be 1·4, which is ·07 per cent.)

In order that the air may be easily renewed without giving rise to excessive draught, a certain amount of cubic space must be allotted to each man. Each adult should have in a room 1000 cubic feet of space, and be supplied every hour with 2000 to 3000 cubic feet of air.

Effects of the Respiratory Movements on the Circulation.

If we examine a tracing of the arterial blood-pressure, we notice that it presents certain periodic oscillations which accompany the movements of respiration. With each inspiration the blood-pressure rises; with each expiration it falls. The synchronism of the rise and fall with the respiratory movements is not exact, since the rise continues for a short time after the beginning of expiration, before it begins to fall, and the fall continues right into the beginning of the next inspiration, so that

the highest point of the curve occurs at the beginning of expiration and the lowest point at the beginning of inspiration. During the fall which accompanies expiration, the heart-beats, as shown in the diagram (Fig. 86), become

FIG. 86.

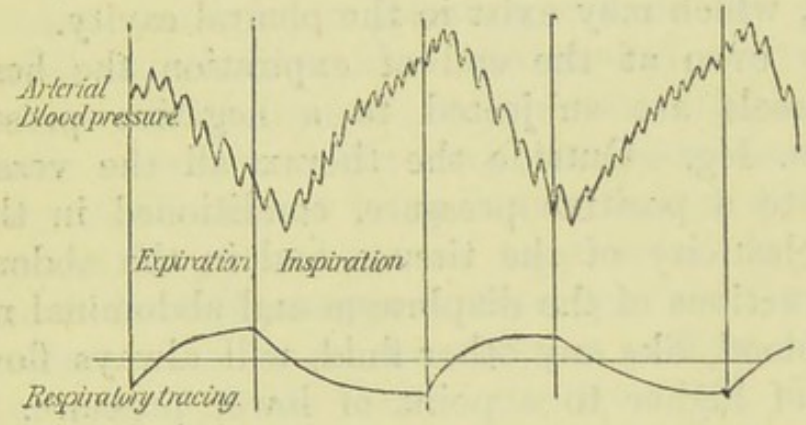


Diagram of blood-pressure curve, showing effects of the respiratory movements on blood-pressure and pulse-rate.

less frequent, and an obvious explanation of the fall of pressure would be to ascribe it to a reflex inhibition of the heart. On dividing both vagi, this difference in the pulse-rate during inspiration and expiration disappears, but the main features of the blood-pressure curve remain the same; so that we must look for some mechanical explanation of the respiratory undulations.

We have already seen that under normal conditions the lungs are in a state of over-distension, and that in consequence of this condition they are constantly tending to collapse, and are therefore exerting a pull on the chest-wall. As soon as we admit air into the pleural cavity by perforating the chest-wall, the lungs collapse. The force with which the lungs are normally trying to collapse amounts to 6 mm. Hg., so we say that in the pleural cavity there is normally a negative pressure of -6 mm. Hg.

As the chest expands in inspiration, it drags the lungs still more open. As these become more distended, their tendency to collapse becomes greater, and hence the

negative pressure in the pleura may be increased during forcible inspiration to − 30 mm. Hg.

Now it must be remembered that the heart and great veins and arteries are in the thorax only separated from the pleural cavity by a thin, yielding membrane, so that they are practically exposed to any pressure, positive or negative, which may exist in the pleural cavity.

Hence even at the end of expiration the heart and large vessels are subjected to a negative pressure of − 6 mm. Hg. Outside the thorax all the vessels are exposed to a positive pressure, conditioned in the neck by the elasticity of the tissues, and in the abdomen by the contractions of the diaphragm and abdominal muscles.

Now blood, like any other fluid, will always flow from a point of higher to a point of lower pressure. There must therefore be a constant aspiration of blood from peripheral parts into the thorax. This aspiratory force will, however, not affect arteries and veins alike. The arteries, having thick, comparatively non-distensible walls, will be very little affected by the negative pressure obtaining in the thoracic cavity, whereas the thin-walled distensible veins will be very largely affected by the same influence. The total result, then, of the negative pressure in the pleural cavities is to increase the flow of blood from the veins into the heart, without affecting to any appreciable degree the outflow of blood from the heart into the arteries. The more pronounced the negative pressure in the thorax, the greater will be the amount of blood sucked into the heart from the veins. During inspiration, therefore, the heart will be better supplied with blood than during expiration, and this factor in itself will tend to raise the arterial blood-pressure.

The inspiratory descent of the diaphragm will, moreover, tend to increase the inflow into the heart by raising the positive pressure in the abdomen, so that blood is *pressed* out of the abdominal veins and *sucked* into the heart and thoracic veins.

Still more important, however, is the influence of the respiratory movements on the circulation through the lungs. In trying to understand this influence, it must be remembered that the pulmonary capillaries lie in a certain amount of elastic and connective tissue, and are separated on the one side by the alveolar epithelium from air at the ordinary atmospheric pressure, and on the other by the pleural endothelium from the pleural cavity, where the pressure varies from 6 to 30 mm. Hg. below the atmospheric pressure. We may therefore consider the pulmonary capillaries as lying between, and attached to, two concentric elastic bags, as represented in Fig. 87. Under normal conditions, since these bags are always tending to collapse, the inner one must be pulling away from the outer one, and the outer one from the chest-wall. Hence there must be a negative pressure in the tissues between these two bags—a negative pressure which, in the expiratory condition, will be something between 0 and − 6 mm. Hg., and in the inspiratory condition between 0 and − 30 mm. Hg. If we regard the average pressure within the pulmonary capillaries as constant, it is evident that in the inspiratory condition these capillaries must be more dilated than in the expiratory condition, as shown in the diagram (Fig. 87). Now this dilatation of the pulmonary capillaries will have two effects. Their capacity will be increased, and the resistance they present to the flow of blood will be diminished.

Let us now consider what effect these changes will have on the general arterial blood-pressure. We will assume that during expiration (Fig. 87 A) the pulmonary vessels have a capacity of 25 c.c., and that the beat of the right heart is forcing through them 10 c.c. of blood per second. So long as the chest remains in the expiratory condition, 10 c.c. of blood will be flowing into the left heart and into the aorta, so that the systemic blood-pressure will remain constant. Now let us suppose that an inspiratory enlargement of the thorax takes place (Fig. 87 B). The negative

FIG. 87 A.

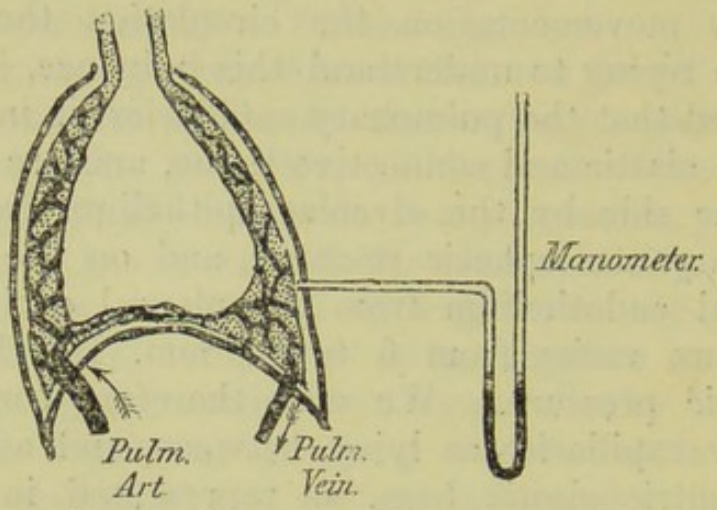


Diagram to show condition of pulmonary vessels in expiration.

pressure in the pleura is increased, the two walls of the lung are pulled farther away from one another, and there is a general enlargement of the pulmonary capillaries. We will assume that this enlargement increases the capacity

FIG. 87 B.

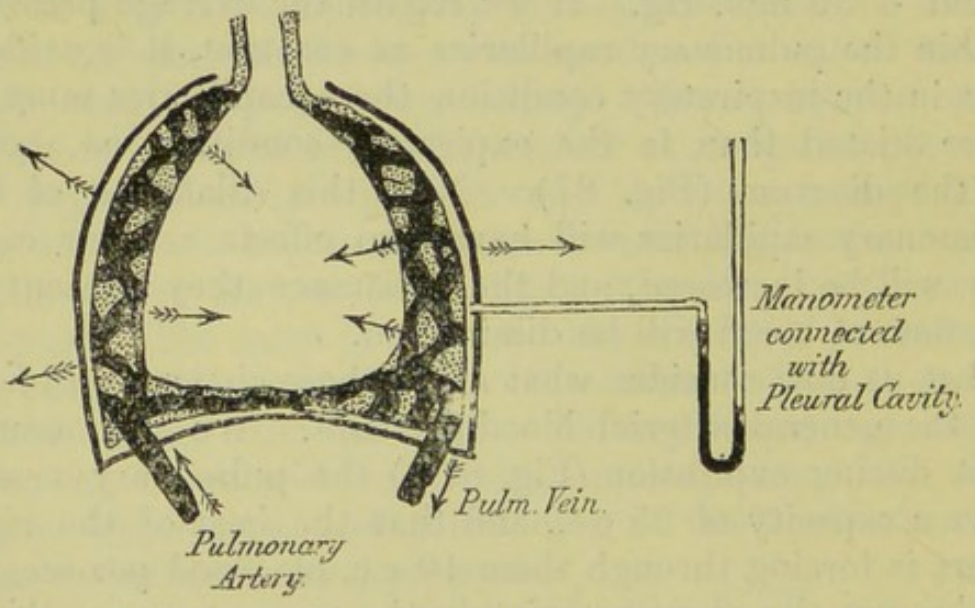


Diagram to show condition of pulmonary vessels in inspiration.

of the pulmonary capillaries from 25 to 30 c.c. Owing to this increased capacity, the first 5 c.c. of blood which flows into the lungs after the beginning of inspiration will not

flow out through the pulmonary vein, but will simply serve to bring the capillaries into the same state of distension as before. Hence at the beginning of inspiration the flow through the pulmonary vein will be diminished; there will be less blood discharged into the left heart, and therefore a fall in systemic pressure. As soon, however, as the increased capacity of the pulmonary vessels is made up, the dilating effect of the inspiratory movement on these vessels will aid the flow through the lungs, in consequence of the diminution of resistance, so that the same force of the right heart which drove 10 c.c. of blood per second through the former resistance during expiration, will now drive more, say 12 c.c. of blood. There is thus more blood entering the left heart, and therefore a rise of systemic pressure during the last three quarters of the inspiratory movement.

Expiration will have exactly the reverse effect. At the beginning of expiration there is a diminution of capacity in the pulmonary vessels from 30 to 25 c.c. Hence during the first second of expiration the outflow of blood from the pulmonary vein into the left heart will be 17 c.c. (12 c.c. + 5 c.c.). After this, the increased resistance in the pulmonary capillaries in consequence of their constriction will come into play, and the flow of blood through them will fall once more from 12 c.c. to 10 c.c. Hence at the beginning of expiration the inflow of blood from the pulmonary vein into the left heart is greater than at any other period. The arterial pressure will therefore rise to its greatest height at the beginning of expiration, and will fall during the last three quarters of expiration, but will attain its minimum only at the beginning of the next inspiration.

We see that in this way the effect of the respiratory movements on the systemic blood-pressure can be entirely explained by the influence they exert on the lung-vessels or lesser circulation.

Voice and Speech

Voice.—The voice is produced by an expiratory blast of air being forced through the narrow interval between the true vocal cords. These, which are thin, membranous, and elastic, are set into vibration by the current of air, and the vibrations are communicated in turn to the air in the upper air-passages. The pitch of the sound produced depends on the rapidity of vibration of the vocal cords.

During ordinary respiration, the glottis or opening between the vocal cords remains about half open, being rhythmically widened with every inspiration. For the production of voice, the free borders of the vocal cords must be brought so near to one another that they almost touch, and a narrow chink with parallel sides is produced. At the same time they must be more or less tense, according to the pitch of the note to be produced. Both these changes are effected by the agency of muscles, the narrowing of the glottis by the contraction of the lateral crico-arytænoid muscles acting in conjunction with the posterior arytænoid and the external thyro-arytænoid muscles. The tightening is brought about by the contraction of the crico-thyroid. This muscle raises the anterior part of the cricoid cartilage so that its upper part, to which the arytænoids are attached, is carried backwards, and thus the vocal cords are put on the stretch. At the same time the tension may be regulated by the contraction of the internal thyro-arytænoid muscles. The pitch of the tone depends on—

1. The length of the vocal cords. It is well known that the pitch of a stretched string varies inversely as its length. A piece of catgut one foot long will, on being struck, give a note an octave higher than a similar piece two feet long, if both are under the same tension.

Comparative measurements show that the vocal cords of men are one and a half times the length of those of women,

and this explains the difference in the pitch of their voices. Among men those with a tenor voice have shorter vocal cords than those with a bass one.

2. Tension of the vocal cords, which is modulated as we have said by the degree of contraction of the crico-thyroid muscle.

The intensity or loudness of the voice depends on the strength of the expiratory blast of air, since the more powerful this the greater the amplitude of the vibrations of the vocal cords produced.

The changes in the glottis accompanying phonation are best studied with the aid of the laryngoscope. This consists essentially of two mirrors; the larger, which has a small hole in the middle, is fastened on to a spectacle frame, which the observer wears. This mirror is used to reflect powerful light into the back of the pharynx of the person to be observed. A small round mirror about half an inch in diameter, mounted on a handle, is then introduced into the pharynx until it is directly over the opening of the larynx. The observer then sees in the small mirror a reflected image of the epiglottis and arytænoid-epiglottidean folds, with the true and false vocal cords lying in between them.

The human voice extends to about $3\frac{1}{2}$ octaves, although it is rare to find any individual compass extending over two octaves. In men two kinds of voice can be distinguished, the chest register and the head register or falsetto. In the latter form of voice it is said that the vocal cords are wider apart, and that only their innermost margins are set into vibration by the current of air.

Speech.—Articulate speech is produced, not in the larynx, but in the mouth and pharynx. If these parts alone are called into play, the expiratory blast of air is so modified as to give rise to whispering speech; if at the same time there is a production of voice in the larynx, ordinary speech is produced.

The sounds that take their origin in this way are divided into vowel sounds and consonants.

The *vowels* a, e, i, o, u (pronounced ah, eh, $\overline{ee}$, o, $\overline{oo}$) are *tones*, *i. e.* are reproduced by a regular series of vibrations.

The special characters of each vowel sound were shown by Helmholtz to be due to the combination of overtones, which is different for each vowel. This was determined in the following way :—A person was made to tone the vowel sounds on one particular note, and by means of resonators the component vibrations of each vowel sound were analysed. These being found, the experiment was completed by re-forming the vowel sounds synthetically by means of tuning-forks arranged to vibrate at the same notes as the notes of the resonators that picked out the sounds in the first experiment.

Thus if *b* be taken for the fundamental tone,

$b + b_1 =$ u ($\bar{o}\bar{o}$).

$b + b_1$ (loud) + f_2 (soft) = o.

$b + b_1$ and f_2 (moderately loud), f_1 (louder), f_3, a_3 and b_3 (loud) = e (eh).

$i = \overline{ee}$ could not be reproduced, since its higher overtones could not be artificially represented by means of tuning-forks.

The difference in the overtones accompanying the fundamental tone, and therefore in the vowel sounds, is brought about by changes in the shape of the cavity of the mouth and pharynx. When *O* and $\overline{oo}$ are sounded, the mouth-cavity has the shape of a flask without a neck, the opening being situated at the mouth. The opening is narrow when $\overline{oo}$ is sounded, wider with *O*.

When *a* (*ah*) is sounded, the mouth-cavity assumes a wide conical form, the widest part of the cone being at the mouth. With *e* (*eh*) and *i* ($\overline{ee}$) the cavity assumes the form of a flask with a long narrow neck which is formed by the raising of the tongue, leaving a narrow canal between this organ and the hard palate.

These changes can be observed roughly by anyone on himself if he intones *oo*, and then gradually changes the sound

to *o*, *ah*, *e*, *i*, directing close attention to the changes that he is bringing about in his mouth.

The vowel sounds, then, we may conclude, are brought about by changes in the shape of the cavity of the mouth and pharynx, which alter the quality of the tone produced in the larynx by intensifying some and suppressing other harmonics or overtones.

Diphthongs are produced by changing the form of the mouth-cavity from that of one vowel sound to the other, so that one sound follows directly after the other; thus *ai* = *ah-ee* run together and abbreviated. Consonants are sounds produced by a sudden check being placed in the course of the expiratory blast of air by closure of some part of the pharynx or mouth. They are classified into labials, dentals, or gutturals, according as the check takes place at the lips, between teeth and tongue, or between back of tongue and soft palate.

In the production of *nasal* sounds, such as *m*, *n*, or *ng*, the mechanism is the same as for the production of *b*, *d*, and *g*, except that the posterior opening of the nares is not kept shut by the soft palate, so that part of the sound comes continually through the nasal passages, when it acquires a peculiar resonance. These sounds are on this account often spoken of as *resonants*. The *aspirates* are produced by the passage of a simple blast of air through a narrow opening which may be at the throat as in *h*, between tongue and teeth as in *th*, or between lips and teeth as in *ph* or *f*.

CHAPTER IX

EXCRETION—FUNCTIONS OF THE KIDNEYS AND SKIN

THE consideration of the lungs, which are organs engaged at the same time in absorption and excretion, leads us on naturally to those organs by which the remaining waste products of the organism are eliminated, *i. e.* the kidneys and skin.

The main work of the kidneys is the excretion of urea, the product of the nitrogenous waste of the body. This is turned out dissolved in water, together with certain other nitrogenous extractives, salt, and water, which together make up the urine.

Human urine in a fresh condition is a clear yellow fluid, with characteristic odour and sour reaction. Its specific gravity is on the average 1016—1020. It is free from organised elements. An average man of 66 kilos. weight passes in twenty-four hours about 1500 grms. of urine. This contains about 73 grms. of solids, which are made up as follows :

Urea	33 grms.
Uric acid	·5 „
Hippuric acid	·4 „
Creatinin	·9 „
Pigment and other substances	10 „
Sulphuric acid	2 „
Phosphoric acid	3 „
Chlorine	7 „
Potassium	2·5 „
Sodium	11 „
Ammonia, Calcium, Magnesium	3 „

It also contains about 15 volumes per cent. of gas, consisting chiefly of carbon dioxide, with a small amount of nitrogen.

Of these constituents, UREA is by far the most important. A description of the chemical relationships of this body has already been given (see p. 41). On treatment with an alkaline hypobromite it is decomposed with the formation of free nitrogen and carbon dioxide :

$$CO(NH_2)_2 + 3NaBrO = CO_2 + N_2 + 3NaBr + 2H_2O.$$

This reaction is taken advantage of in the quantitative estimation of urea. 5 c.c. of urine are treated in a closed vessel with about 20 c.c. of alkaline sodium hypobromite solution. The CO_2 evolved is dissolved by the excess of alkali present, and the nitrogen is collected in a graduated cylinder over water. From the amount of nitrogen given off, the amount of urea present in the urine may be calculated. 35·4 c.c. of nitrogen correspond to one decigram of urea.

Since urea is the end-product of the metabolism of the proteids taken in with the food, whether these have been built up to form constituent parts of the living cells of the organism or have been broken down at once on their entry into the body, the amount of it excreted in the day is an index to the activity of the proteid metabolism. Hence it is increased by a large proteid diet ; as well as under conditions such as fevers, when a rapid disintegration of the tissues is going on. It is, moreover, increased by administration of nitrogenous extractives, such as glycin or leucin, or combinations of ammonia with carbon dioxide or vegetable acids, or of large quantities of water.

Origin of urea.—Urea is not formed in the kidneys. If the kidneys of an animal be extirpated, urea accumulates in all the tissues and organs of the body, in which it is found at death in large quantities. Circulating blood constantly contains a small proportion of urea, and the kidney-cells merely take up this urea and turn it out into the urinary

tubule. So we have to inquire what are the immediate precursors of urea, and in what organ or organs their transmutation into this body is effected.

Since urea is an amido-body (carbamide), it is natural to look upon the amido-acids (*e. g.* leucin) that are formed during digestion, as well as those that occur in combination with other bodies (such as glycin and taurin), as possible precursors of urea. And, indeed, as I have just mentioned, administration of these bodies gives rise to a corresponding increase in the amount of urea in the urine. The conversion into urea of the amido-acids formed during digestion will account to some extent for the increased urea-excretion after a meal rich in proteids. It is impossible, however, to conceive chemically the direct conversion of these amido-acids into urea. These bodies all contain a much larger proportion of carbon to nitrogen than does urea, and we must therefore assume that the first stage in the change is one of oxidation. The carbon-holding part of the molecule is oxidised to CO_2, and part of this CO_2 unites with the ammonia of the amido-radical to form ammonium carbonate, from which, by a simple process of dehydration, carbamide or urea may be formed :

(1) $$2\left|\begin{matrix}CH_2.NH_2\\ \\ CO.O.H\end{matrix}\right. + 3O_2 = CO\begin{matrix}\diagup O.NH_4\\ \\ \diagdown O.NH_4\end{matrix} + 3CO_2 + H_2O$$

Glycin. Ammonium carbonate.

(2) $$CO\begin{matrix}\diagup O.NH_4\\ \\ \diagdown O.NH_4\end{matrix} - 2H_2O = CO\begin{matrix}\diagup NH_2\\ \\ \diagdown NH_2\end{matrix}$$

Carbamide or urea.

If ammonium carbonate be administered to an animal, no increase is found in the ammonia of the urine, but a large increase in the urea, showing that the ammonium carbonate has been converted into urea. Recent experiments have shown that this conversion takes place in the liver. If defibrinated blood mixed with ammonium carbonate be

passed through the blood-vessels of a recently excised mammalian liver, the urea in the blood is found to be increased 200 or 300 per cent., and there is a corresponding decrease in the amount of ammonium carbonate in the blood. The decisive experiment of extirpation of the liver cannot be performed on mammals, since these animals die almost immediately after this operation, or after ligature of all the vessels going to the liver.

Birds, however, may survive the operation for some time. In this class, unfortunately for our present question, the greater part of the nitrogen is excreted as uric acid, and not as urea. Extirpation of the liver causes an almost total disappearance of the uric acid in the urine, and a corresponding appearance of ammonia. In healthy geese, for instance, the nitrogen eliminated as uric acid amounts to from 60 to 70 per cent., and as ammonia to from 9 to 18 per cent. of the total nitrogen. After removal of the liver the uric acid nitrogen represents only 3 to 6 per cent., and the ammonia 50 to 60 per cent. These figures show clearly that in birds ammonia is a precursor of uric acid, and that the presence of the liver is essential for its conversion into this substance.

It is probable that the liver is also active in the transformation of the amido-acids into ammonium carbonate. In acute yellow atrophy of the liver and in the atrophy produced by the administration of phosphorus, the urea disappears from the urine, its place being taken by leucin and tyrosin, as well as ammonia.

Another important precursor of urea is represented by *creatin*. This nitrogenous substance occurs in far larger quantities in the organism than any other extractive. The body of a normal-sized man contains about 90 grms., chiefly in the muscles. On boiling creatin with baryta water it is split up into urea and sarcosin—an amido-acid; and it is conceivable that a similar decomposition takes place in the muscles, the sarcosin passing on to the liver, and there being converted into ammonium carbonate and

then into urea. The following fact seems at first against this view. Creatin taken with the food or injected into the blood calls forth no increase of urea in the urine, the whole quantity being excreted as creatin or creatinin. We must conclude from this experiment that the creatin does not leave the muscle as such, but that it is broken down in the muscle into urea and an amido-acid, or still further oxidised into ammonia and carbonic acid, which are then turned out into the lymph and blood-stream.

URIC ACID ($C_5H_4N_4O_3$), which occurs constantly in the urine in small quantities, is a weak dibasic acid. It is almost insoluble in cold water—a little more soluble in hot water. It is easily soluble in alkaline solutions and in solutions of the alkaline phosphates. In solutions of the latter salts a chemical change takes place, the uric acid withdrawing a part of the alkali from the phosphate to form an acid urate of the alkali, which is more soluble in water than uric acid. Thus :

$$Na_2HPO_4 + C_5H_4N_4O_3 = NaH_2PO_4 + NaC_5H_3N_4O_3.$$

The acid reaction of the urine is due to the presence of the acid sodium phosphate. If the urine be allowed to cool, it is often found that crystals of uric acid separate out, and the urine becomes less acid or even alkaline. This is due to the fact that in cooling the mass-influence of the uric acid is diminished. The phosphoric acid of the phosphate combines with the soda of some of the acid sodium urate, forming the disodium phosphate and setting free uric acid, which is precipitated. If the urine be warmed again to the temperature of the body, the converse reaction takes place, acid sodium urate and acid sodium phosphate being formed, and the uric acid is dissolved.

The yellow colour of the crystals is due to the fact that they carry down with them part of the pigment of the urine. If the urine is concentrated, there is very often a brick-coloured precipitate produced on cooling, which dissolves up again if the urine be warmed. This is spoken of

as the 'lateritious' deposit, and consists of the mixed urates of potassium, sodium, calcium, and ammonium.

Uric acid is chemically allied to urea, and may be prepared from that body by heating it with glycin in a closed tube for some hours.

Test for uric acid.—A few crystals of uric acid are warmed with a little concentrated nitric acid in a porcelain capsule until the nitric acid is evaporated. On adding a drop of ammonia to the yellow residue, a brilliant purple colour is produced (murexide). If potassium or sodium hydrate be used the colour is blue.

Quantitative determination.—Hopkins' method for the estimation of uric acid is founded on the fact that saturation of a fluid containing uric acid or urates with ammonium chloride causes complete separation of all the uric acid present in the form of ammonium urate. In applying this method the urine is saturated with crystals of ammonium chloride. The precipitate of ammonium urate which forms is collected on a filter, washed into a beaker, and boiled with dilute hydrochloric acid. The urates are broken up, and the uric acid thus set free is deposited in a crystalline form on cooling. The precipitate of uric acid is collected on a weighed filter, dried, and weighed.

Origin of uric acid.—We have already seen that uric acid in birds is manufactured to a large extent in the liver, and that a salt of ammonia—probably lactate—is its immediate precursor. It is said that in mammals, however, administration of uric acid in the food only gives rise to increased urea in the urine. The circumstances under which the uric acid excretion is increased are—1st, large meat diet; 2ndly, various pathological conditions associated with an increased number of leucocytes in the blood, especially in leucocythæmia. It has therefore been thought that the uric acid is the product of the nitrogenous metabolism of the leucocytes, which in this respect may be looked upon as lowly organisms inhabiting the blood, leading an almost independent existence, and having a special nitrogenous

excreta of their own. A distinct relationship appears to exist between the amount of nucleins in the food and the excretion of uric acid. On treating nucleins (the phosphorised moiety of nucleo-albumens) with hydrochloric acid at a high temperature they are broken down, and among their products of decomposition are found bases such as xanthin, hypoxanthin, &c., which are closely allied to uric acid. Many authorities are, therefore, of opinion that the sole source of uric acid in mammals is the disintegration of the nucleins of the food and tissues.

Creatinin.—The creatinin in the urine is nearly all derived from the creatin contained in the meat that is taken as food. It does not, however, quite disappear in hunger, so that a certain amount must arise in the metabolic processes of the body itself. It may be that this quantity merely represents a small percentage of creatin which has escaped further decomposition in the muscles.

Hippuric Acid.—This is only present in small quantities in human urine. The large amount found in the urine of herbivora is due to the fact that in their food are bodies belonging to the aromatic group—the benzoic acid series. If benzoic acid be administered to a man, it is excreted in the urine as hippuric acid, which is a combination of glycin with benzoic acid, with the elimination of a molecule of water:

$$\underset{\text{Benzoic acid.}}{C_6H_5-COOH} + \underset{\text{Glycin.}}{\begin{matrix}CH_2.NH_2\\ |\\ COOH\end{matrix}} = \underset{\text{Hippuric acid.}}{\begin{matrix}CH_2NH-CO.C_6H_5\\ |\\ CO.OH\end{matrix}} + H_2O$$

This synthesis is effected by the living cells of the kidney. If defibrinated blood containing benzoic acid and glycin be passed through the vessels of the kidney for some time, it will be found that their place has been taken by hippuric acid. In the same way, a small amount of hippuric acid is formed if the kidney be chopped up and mixed with blood containing benzoic acid and glycin. If

the kidney cells be first killed by exposure to a temperature of 65°, or to the action of alcohol, no hippuric acid is formed, showing that this synthesis is not effected by a mere ferment action, but is intimately dependent on the life of the cell.

SALTS.—The greater part of the salts of the urine is derived directly from the salts taken in with the food. The combinations of the vegetable acids with alkalies, *e.g.* citrates and tartrates, are oxidised to carbonates, and are in this form eliminated with the urine.

The *phosphates* originate partly from the breaking down of complex phosphorised molecules, such as lecithin, nuclein, and the nucleo-albumens, partly from the phosphates taken in with the food. When the urine becomes alkaline, the calcium and magnesium phosphates are deposited as an amorphous precipitate. If the urine is ammoniacal, ammonio-magnesium phosphate may be formed and precipitated in a crystalline form.

The *sulphur* in the urine arises partly from the sulphates of the food, and partly from proteid metabolism. It is found in the urine in three forms:

1. Small traces of an unoxidised sulphur compound, allied to cystin.
2. As simple sulphates of the alkalies.
3. As conjugated sulphates.

These latter bodies are important from the fact that they are dependent on putrefactive changes occurring in the intestine, so that their quantity in the urine is an index to the extent of these processes. In the bacterial putrefaction of proteids, bodies of the aromatic series, such as skatol, indol, and phenol, are formed. These, after absorption, unite in the blood-stream with an alkaline sulphate to form conjugated sulphates, and as such are excreted by the kidneys. The poisonous aromatic body is thus rendered innocuous.

$$C_6H_5OH + SO_2\begin{matrix}\diagup OH \\ \diagdown OK\end{matrix} = SO_2\begin{matrix}\diagup O.C_6H_5 \\ \diagdown OK\end{matrix} + H_2O$$

Phenol. Acid potassium sulphate. Potassium phenyl sulphate.

Indoxyl sulphate of potash is often spoken of as indican, since on oxidation it yields indigo blue. If urine containing this body be treated with hydrochloric acid and a drop of chlorine water, a bright blue colour is produced from the formation of indigo.

PIGMENTS.—An exact knowledge of the pigments of the urine is still wanting. The chief colouring matter is a body known as *urochrome*. The chemical relationships of this body have yet to be discovered. It has no distinctive absorption spectrum. Among the other pigments of the urine the best known is *urobilin*, which is a body with a distinctive spectrum. This body does not, however, exist in normal urine, which presents no absorption bands. On precipitating normal urine with lead acetate, and extracting the precipitate with acid alcohol, a small trace of urobilin is obtained. Normal urine, therefore, contains a small amount of a chromogen, which on appropriate treatment may give rise to urobilin. In certain diseases, especially cirrhosis of the liver, the urine may contain large amounts of pre-formed urobilin. The pigments are probably all derived from the disintegration of hæmoglobin. The affinity of urobilin with the blood and bile-pigments is shown by the fact that a similar substance, hydrobilirubin, may be formed by the action of sodium amalgam on bile-pigments or on hæmatin.

REACTION.—The acidity of the urine is due to the presence of acid sodium phosphate, and is equivalent to about two grms. of oxalic acid in twenty-four hours. While active digestion is going on, the urine may be for a while alkaline, owing to the secretion of hydrochloric acid by the stomach. It varies with the nature of the food. In herbivora the urine is normally alkaline, becoming acid only when they have had no food. In this condition their

metabolism is going on at the expense of their own bodies, so that they may be regarded as carnivorous for the time being. The diminution of the acidity of the urine on standing has been already mentioned. If exposed to the air, a development of micro-organisms (*Micrococcus ureæ*) takes place in the urine. By their agency the urea is combined with two molecules of water to form ammonium carbonate, and the urine becomes strongly alkaline and ammoniacal.

Secretion of Urine

The kidney may be considered as a compound tubular gland. The urinary tubule starts in the cortex in a small dilatation—the Malpighian capsule, which is lined by a single layer of flattened cells. Into this capsule projects the glomerulus, a little bunch of capillary blood-vessels, also covered by flattened cells. The capsule leads into the first convoluted tubule, lined with peculiar 'rodded' epithelium. The tubule now becomes much narrower, and dips down into the medullary pyramids as the descending loop of Henle, lined with flattened hyaline epithelium. It then widens as it turns up again, and on reaching the cortex forms the irregular tubule and the second convoluted tubule. These three last-named parts are lined with rodded epithelium. From the second convoluted tubule a junction tubule leads into the collecting tubules, lined with hyaline cylindrical cells. There are thus four different varieties of epithelial cells in the various parts of the tubule, *i. e.* scaly cells in the Malpighian capsule, peculiar rodded epithelium in the convoluted and irregular tubules, flattened cells in the descending loop of Henle, and ordinary cylindrical cells in the straight collecting tubes.

There are also certain peculiarities connected with the blood-supply to the kidney. The renal artery breaks up into numerous vessels at the boundary zone between the

pyramids and the cortex. From these the straight interlobular arteries pass towards the surface, giving off lateral branches which form the afferent arteries of the neighbouring Malpighian capsules. These break up in the glomerulus into a cluster of fine capillaries, which unite again to form the efferent vessel, which is only two thirds the size of the afferent vessel. The efferent vessel leaves the glomerulus and breaks up again into capillaries which supply the walls of the convoluted tubules. We thus see that the arrangement of the portal system of vessels is repeated in the kidney on a microscopic scale—the vessel taking the blood from the glomerulus, breaking up again into a system of capillaries, just as the portal vein does in the liver. The pyramids are supplied by branches of the vasæ rectæ which pass inwards from the arteries in the boundary zone.

This arrangement of blood-vessels must determine a high pressure in the capillaries of the glomerulus, and a low pressure in the vessels supplying the remaining parts of the tubule. Since these capillaries are covered only by a thin layer of scaly epithelium, it has been thought that filtration plays a great part in the secretion of urine, and that perhaps the fluid parts of the blood are merely filtered off in the capsule, and the useful constituents of the filtrate, together with the excess of water, reabsorbed while the blood-pressure is low. The close relationship found to exist between the supply of blood to the kidney at any movement and the amount of urine excreted seemed at first to favour this hypothesis. We have seen that the volume of the kidney is intimately dependent on the supply of blood to it, so that the latter may be determined by means of the oncometer. As I have already pointed out, a general rise of blood-pressure, due to increased activity of the heart, causes a swelling of the kidney. If the renal nerves be cut, and a rise of pressure called forth by stimulation of the splanchnic, the kidney swells, owing to the increased pressure in its vessels.

Under all these circumstances, in which the kidney increases in volume, the amount of urine excreted by it is increased. But we have here two factors, either of which may determine an increased flow of urine—1st, increased blood-pressure in the glomerulus; and 2ndly, increased flow of blood through the kidney. It will be remembered that the flow of lymph from a limb is markedly increased by ligature of the veins; and this increase is due chiefly to the enormous rise of pressure that takes place in the capillaries, larger than can be brought about by the constriction of the arterioles in any other part of the body. If the secretion of urine was similarly dependent on the intra-capillary blood-pressure, ligature of the renal vein would also cause an increase in the urine excreted. This is not the case. Ligature of the renal vein entirely stops the secretion of urine, which must therefore be conditioned by the amount of blood flowing through the kidney in a given time.

It is interesting to note that if the renal vein be obstructed for a short time, the urine that is excreted after the removal of the obstruction contains albumen, showing that the short deprivation of oxygen undergone by the cells has injured them, so that they are no longer able to prevent the passage of the proteid constituents of the plasma.

We are yet far from knowing the exact part played by the various kinds of cells of the tubules in the excretion of the urine. The idea that the glomerular epithelium merely allows a watery plasma to filter through is at once negatived by the fact that under normal circumstances no albumen is to be found in the Malpighian capsules.*

Bowman, on rather insufficient evidence, came to the

* The presence of albumen in the Malpighian capsules is easily proved under certain abnormal conditions. By throwing small bits of the kidney at once into boiling water, the albumen is coagulated and can be seen in microscopical sections as a solid mass, occupying the space between the glomerulus and capsule.

conclusion that the glomerulus allowed simply water and salts to pass, while the urea was excreted by the cells of the convoluted tubes. This view, however, has received confirmation from later researches of Nussbaum and Heidenhain.

The kidneys in the frog have a double blood-supply, the glomerular arteries being branches of the renal artery, whereas the urinary tubules derive their blood from a branch of the femoral vein which forms what is called the renal-portal system. It is found in these animals that when the renal arteries are tied and the glomeruli therefore shut off from the circulation, the injection of urea into the blood gives rise to a secretion of urine, showing that this substance is excreted by the epithelium of the tubules, together with a certain amount of water. On the other hand, certain substances, such as sugar and peptone, which are readily excreted by a normal kidney, are not excreted if the renal arteries have been tied, even if a flow of urine be called forth by the simultaneous injection of urea into the blood. It is concluded, therefore, that sugar and peptone pass into the urine through the glomerular epithelium. It must be admitted, however, that these experiments, though apparently so convincing in their results, are subject to several grave objections which tend to deprive them to a large extent of their importance. Thus it has been shown that ligature of the renal arteries does not stop the flow of blood through all the glomeruli, so that it is impossible to arrive by this method at certain conclusions.

If sodium sulphindigotate be injected into the blood of a mammal, and the animal be killed some time afterwards, this substance is found to have been turned out by the kidneys. On cutting sections of these organs, the blue colouring matter is only to be seen in the cells of the convoluted tubules and in the tubules below these, the capsules being entirely free. By previous section of the cervical spinal cord, the blood-pressure sinks so low that no urine is excreted. Under these circumstances the

sodium sulphindigotate, not having been washed down into the lower parts of the tubule by any flow of urine, is only found in the cells of the convoluted tubules. It is supposed that urea is excreted in the same way as the sodium sulphindigotate.

Regulation of urinary secretion.—In most other glands of the body we have seen that their activity was subject to nervous influences. The submaxillary gland is supplied by secretory nerves, stimulation of which calls forth a flow of saliva independently of any change in the blood-stream. The conditions in the kidney, however, are different. The function of this organ is to purify the blood of its waste products, and hence it is only necessary that the cells should react to changes in the composition of the blood. If the blood becomes more watery, the excess of water must be turned out into the urine; if it contains too much urea or sugar, these bodies must be excreted, in order that the blood may act as a normal living medium, and not as a poison to the tissues which it traverses. There is, indeed, no evidence of secretory nerves to the kidney. The urinary secretion is conditioned only by the composition and amount of blood supplied to it. Injection of water or of diuretics, such as sodium acetate or urea, into the blood, causes an expansion of the kidney from dilatation of its vessels, and increased flow of urine, until the blood is restored to its normal composition. The nervous system can influence this secretion of urine, but only by its action on the vessels. In this way may be explained the copious flow of dilute urine which may occur under the influence of emotions or in hysteria. Increased secretion of urine brought about by the application of cold to the skin may be due to reflex dilatation of the blood-vessels.

In the dog the vaso-motor nerves to the kidney pass from the spinal cord chiefly through the anterior roots of the 11th, 12th, and 13th dorsal nerves, and stimulation of the peripheral ends of these roots causes shrinking of the

kidney. If slowly repeated rhythmical stimulation instead of the ordinary faradic current be applied to these nerves, swelling of the kidney may be produced, showing that these roots also contain vaso-dilator fibres.

On the Work done by the Kidney

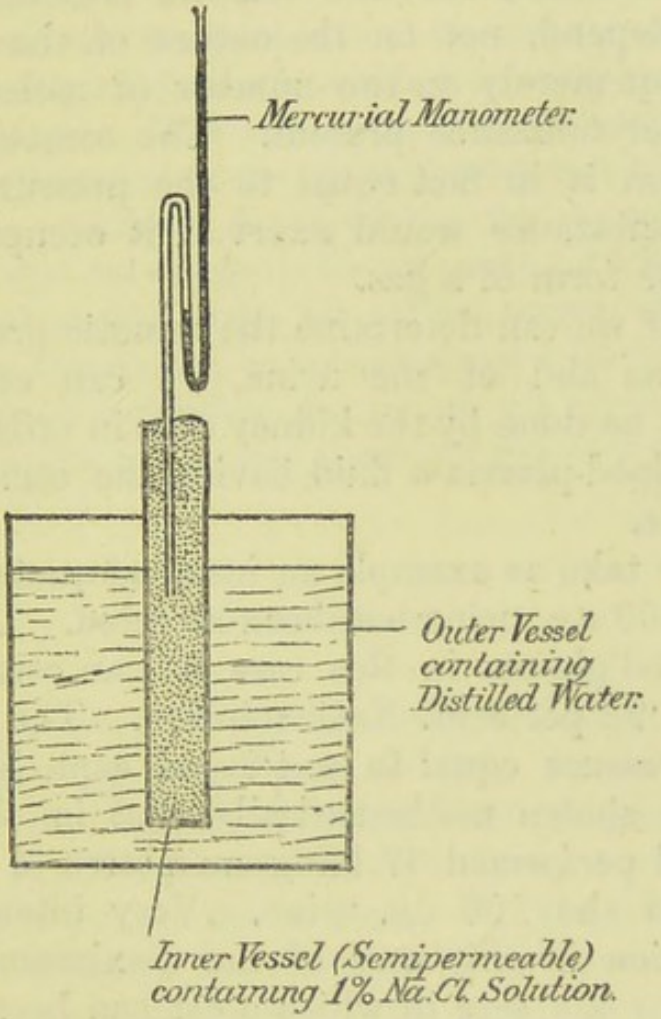
I have already mentioned certain arguments against the hypothesis that the urine is separated from the blood circulating in the kidney by a simple process of filtration. A still stronger argument, however, is furnished by the fact that we can measure the work done by the kidney in the secretion of urine, and find that it is enormously more than could be accomplished by the pressure of the blood in the renal capillaries.

The measurement of the work done by the kidney depends on a determination of the *osmotic pressures* of the blood-plasma and urine respectively. Before describing these results, it will be necessary to say a few words as to what is meant by the term osmotic pressure.

It is well known that, if a bladder containing strong salt solution be placed in a vessel of distilled water, water passes into the bladder by diffusion or osmosis, so that the bladder swells and becomes tense. A manometer connected with the bladder will show a considerable rise of pressure (osmotic pressure). It is evident, however, that we cannot expect under these conditions to get the total possible rise of pressure in the bladder; since the salt diffuses out of the bladder while the water is diffusing in, and moreover the animal membrane permits of a distinct filtration, *i. e.* leaks, as soon as the pressure within it has attained a certain height. It is necessary, then, in order to measure the osmotic pressure of a solution, to enclose it in some vessel whose walls will only allow of the passage of water, and will not permit salt to pass out either by diffusion or by filtration. Such a vessel may be made by washing out a porous cell, first with copper sulphate and

then with potassium ferrocyanide. An insoluble precipitate of copper ferrocyanide is deposited in the pores of the

FIG. 88.



earthenware, and it is found that these now only allow water to pass through, and are perfectly impermeable to dissolved salts. If we arrange such a cell as in the diagram, and fill it with 1 per cent. NaCl solution, and then suspend it in distilled water, we find that water diffuses in until the pressure, as shown by the attached manometer, has attained a great height. The osmotic pressure of a 1 per cent. NaCl solution is equal to about 5000 mm. Hg. If we increase the pressure in the cell, by artificial means, above this height, water will be pressed through the semi-permeable walls of the cell, and the solution will become

more concentrated. In order, then, to make a 1 per cent. NaCl solution more concentrated, we must employ a pressure greater than 5000 mm. Hg.

Now it is found that the osmotic pressures of various solutions depend, not on the nature of the substance in solution, but merely on the number of molecules of this, or any other substance present. The osmotic pressure of any solution is in fact equal to the pressure which the dissolved substance would exert if it occupied the same space in the form of a gas.

Hence, if we can determine the osmotic pressures of the blood-plasma and of the urine, we can estimate what work must be done by the kidney cells in order to separate from the blood-plasma a fluid having the osmotic pressure of the urine.

We may take as example an instance quoted by Dreser in which 200 c.c. urine had been secreted.

The blood-plasma in this case had an osmotic pressure equal to a ·92 per cent. NaCl solution. The urine had an osmotic pressure equal to a 4·0 per cent. NaCl solution. It may be shown mathematically that in this case the kidney had performed 37 kilogram-metres of work in the secretion of the 200 c.c. urine. Very interesting is the determination in this way of the maximum force of the kidney. In one case in which a cat had been deprived of water for three days, the urine was so concentrated that it was equivalent to an 8 per cent. salt solution. The blood-plasma in the same animal had an osmotic pressure equal to 1·1 per cent. NaCl. The difference of osmotic pressures in this case was equal to 498 metres of water, so that the kidney had separated the urine from the blood against a pressure of 49,800 grams per square centimetre. The absolute force of human muscle (*i. e.* the weight it can *just* raise) is 8000 grams per square centimetre; hence we see that the mammalian kidney can exert a force six times greater than the maximum performance of voluntary muscle.

Some recent observations of Bradford show that we have not exhausted the subject of the functions of the kidney when we have described its action as an excreting organ. If in dogs one kidney be first excised, and at a later period half or two thirds of the other kidney, it is found that the urine after the second operation is largely increased in quantity, and contains much more urea than it did under normal circumstances. This urea comes from the disintegration of the nitrogenous tissues, since the animal wastes rapidly and dies in a few weeks. An explanation is yet wanting for the paradoxical fact that an animal with one fourth its normal amount of kidney substance should form and excrete double the normal amount of urea. It is evident that the kidneys play an important and hitherto unlooked-for part in nitrogenous metabolism, but we are not yet in possession of sufficient facts to decide the exact extent and nature of this function.

Micturition

The urine is secreted continuously, although the amount secreted may vary from time to time according to the condition of the animal. Partly through gravity, partly through the pressure under which it is secreted, the urine is driven on through the ureters. If these be occluded, the secretion of urine continues until its pressure reaches 40 mm. Hg., when it ceases. This pressure is sufficient to widely distend the upper part of the ureters and the pelvis of the kidney. In the ureters, which are muscular tubes lined with transitional epithelium, the urine is driven on by peristaltic contractions, which travel from the upper to the lower part of the ureter. These contractions occur from three to ten times a minute, and seem to originate in the muscular substance of the ureter itself, since they are to be seen in an excised ureter. The urine in this way gradually accumulates in the bladder; its reflux into the ureters is prevented by the oblique manner in which these enter the bladder, a sort of valvular opening being thus formed. At intervals the urine that is collected in the

bladder is expelled by contraction of its muscular wall. This act of micturition is in the young child purely reflex, and dependent on the tension in the bladder. With advancing age, however, the individual acquires more or less voluntary control over the reflex act. It will be convenient to first consider the purely reflex act of micturition.

It is found that in the dead subject the bladder is able to hold fluid at a pressure of 18 to 20 c.c. of water. In a living animal fluid can be injected until the pressure reaches 100 c.c. of water before it begins to dribble away. If, however, the lumbar spinal cord be destroyed, the dog is reduced to the same condition as the dead dog, and its bladder can only hold fluid up to a tension of 20 c.c. of water. The retention of urine in the bladder is effected by the tonic contraction of the external sphincter muscle round the prostatic part of the urethra, and the tone is maintained reflexly by means of a centre in the upper part of the lumbar spinal cord.

As urine is gradually secreted, the tension in the bladder rises. When the tension reaches a certain height, slow rhythmical contractions of the bladder-wall begin—weak at first, but growing stronger. After a time one of these contractions is sufficient to overcome the resistance of the sphincter and drive a little urine into the urethra. The stimulus to the urethra sets the whole reflex chain going. The sphincter, by the intermediation of the spinal centre, is inhibited, and at the same time the longitudinal and circular fibres of the bladder-wall contract, thus emptying the bladder. This evacuation may be aided by an associated contraction of the abdominal muscles. At the end of the act the last drops are expelled from the urethra by rhythmical contractions of the perinæal muscles, especially the accelerator urinæ and levator ani. We thus see that both the retention of urine and its evacuation are brought about reflexly through the agency of the spinal centre.

The nerve-supply of the bladder is shown in the accompanying diagram (Fig. 89). It will be seen that it receives nerves from two sources: firstly, from the upper lumbar

FIG. 89.

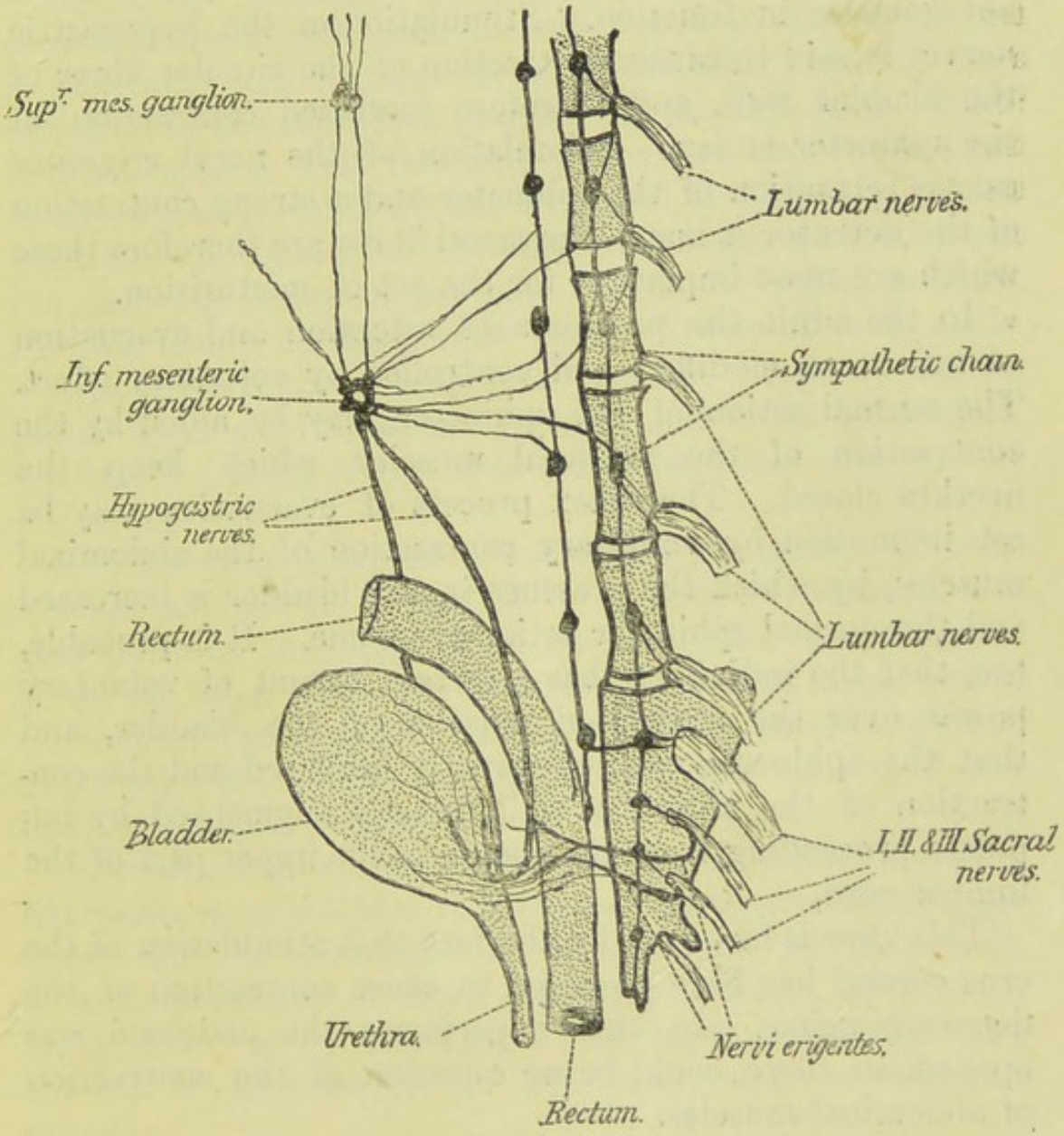


Diagram of nerve-supply to bladder. (Nawrocki and Skabitchewsky.)

nerves: and secondly, from the second and third sacral nerves. The fibres from the latter source run direct to the bladder in the nervi erigentes. Those from the upper

lumbar cord have a more circuitous course, by the *rami communicantes* to the sympathetic chain, thence to the collection of ganglion cells surrounding the inferior mesenteric artery, and from this by the two hypogastric nerves to the bladder. These two sets of fibres seem to be antagonistic in function. Stimulation of the hypogastric nerves is said to cause contraction of the circular fibres of the bladder wall, and therefore increased contraction of the sphincter vesicæ. Stimulation of the nervi erigentes causes relaxation of the sphincter and a strong contraction of the detrusor urinæ. The sacral fibres are therefore those which are most important for the act of micturition.

In the adult the processes of retention and evacuation of urine are modified and controlled by voluntary effort. The normal action of the sphincter may be aided by the contraction of the perinæal muscles which keep the urethra closed. The reflex process of evacuation may be set in motion by voluntary contraction of the abdominal muscles, by which the pressure in the bladder is increased and the normal sphincter action overcome. It is probable, too, that the individual has a certain extent of voluntary power over the unstriated muscles of the bladder, and that the sphincter may be directly inhibited and the contraction of the muscular wall directly augmented by impulses proceeding from the cortex to the upper part of the lumbar cord.

This view is favoured by the fact that stimulation of the crus cerebri has been observed to cause contraction of the detrusor urinæ. In this experiment the abdomen was opened, so there could be no question of the contraction of abdominal muscles.

Skin

Two forms of glands are found in the skin, the *sebaceous* and the *sweat* glands. The former are in connection with the hair-follicles. They are interesting physiologically from the fact that their secretion represents the actual

cells of the glands themselves, which have undergone a peculiar fatty degeneration. The secretion is composed of various neutral fats mixed with fatty acids, and has an acid reaction.

Sweat, the secretion of the sweat-glands, is a clear, colourless fluid, with peculiar odour and a salt taste. It is generally acid in reaction, from the admixture of the secretion of the sebaceous glands. If the skin from which it is collected be first thoroughly cleansed, the sweat that is subsequently collected has a neutral or slightly alkaline reaction. It contains a few epithelial scales derived from the skin and about 2 per cent. solids, of which sodium chloride makes up the greater part. Traces of fatty acids —formic, butyric, and propionic—are also present. Under pathological conditions, urea, sugar, and other substances are found. Many drugs after administration reappear in the sweat.

The secretion of sweat is constantly going on. If only a small amount is formed, it is at once evaporated, and goes off into the atmosphere as insensible perspiration. If, on the other hand, the amount secreted be large, or the surrounding atmosphere moist, so that evaporation cannot easily take place, the sweat collects on the surface of the body as sensible perspiration.

The quantity of perspiration given off is considerable, but varies so much that it is impossible to give an average figure for the amount. It is increased by imbibition of large quantities of fluid, especially if warm, by a warm atmosphere, or by anything which tends to increase the amount of heat formed in the body, such as muscular exercise.

The fact that sweating is so constantly associated with a warm skin seemed at first to show that the secretion of this fluid was called forth by the increased supply of blood to the surface of the body and to the sweat-glands. This view, however, is negatived by the fact that sweating may coincide with a pale anæmic skin, as in the cold

sweats of phthisis or of the death agony, or associated with mental emotion, especially extreme fear. The activity of these glands, as of the salivary glands, is under the control of the central nervous system. Stimulation of the peripheral end of the cut sciatic nerve of the cat causes abundant secretion of sweat on the toes supplied by that nerve. If, on the other hand, the sciatic nerve on one side be cut, and the cat asphyxiated, sweating occurs in the toes of the other three limbs, but not on the limb the nerve of which has been cut. Stimulation of the sciatic nerve causes contraction of the blood-vessels, so that the secretion of sweat cannot be here determined by an increased blood-supply. We can, indeed, excite secretion of sweat by stimulating the sciatic nerve of an amputated leg.

Secretion of sweat may also be excited reflexly. Pungent substances taken into the mouth may cause abundant perspiration on the face.

The sweat-glands may likewise be affected peripherally. Injection of pilocarpin calls forth secretion of sweat between the toes, even after the sciatics have been cut. It is found that the secretion called forth by stimulation of the sciatic is much increased by warming the air surrounding the toes. The importance of this secretion for the regulation of the body-temperature will be spoken of in the next chapter.

In the frog, a large amount of gaseous interchange takes place through the skin, so that the animal may live a considerable time after the extirpation of the lungs. In man, the skin and dead cuticle are much too thick to allow any great interchange to take place between the gases of the blood and the surrounding atmosphere. It is reckoned that on the average from 5 to 8 grms. of CO_2 are given off by a man from the skin in twenty-four hours, and a considerably smaller amount of oxygen is absorbed through the same agency.

It was formerly thought that various poisonous products were excreted with the sweat, and that retention of these

in the body might give rise to symptoms of poisoning. It seems, however, that if a man's skin be clean, the sweat is perfectly innocuous, and it is found that a man may be varnished all over without suffering much harm. In rabbits, which do not sweat, varnishing the body all over causes rapid death of the animal, but this death is due simply to excessive loss of heat, and may be prevented by wrapping the animal in cotton wool. Varnishing this animal seems to cause dilatation of all the superficial capillaries, and hence a great discharge of heat from the surface of the body. The only function of any importance, therefore, that can be ascribed to the secretion of sweat, is the regulation of the heat discharge from the body.

Excreting Organs:

Skin - Sweat, Salts, CO_2, Epithelial scales.

Kidneys

Lungs CO_2, H_2O, Organic matter,

Alimentary Canal. Faeces.

Liver (?)

CHAPTER X

FATE OF FOODSTUFFS IN THE ORGANISM—METABOLISM

HAVING studied the paths by which foodstuffs are absorbed and waste products removed from the body, it remains to inquire into the changes that take place in the food after its absorption. We assume from our experience with the various tissues, especially muscle, that the combustible parts of the food are built up, together with oxygen, into the living protoplasm of the cell to form a highly unstable molecule with large potential energy. In the breaking down of this molecule there is a rearrangement of atoms to form more stable compounds, the carbon and oxygen combining into carbon dioxide with the evolution of energy, which may be displayed either as heat or work.

We are still far from being able to follow the changes that the foodstuffs undergo on entering into the living protoplasmic molecule. Up to this point, however, we can, though with many gaps in our chain of facts, follow the fate of foodstuffs in the body; and a short account of these facts, which are grouped together under the term metabolism, is the object of the present chapter.

In all experiments on metabolism we must be able to make an exact comparison of the Income and Output of the body. To this end the food must be weighed and analysed, and the oxygen taken in measured by means of some respiratory apparatus. The output of the body includes the carbon dioxide and water expired by the lungs; the urine, containing chiefly the nitrogenous excreta; the fæces; the carbon dioxide and water given out by

the skin as perspiration, and a slight loss dependent on the wearing away of the cuticle. In a balance-sheet of the organism the fæces should be subtracted from the income, since they represent the undigested parts of the food.

It has been thought that in a normal animal the excreta may possibly have a twofold origin, and may come partly from the breaking down of the living protoplasm of the body, partly from the direct oxidation of the food that is continually being taken in. It must be remembered, however, that we have no evidence of any oxidative destructive changes in the tissue juices or blood, and that the whole weight of experiment points to the cells being the sole seat of all metabolic changes. It will be convenient to consider first the simplest condition, in which the animal takes no food, in order that we may have only the metabolism of the living tissues themselves to deal with.

In starving animals the income of the body is limited to the inspired oxygen, and, in most experiments, to a certain amount of water. During an experiment of this sort, the animal is weighed every day, and the amount of nitrogen excreted and CO_2 given off by the lungs carefully estimated. Preliminary experiments have shown us the amount of nitrogen contained in muscle, so that from the amount of nitrogen excreted we can estimate the degree of disintegration of the muscular tissues that has gone on. From the quantity of CO_2 eliminated we can determine the loss of the carbonaceous part of the body. This may be regarded as composed entirely of fat, since the amount of glycogen and carbohydrates in the body is small in comparison with the fat present. These two amounts (proteid + fat lost) subtracted from the total daily loss of weight leave a remainder which represents the output of water. Adult animals, supplied with water only, live for four or five weeks. During this time they suffer gradual loss of weight, and at death have lost about 50 per cent. of their weight. The excretion of CO_2 and water sinks continually until death takes place. The

urea excretion falls considerably within the first four or five days, and then remains almost constant at a low level for about four weeks. At the end of the fourth week there may be a sudden rise in the amount of urea excreted. At this period every trace of fat has disappeared from the body. The animal has no further store of carbonaceous material to draw upon, and so must consume the proteid of its tissues in order to supply the necessary proportion of heat and work. In the emaciation consequent upon starvation it is observed that the tissues whose energies are most necessary for the carrying on of the vital functions suffer least. Thus the heart and the central nervous system only lose 3 per cent. of their weight. Of the fat, on the other hand, 97 per cent. disappears, of the muscles 30 per cent.; and a considerable decrease of weight is also observed in the bones, liver, blood, and alimentary canal.

The nitrogen that is eliminated during starvation must necessarily arise from the disintegration of the proteids of the body. As we have just seen, this amount during certain periods of starvation is fairly constant from day to day. It might be thought that if an amount of proteid were given to the animal containing a proportion of nitrogen equivalent to that which the starving animal was excreting, the loss of nitrogen to the body would be checked, the loss of nitrogen in the urine being replaced in the tissues by the nitrogen of the food. This is, however, not the case. After the administration of the proteid to the starving animal the quantity of urea excreted is almost doubled, showing that nearly the whole of the proteid taken in is disintegrated within twenty-four hours and excreted with the urine. In order to produce a condition in which the amount of nitrogen eliminated is equal to the amount of nitrogen taken in with the proteids of the food, it is necessary to give the animal two and a half times the amount of proteid corresponding to the nitrogen that is excreted during starvation. In this case the animal is said to be in a condition of 'nitrogenous equilibrium.'

The condition of the proteid metabolism in an animal that is in a state of nitrogenous equilibrium deserves a little further consideration. The fact that, to maintain the animal in this condition, two and a half times as much proteid is required as is necessary to replace disintegrated nitrogenous tissues in the body, has been regarded as showing that not all the proteid in the food can be devoted to this object. It has been supposed that the proteid taken in with the food has a twofold destination in the body, part of it going to supply the tissue waste, and being built up into the living protoplasm of the tissues (morphotic or tissue proteid); while the other and probably greater moiety passes into the juices that bathe the protoplasmic elements of the cells, and is rapidly broken up and oxidised there without at any time forming an integral part of the protoplasm. This is spoken of as circulating proteid.

I have, however, already drawn attention to the numerous experiments on the subject, carried out chiefly by Pflüger and his pupils, all of which tend to prove that the sole seat of oxidative processes in the body is the living cell. All the proteid, therefore, which is broken down and oxidised to form urea, must at some time have formed an integral part of a living cell, and the tissue proteid is thus the sole source of the urea in the urine. Of course a certain amount of breaking down of the proteid molecule takes place in the intestine, with the formation of leucin and tyrosin; but even in this case these amido-acids have to undergo a series of oxidative changes in the cells of the body (especially of the liver) before they can be turned out in the urine as urea. The behaviour of the nitrogenous excretion in starvation can, therefore, be better explained as follows:

An animal cell desires above all things proteid food, and when it can get enough of this feeds upon (*i. e.* uses up) nothing else. Only when proteid is lacking will it make use of fat or carbohydrate for its needs. Thus while a

dog is fed on a rich mixed diet, he lives practically on proteid alone, storing up the fats and carbohydrates of the food as fat. If food be now withdrawn, the animal must live either at the expense of his own living tissue (proteids) or must attack the stored-up fats in his body. The latter, as a matter of fact, takes place. The animal now spares the precious proteid and lives on the fat of his own body. Hence comes the great fall in the excretion of urea that is observed in starvation, the consumption of proteid sinking to the indispensable minimum. If now a proteid meal be given, the cells of the body return to their former way of living, and satisfy as much of their needs as possible at the expense of proteid, so that the urea excretion rises almost in proportion to the food given. In order to attain nitrogenous equilibrium on a purely proteid diet, it is necessary to give the cells enough proteid for their total requirements, *i. e.* two or three times as much as would correspond to the nitrogenous excretion during hunger.

If a larger amount of proteid be given than is necessary for the maintenance of nitrogenous equilibrium, a certain amount of nitrogen is retained in the body, probably as proteid, and the animal increases in weight. The amount of urea excreted by an animal is proportional not only to the quantity of proteid taken in with the food, but also to the weight of the animal; so the animal which has grown heavier in consequence of increased supply of nitrogenous food will need a larger amount of proteid to maintain its nitrogenous equilibrium, which will be produced with the same amount of proteid as soon as the animal has increased in weight to a certain extent. In order, therefore, to maintain the increase in weight, it is necessary to give ever-increasing quantities of proteid, and the stuffing process is finally put an end to by the refusal of the digestive organs to digest any more.

The experiments on feeding with purely proteid food have been made chiefly on dogs. In men it is found that administration of an exclusively proteid diet very soon

gives rise to digestive disturbances, and the experiment has to be discontinued.

It is necessary to consider the effect on metabolism of mixing fats or carbohydrates with the proteid in the food. It is found in dogs that if fat be given at the same time as proteid, the animal requires about 7 per cent. less proteid in order to maintain his nitrogenous equilibrium. It is apparent that the fat exercises a 'sparing' effect on the proteid, and is able to replace a certain amount of the proteid in the metabolism of the body. With this mixed diet the animal now draws part of the energy required from the consumption of fats instead of from the consumption of proteids. Carbohydrates have a still further sparing effect on the proteid, so that about 10 per cent. less proteid is required for the production of equilibrium. In fact, if very large quantities of carbohydrates and fats be given, nitrogenous equilibrium may be attained on an amount of proteid food which only just corresponds to the nitrogenous excretion during starvation.

Formation of Fat

If, while the animal is in a state of nitrogenous equilibrium, larger amounts of fat or carbohydrates be given than are necessary for its daily consumption, the animal increases in weight, and the excess of carbonaceous material is deposited in its body in the form of fat. It is probable that fat may be formed in the body from all three classes of foodstuffs. On a purely proteid diet no very large amount of fat, if any, is ever deposited in the body. A formation of fat from proteid, though not indubitably proved under normal circumstances, certainly occurs under pathological conditions in the higher animals and in many lower organisms. Thus, if dogs that have been starved till all fat has disappeared from the body be poisoned with phosphorus, a large increase in the nitrogen excretion is

observed, and when the animal dies all its organs are found to be in a state of fatty degeneration, and to contain two or three times the normal amount of fat. Here there is evidently a splitting up of the proteid molecules of the tissues into a nitrogenous moiety, which is excreted, and a carbonaceous moiety, which is retained in the cells in the form of fat. In the ripening of cheese, which is accomplished by the agency of low organisms, there is a conversion of proteid into fat. If the eggs of fly-maggots be allowed to develop on a blood-clot, the maggots, when full grown, will be found to contain ten times as much fat as there was previously in the blood-clot and eggs together ; so that in this case the maggots have been able to convert the proteid of the blood-clot into fat. We must conclude, therefore, that proteids may be converted into fat in the living organism, although we are at present unable to say how far such conversion takes place under normal conditions.

It was long doubted whether the fat in the food could be directly deposited in the body as such. It was supposed that the fat in the food exerted merely a sparing effect on the fat in the body formed from the proteids—that the fats absorbed from the alimentary canal served to supply the organism with an oxidisable material, and so shielded from oxidation the fat in the tissues that had been formed from proteid. We have, however, conclusive evidence that the fats taken in with the food are deposited in the body as such. Thus two dogs were fed, one with linseed oil, the other with mutton suet, for a considerable period. The fat in the tissues of the former was liquid at 0° C., while the fat of the latter had a melting-point at above 50°. In another experiment, in which a dog had been fed with colza oil, erucic acid, which is an ingredient of colza oil but absent from animal fat, was found in the fat of the dog after death.

Not only are neutral fats thus absorbed from the intestine and deposited in the body, but also fatty acids.

If these be administered to an animal the greater part is absorbed, and it is found that in the chyle of the thoracic duct nearly the whole of the fat is present as a neutral fat and not as a fatty acid, showing that in the passage of the fat from the intestine through the wall of the villi into the lacteals there has been a synthesis of fatty acid with glycerin. This is an interesting fact, since glycerin is at no time found free in the animal body, although we see that the epithelial cells of the intestine can supply sufficient of it to unite with nearly the whole of the fatty acid absorbed.

Long experience has shown the farmer the value of carbohydrates as fattening food. As in the case of fats, the question has arisen whether the carbohydrates are converted into fat, or whether they only effect a sparing influence on the hypothetical fat formed from the proteids of the food. That the former is the case is shown by the following experiment. Two young pigs, ten weeks old, of the same litter, with approximately equal weights, were taken. One was killed, and the fat and total nitrogen in the body estimated. From the amount of nitrogen the maximum possible quantity of proteids present was calculated. The second was fed on barley for four months. The barley was measured and analysed, as well as the amount of undigested fat and proteid that passed through the animal. At the end of the four months the second animal was killed and analysed. It was found that the animal contained 1·56 kilos. more proteid, and 8·6 kilos. more fat. It had taken up with the food 7·49 kilos. more proteid, and 0·66 kilo. fat. If we subtract the proteid added to the body (1·56) from that taken up with the food (7·49), there is a remainder of 5·93 kilos. which might possibly have given rise to fat. But 7·9 kilos. of fat had been added in the body—a far larger amount than could possibly have arisen from the maximum amount of proteid left over for the purpose. At least 5 kilos. of fat in this experiment must have been derived from the

direct conversion of the carbohydrates of the food. We must conclude that fat can be formed directly from carbohydrates, although how and where this conversion takes place is at present quite unknown. We have, however, parallel instances in the formation of butyric and other acids of the fatty acid series from sugar by means of certain organised ferments.

As we should expect, peptones may be used entirely to replace the proteids of the food, and the animal will maintain or even increase its weight on such a diet.

Gelatin cannot take the place of proteids in the food. As we have seen, it differs from ordinary proteids in certain important chemical relationships. If given in the food, it has, like carbohydrate and fat, a sparing effect on the proteid, so that nitrogenous equilibrium is attained with a smaller amount of proteid than would be the case if no gelatin were given. If a dog be fed on gelatin and fat, the excess of the nitrogen excreted over the nitrogen taken in is less than when the same dog is fed on fat alone, showing that the gelatin has sheltered from disintegration some proteid constituents of the body. It has been said that gelatin can take the place of circulating, not of tissue proteid.

History of Carbohydrates in the Body

Normally, the blood of man and dogs contains from 0·05 per cent. to 0·15 per cent. of sugar (dextrose). If this amount be artificially increased by injection of sugar into the blood, it is found that as soon as the amount of sugar rises above 0·3 per cent., the excess is eliminated by the kidneys and appears in the urine. After a meal rich in carbohydrates, such as the Irishman's mess of potatoes, an enormous amount of sugar passes into the blood of the portal vein. Several hundred grammes, however, of carbohydrates may be ingested without any sugar appearing in the urine. Again, in the intervals between meals when

no sugar is passing into the blood, the amount of sugar remains constant, although we have reason to believe that it is incessantly being used up by the muscles and other tissues of the body. There must be some means, therefore, by which the overloading of the blood with sugar is guarded against, at the same time that the sugar percentage of the blood is maintained constant during periods of temporary starvation. This function is subserved by the liver, the great chemical factory of the body. This is shown by the fact that if a solution of dextrose be slowly injected into a mesenteric vein, no sugar appears in the urine, whereas glycosuria is at once produced if the injection be made into the jugular vein.

Just as plants have the power of transforming sugar into starch, which is deposited as a reserve material in their tubers and similar organs, so the liver has the power of seizing upon the excess of sugar passing through its capillaries and transforming it into a colloidal substance, which is deposited in the meshes of the cell-protoplasm. This colloidal substance belongs to the group of starches, and is called glycogen or animal starch.

Preparation of glycogen.—A rabbit is well fed with carrots for a couple of days. It is then killed by decapitation, the liver cut out and thrown into boiling water, and boiled for about ten minutes. The pieces are then ground up with sand to a fine paste, returned to the same water, and boiled for half an hour. While the mixture is still boiling a few drops of acetic acid are added until the reaction is very faintly acid. In this way nearly all the proteids are coagulated. The mixture is then thrown on a filter, and an opalescent fluid runs through containing only the merest traces of proteid. From this fluid the glycogen is precipitated as a white amorphous powder by addition of two volumes of 90 per cent. alcohol. It may be purified by solution in water and reprecipitation by alcohol; it is finally washed with alcohol and ether and dried. It may be freed from adherent traces of proteid

by boiling with alcoholic solution of potash, in which the glycogen is insoluble.*

In the liver treated in this manner we find only the merest traces of sugar. If, however, the liver be left for some hours after the death of the animal before extraction with boiling water, the extract will be found to contain much less glycogen, but very large quantities of sugar. We see that after death a process takes place in the liver by which the glycogen is converted into sugar. This sugar is dextrose. This conversion may take place even after the cells have been subjected to the action of absolute alcohol for a considerable time. This fact shows that the conversion is due to the presence in the liver of some substance which may act as an amylolytic ferment, converting starch or glycogen into sugar. This ferment is destroyed by heat, and it is on this account that the liver is thrown into boiling water in order to obtain the maximum yield of glycogen.

Circumstances influencing the formation of glycogen.—The amount of glycogen present in the liver at any given time is intimately dependent on the food taken. If an animal be starved the glycogen in the liver diminishes quickly at first, and more slowly afterwards. After prolonged starvation the liver contains only the merest traces. If a rabbit deprived of glycogen in this way by starvation be given a meal of carbohydrates and killed a few hours later, the liver will be found to contain large quantities of glycogen.

Although carbohydrates furnish the chief material for the manufacture of glycogen, yet we have evidence that the organism is able to form glycogen out of proteids. If a dog, deprived of glycogen by long starvation and work, be fed for a few days on a diet of washed fibrin perfectly free from carbohydrates, the liver will be found to contain a fair quantity of glycogen, though the amount is many times less than that formed on a diet of carbohydrates.

* For Chemical Properties of Glycogen see Chap. II, p. 46.

Fats have no influence on the formation of glycogen. The glycogen disappears as rapidly in an animal fed on fat alone as in starvation.

Much more efficacious than starvation in causing disappearance of the hepatic glycogen is muscular work. If a dog be starved for a day and be then made to drag a heavy milk-cart about all the next day, there will only be found the merest traces of glycogen in its liver.

Glycogen is also found in the muscles, where it probably serves as a local supply of reserve material for the furnishing of muscular energy. The glycogen must be conveyed from the liver to the muscles and other organs of the body in the form of sugar, since we cannot detect any glycogen in the blood. The importance of glycogen as a reserve material is shown by the fact that it is present in enormous quantities in embryonic muscle, just when the formation of new muscular fibres is going on most intensely.

We may also look upon glycogen as a source of heat. If the temperature of a rabbit be lowered by immersing it in a cold bath, the glycogen is found to have disappeared from the liver after a few hours.

Under certain circumstances the power of the liver to store up glycogen may be temporarily destroyed. If a puncture (*piqûre*, or diabetic puncture) be made in the floor of the fourth ventricle between the origins of the auditory and vagus nerves, the animal for the next twenty-four or thirty-six hours will suffer from glycosuria ; that is to say, sugar will pass into the urine. At the end of this time the liver will be found to be quite free from glycogen. If, on the other hand, the animal be first deprived of glycogen by starvation and work, the diabetic puncture will be without effect, showing that the glycosuria is due to the rapid conversion of the hepatic store of glycogen into sugar. This is turned out into the blood-stream, where it raises the percentage amount of sugar so high that the excess is excreted by the kidney-cells and appears in the urine. Temporary glycosuria may be

brought about by various other means, such as poisoning by strychnine or curare. After administration of chloral and some other drugs, a reducing body appears in the urine, which was formerly thought to be dextrose. It has been proved, however, that in this latter case the reducing body is not dextrose, but an oxidation product of dextrose, *glycuronic acid* ($C_6H_{10}O_7$).

The results of the administration of phloridzin throw some light on the carbohydrate metabolism of the body. Phloridzin is a glucoside found in the root cortex of apple and cherry trees. If a certain amount of this be administered to a dog, sugar appears in the urine after a few hours, and the glycosuria lasts for two or three days. If the dog be killed at the end of this time, the liver and muscles are found totally free from glycogen. We might thus come to the conclusion that the sugar was divided from the glycogen stored up in the body, and from that alone, as is the case after the diabetic puncture. But if, when the glycosuria has ceased and the body is quite free from stored-up glycogen, a second dose of phloridzin be given, a still larger amount of sugar is excreted.

As the dogs were starved during the experiment, this sugar must have been derived from proteid. Thus we see that sugar as well as glycogen may be manufactured in the body directly from proteid.

In the disease known as diabetes the patient passes large amounts of sugar with the urine. Some of these cases may be due to defective power of the liver to store up glycogen, so that the excess of sugar taken in with the food passes at once into the general circulation, and is excreted by the kidneys. Such cases may be successfully treated by limiting the amount of carbohydrates taken in with the food. This, however, cannot be the explanation of the ordinary cases of severe diabetes. In these the patient passes sugar even during starvation or on a pure proteid diet, just as in the case of a dog poisoned with phloridzin. In these cases glycogen is found in the liver

after death, so that this function of the liver is certainly not wanting. The passage of sugar into the urine probably depends on the inability of the organism to utilise the sugar taken in with the food or split off from the proteids of the body. It is found, therefore, that the excretion of urea is also increased. In fact, the man is in a condition of an animal fed on proteids alone. Since the carbohydrates cannot be utilised, the organism has recourse to the proteids to cover the whole expenditure of energy, and hence the increased excretion of urea.

Why the power of utilisation of the sugar is defective we do not know. It may be that the sugar has to be further elaborated in certain organs before it can be used up by the general tissues of the body. Such a function of elaboration may possibly belong to the pancreas. If this organ be extirpated in a dog, the animal acquires severe diabetes, which proves fatal in a few weeks. Ligature of the duct is insufficient to produce this result. If a small fragment of the gland be left, the animal does not get diabetes. We thus see that we are far from having exhausted the functions of the pancreas when we have described its *rôle* in digestion; and it is possible that many organs of the body have similar mysterious and at present undreamt-of parts to play in the complicated processes of the body included under the term metabolism.

The whole question of diabetes is, however, too difficult to be dealt with at greater length here. Although the researches into its causation have thrown some light on the normal carbohydrate metabolism of the body, yet the light is at present only sufficient to intensify the black shadows of ignorance that obscure almost every part of our knowledge of the subject.

The Source of Muscular Energy

It was always maintained by Liebig that the foodstuffs might be divided into two main groups—the carbohydrates

and fats that gave rise to the heat produced in the body, and the proteids which were the source of muscular energy. This view was, however, refuted once and for all by the classical experiment of Fick and Wislicenus (1865). These observers ascended to the summit of the Faulhorn, which is 1956 metres high. The urine they secreted during the six hours' ascent and during the succeeding six hours was collected, and from the amount of nitrogen contained in this was calculated the amount of proteid that was used up during this time. It was found that in the case of Wislicenus 37 grms. proteid had undergone oxidation. It was calculated that the oxidation of this quantity would produce 250 heat units (the unit of heat here employed is that amount of heat necessary to raise the temperature of one kilogramme of water one degree Centigrade). This heat is equivalent to about 100,000 kilogram-metres of work. But Wislicenus weighed 76 kilos., so that in raising his body to the height of 1956 metres he had performed $76 \times 1956 = 148{,}656$ kilogram-metres of work. There was, moreover, a large expenditure of energy in the movements of the heart and respiratory muscles, which is not taken into account here; so that the amount of work done was far larger than could be accounted for by the oxidation of proteids.

If the income and output of a man be compared for several days, on some of which work is done, while on others no work is done, it is found that the consumption of oxygen and the production of CO_2 are much larger on the working days than on the resting days, and that in fact the increased oxidation of carbon which takes place is sufficient to account for the energy expended. The nitrogen excretion, on the other hand, is either not altered at all or is only slightly increased. This slight increase may be due to the increased wear and tear of the protoplasmic mechanism of the muscle, and is not nearly sufficient to account for the energy expended.

If a dog be starved for six successive days, and on the

last three be made to do hard work, it is found that the increase in the excretion of urea on the last two days is still quite small. As we have already seen, one day's starvation and hard work is sufficient to get rid of all glycogen from the body. Hence it is evident that in the last two days the energy for the performance of muscular work must have been derived from fats. We must conclude that normally the fats and carbohydrates are the chief sources of muscular energy.

If an animal be fed on a pure proteid diet, work increases the excretion of urea, since the energy in this case has to be derived from the disintegration and oxidation of proteids. The experience that we have acquired from 'training,' in which process large amounts of proteid food are taken while fats and carbohydrates are diminished, seems to show that a muscle perhaps works more economically when fed on proteids than when fed on fats and carbohydrates. At all events, the sweating and distress of a man fed on rich diet as contrasted with the 'fitness' of a well-trained man after muscular exertion, would appear to indicate that in the former the heat formation concomitant with muscular contraction is out of all proportion to the work done. Muscle draws its energy from all three classes of foodstuffs. So long as carbonaceous food is supplied in sufficient quantity, or is present in the body in the form of fat or glycogen, the muscle chiefly makes use of this for the energy required in the contraction. If this is not given, or if the carbonaceous stores of fat and glycogen are used up, muscular work must be maintained by the disintegration of proteid.

Animal Heat

All the energy that is set free by the decomposition and oxidation of the foodstuffs appears as work or heat. It has been reckoned that about nine tenths of the energy

set free in the body appears in the form of heat, and one tenth is represented by the work done. In the chapter on Muscle we saw that its efficiency as a heat-engine varied within very wide limits, the proportion of heat evolved to work done in muscular contraction being from 5 : 1 to 25 : 1. Even if we take the lowest of these estimates, we see that a very large proportion of the heat produced in the body must be evolved by the muscles. The increased production of heat attendant on bodily exercise is familiar to every one. If the spinal cord of an animal be excited by faradic currents, so as to cause tetanic contraction of all the limbs, the production of heat in the muscles is so large that the temperature of the animal may rise to 110° or 112° Fahr. —a rise which is fatal.

Next to the muscles in importance as a source of heat to the body is the liver. In fact, under normal circumstances the temperature of the blood in the hepatic vein is higher than in any other part of the body. Wherever active processes of katabolism are going on there is an evolution of heat. Probably there is a similar evolution of heat accompanying the activity of every gland in the body.

We must also look upon the brain as a source of heat, since thermometers inserted in it may register a higher temperature than that of the blood which is supplied to the brain. The amount of heat produced here is, however, insignificant compared with that formed in the muscles and liver.

On the processes of metabolism—the decomposition and oxidation of foodstuffs—depends the maintenance of life. Hence all living animals are continually producing heat and imparting it to the surrounding bodies; and they must, therefore, always have a higher temperature than the surrounding medium, although the difference may not amount to more than two or three degrees in cases where metabolic processes are going on sluggishly.

With respect to their internal temperature, animals may be ranged into two main classes : (1) those which have a

fixed temperature, which is within certain limits independent of the surrounding medium—*homœothermic* animals; (2) those in which the temperature varies with that of the surrounding medium—*poikilothermic* animals. To the first class belong birds and mammals, including man; they are often spoken of as warm-blooded animals. The lower Vertebrata, including reptiles, amphibians, and fishes, and the Invertebrata, belong to the second class of poikilothermic animals.

We must now inquire into the means by which this regulation of the internal temperature in warm-blooded animals is effected. The temperature of an animal is the product of two factors—the amount of heat produced and the amount of heat lost in a given time. If, while the heat production remains constant, the amount of heat imparted to the surrounding medium be increased, the temperature will fall. If, on the other hand, heat loss remaining constant, heat production be raised, the temperature will rise in the same proportion. So the temperature may be regulated by alterations in the heat production or in the heat loss; and if the temperature is to remain constant, there must be an accurate correlation between the two processes.

Regulation of production.—It has already been mentioned that if a frog or other cold-blooded animal be exposed to a higher temperature, its internal temperature will also rise. If, at the same time, we measure the respiratory interchanges of the frog, we find that at the higher temperature more carbon dioxide is evolved and more oxygen taken up, showing that in this case a rise of temperature in the surrounding medium causes a rise in the temperature of the frog, and at the same time increases the activity of its metabolic changes. Cooling has the reverse effect. If a frog be cooled to 0° C., the chemical changes in its tissues are so reduced that it may be kept alive for some days in an atmosphere devoid of oxygen. The case is quite otherwise with warm-blooded animals. Exposure of one of

them to a cold medium raises the amount of carbon dioxide given off and oxygen taken in, while the temperature of the animal remains unaltered. This power of the animal to *react* to changes in the temperature of the surrounding medium is dependent on the integrity of the nervous system and its connection with the muscles. If a dog or rabbit be poisoned with curare (which paralyses the muscle end-plates), or if its spinal cord be divided just below the medulla, its temperature sinks continuously. It is then found that the animal reacts to changes in the temperature of the surrounding medium precisely like a cold-blooded animal—rise of the external temperature causing rise of the internal temperature and increased elimination of CO_2, while a fall of the external temperature has the reverse effect.

It is still a subject of debate, what is the exact nature of the action of the central nervous system on the heat production of the body. It is evidently effected through the muscles, and partly, at all events, by means of muscular contractions. The increase of the tone in the muscles, and the general stringing up of the body after a cold bath, is an example of this. If the cold be more severe, the reflex contractions are more pronounced, and take on a clonic character, as shivering and chattering. A man, too, instinctively has recourse to muscular exercise to ward off the effects of extreme external cold. It has been thought, however, that the nervous system has a distinct influence on the thermogenic properties of muscles, apart from its action in producing muscular contraction; and that nervous impulses may call forth chemical changes in the muscle which give rise to heat and heat only. This view is supported by several phenomena, such as the increased production of heat in fevers, accompanied by a rapid wasting of the muscles, although the muscular tone in these cases is depressed rather than heightened. If the anterior part of the corpus striatum be pricked or stimulated, the animal suffers from pyrexia or rise of internal

temperature for a day or two; and this rise is accompanied by increased elimination of CO_2 and production of heat. No special motor phenomena are observed in these experiments, and it has therefore been concluded that the increased heat production is due to a direct thermogenic action of the injury.

Far more important, however, than the regulation of the temperature by the production, is the regulation by the loss of heat. The channels of loss of heat may be classified as follows:

1. By the urine and fæces. In the warming of the food and drink taken into the body there must be a certain abstraction of heat from the tissues surrounding the alimentary canal, though this heat is not lost to the body till the warmed urine and fæces leave it. The amount lost in this way has been calculated to be about 3 per cent. of the total heat loss.

2. By the inspired air. The inspired air is taken in at the temperature of the surrounding atmosphere, and contains only a small amount of aqueous vapour. The expired air has a temperature of about one degree lower than the body temperature, and is saturated with watery vapour. Heat is therefore lost in respiration in two ways: 1st, in warming the inspired air; and 2nd, in the evaporation of large quantities of water. These two sources of loss constitute about 20 per cent. of the total heat loss.

3. By the skin. Here, again, the loss of heat is effected in two ways. 1st. By radiation and convection. By these means an interchange of heat takes place between the surface of the body and surrounding objects, tending to cool the body under ordinary circumstances when the external temperature is below 98·4° F., or 37° C., or to warm the body when the external temperature is higher than this, as during the hot season in the tropics or in a Turkish bath. The amount of interchange of heat between two bodies is directly proportionate to the difference of

temperature between them. Thus the warmer the surface of the body in comparison with that of surrounding objects, the greater will be the amount of heat interchange, which in this case implies a loss of heat to the body. Since very little heat is generated in the skin itself, its temperature is intimately dependent on the amount of blood flowing through it, and this in its turn on the condition of the blood-vessels of the skin. When these are dilated, there is a constant supply of warm blood from the deeper parts of the body to the skin, which therefore is kept warm and feels warm, both subjectively and objectively. Hence dilatation of the blood-vessels of the skin, under normal circumstances, brings about increased loss of heat. If, on the other hand, the vessels are constricted, the small amount of blood supplied to the skin rapidly becomes cooled, and the skin is also cool, and the loss of heat small.

2nd. By the evaporation of the sweat. In the conversion of water into watery vapour a large amount of heat becomes latent. This principle is made use of in making ice, or in cooling a bottle of water by surrounding it with damp cloths which are exposed to a draught of air to facilitate evaporation. If the secretion of sweat is small it evaporates as it is secreted, and the skin remains dry. This is spoken of as insensible perspiration. If the secretion be very copious it may be formed faster than it can evaporate, and appears on the skin as drops of sensible perspiration. The formation of sensible perspiration depends, then, on two factors—the amount of sweat secreted, and the rapidity of evaporation, which latter, again, is dependent on the amount of saturation of the surrounding atmosphere with watery vapour.

The loss of heat by the skin amounts to about 77 per cent. of the total heat loss, and is therefore the most important of all the channels for the discharge of heat. The regulation of the total heat loss is also effected chiefly by changes in the loss through the skin. The nervous

channels by which this is carried out are the vaso-motor and the sweat nerves. If the external temperature be below that of the body, the loss by radiation and convection may be sufficient to get rid of the excess of heat produced. If, however, the external temperature be higher than that of the body, radiation and convection will only serve to warm the body still further, and the sole loss of heat that can be effected is by the evaporation of sweat, which is accordingly, under such circumstances, secreted in large quantities.

Often, especially after severe muscular exercise, radiation and convection are not sufficient to carry off the excess of heat produced, and hence there is a copious secretion of sweat as well, even though the external temperature may be cool.

The evolution of heat is aided under such circumstances by two factors, viz. quickened and deepened respiration, by which a greater volume of air is warmed up to the body temperature at the expense of the body heat; and quickened heart-beat, by which more blood is driven through the dilated cutaneous vessels, and so a rapid loss of heat at the surface provided for.

In the dog, where there are no sweat-glands on the general skin, and the loss of heat by conduction and radiation is checked by the thick hairy coat, the quickening of respiration is the most important means for getting rid of the surplus heat produced in the body, and hence the panting and apparent distress of these animals in hot weather.

So perfect is the adaptation of the heat loss to the heat production, that a man may travel from the poles to the equator, may eat or fast, take violent exercise or rest, without causing an alteration in his temperature of 1° C.

The temperature of man, which varies from 97·8° F. to 98·4° F., undergoes certain diurnal variations, which are important, since they are reproduced in an exaggerated form in many fevers. The temperature is lowest between

2 and 4 a.m., and highest in the afternoon between 4 and 6 p.m.

The Normal Diet of Man

We have already seen that to maintain a man in perfect health it is necessary that his food shall contain examples of the five different sorts of foodstuffs,—proteids, carbohydrates, fats, salts, and water. The first three classes serve as sources of energy to the body. Salts and water are equally necessary, although they cannot serve as sources of energy.

Water forms an integral part of all living protoplasm; and the phenomena of life, even in the lowest organisms, are dependent on an adequate supply of this substance. Apart from its function as a constituent of protoplasm, it is also essential as a medium for carrying the foodstuffs to the tissues, and the waste products from the tissues and out of the body. We have seen that water, in being discharged from the body, has two functions—as a solvent of the effete nitrogenous and other material contained in the urine, and as a powerful means by which the excess of heat produced in the body is dissipated. To supply this loss, water must be a constituent of the foodstuffs.

The exact part played by salts in the body we do not know, although it has already been shown that the presence of calcium salts is a necessary condition for two physiological phenomena—the clotting of milk and of blood. It has been shown, moreover, that a frog's heart will go on beating for many hours if fed with a solution containing phosphates and chlorides of potassium, sodium, and calcium, although, if any one of these salts be absent, the heart soon comes to a standstill. Of the salts present in the body and taken in with the food, sodium chloride forms the largest quantity. The presence of potassium and phosphates, however, seems to be of more importance

in the active phenomena of protoplasm, since these are found in largest proportions in organs consisting chiefly of cells, with very little interstitial substance. It will be remembered, too, that potassium and phosphoric acid are the leading base and acid present in muscle and in blood-corpuscles. An animal, if fed on a diet free from salts, dies almost as quickly as an animal that is starved.

At an early period of life the human animal, as all mammalia, is fed exclusively on milk, and the composition of milk agrees almost entirely with the ideal composition of the normal human diet, that has been worked out by numerous authorities as the result of many laborious experiments. Thus it has been found that a man may maintain himself in perfect health, neither gaining nor losing weight, on a diet consisting of—

Proteids	100 grms.
Fats	100 „
Carbohydrates	240 „
Salts and water.	

In cow's milk we find that for every 100 grms. of proteid we take in 107 grms. fat and 140 grms. carbohydrates.

In human milk, for every 100 grms. proteid there are 170 grms. fat and 270 grms. carbohydrates.

The following table represents the average compositions of human and cow's milk:

	Human.		Cow's.
Caseinogen and lactalbumen	2	...	4
Fats	2·75	...	4
Lactose (sugar of milk) .	5	...	4·4
Salts	·25	...	·6
Total solids . . .	10	...	13
Water	90	...	87

Milk when fresh is slightly alkaline or neutral. On standing exposed to the air the lactose is converted by

the agency of micro-organisms into lactic acid. The milk hence becomes sour, and the caseinogen is precipitated.

Human milk has a specific gravity of 1025 to 1035.

The proteids of milk consist of caseinogen and lactalbumen. Caseinogen, which forms by far the greater quantity, is a complex proteid belonging to the group of nucleo-albumens. From milk it may be precipitated by the addition of acetic acid or weak mineral acid. When purified it forms a snow-white powder, insoluble in water, but easily soluble in dilute alkaline solutions, such as soda, ammonia, lime, or baryta water. From these solutions it may be reprecipitated by neutralisation. The purified caseinogen when moist has the power of reddening litmus paper, and is therefore looked upon as a weak acid. In the milk, caseinogen occurs in combination with calcium. Its power of clotting with rennet ferment has been already described (p. 222).

Lactalbumen, which resembles very closely serum-albumen, is only present in traces in cow's milk, but in much more considerable quantities in human milk. The relatively smaller amount of caseinogen in human milk probably accounts for the fact that the clot produced by rennet in the latter is flocculent, and does not form a firm compact mass as in cow's milk.

Fats occur in milk in the form of minute droplets of various sizes. It is the presence of these which gives to milk its brilliant white appearance. If milk be allowed to stand they rise to the surface, forming the layer of cream. The droplets are probably prevented from running together by being surrounded with a proteid envelope, or perhaps this is effected simply by the physical nature of the solution of caseinogen in which they are suspended. If cream be beaten or churned, this physical condition is overcome, and the fat droplets run together to form a mass known as butter. The fats of milk or butter consist of the glycerides of stearic, palmitic, and oleic acids, with

traces of the glycerides of capric, caprylic, capronic, and butyric acids.

The carbohydrates are represented by lactose ($C_{12}H_{22}O_{11}$). The properties of this body have been already described (p. 45).

The salts consist chiefly of the phosphates and chlorides of sodium, potassium, calcium, and magnesium. Of these calcium is present in the largest quantities to supply the material needed for the rapidly growing bones of the young animal. The potassium occurs in far larger amount than the sodium, as would be expected from what has already been said concerning the part played by potassium in the functions of living protoplasm.

Milk also contains small traces of iron in combination with some proteid body.

The food of the adult consists chiefly of meat, eggs, cereals, and green vegetables.

The following may be taken as an example of a complete diet (Waller):

		Carbon.	Nitrogen.
Foundation	1 pound bread	117 grms.	5·5 grms.
	½ pound meat	34 „	7·5 „
	¼ pound fat	84 „	—
Accessories	1 pound potatoes	45 „	1·3 „
	½ pint milk	20 „	1·7 „
	¼ pound eggs	15 „	2 „
	⅛ pound cheese	20 „	3 „
		335	21

This diet is considerably more liberal than that given on p. 337.

Meat consists of several animal tissues. Muscular tissue forms the greater part of it, though it also contains white fibrous tissue in the connective tissue and aponeuroses, and some interstitial fat. There is also a greater or less quantity of fat surrounding the muscles. Meat in

its most general sense, therefore, comprises proteids (myosin and albumen), fats, collagen or (in cooked meat) gelatin, and minute traces of carbohydrate, as glycogen or sugar.*

Eggs consist of two parts, the white and the yolk. The white is simply a solution of egg-albumen, with a small amount of globulin, enclosed in delicate membranes. The yolk contains a peculiar phosphorised proteid, vitellin, a large amount of fats, salts, and traces of sugar and iron. The latter, as in the case of milk, is present in a complex organic compound allied to the nucleo-albumens.

A hen's egg weighing 53 grms. (average weight) contains 31 grms. of white of egg (albumen and water with a small amount of globulin), 16 grms. of yolk, and 6 grms. of egg-shell. A man would have to eat twenty eggs a day in order to obtain the necessary amount of proteid.

The vegetable articles of diet are distinguished from the animal in containing a much larger proportion of indigestible material, chiefly consisting of cellulose. This also encloses much of the digestible portions of the vegetable, so that these also pass out in the fæces undigested. On this account a certain amount of vegetable food is of importance in the normal dietary, since the indigestible residue increases the bulk of the fæces, and aids the normal action of the bowels.

The cereals are the most important class of vegetable foodstuffs. They include wheat, barley, rye, oats, maize, and rice. Wheat-flour, out of which bread is made, contains proteids, carbohydrates, and a small amount of

* Lean beef contains in every 100 parts—

Proteids	18·36
Gelatiniferous substances	1·64
Fat	0·90
Extractives	0·90
Ash	1·30
Water	76·80

fat (less than 2 per cent.). The proteids, forming about 12 per cent., are two in number—a proteid belonging to the class of globulins, soluble in 10 per cent. NaCl, and an albumose. On treatment of flour with water a change takes place in these proteids, and the flour becomes sticky and 'doughy.' In the dough two proteids are found—*gluten*, or vegetable fibrin, and a sticky body, *gleiadin*, which is soluble in alcohol, and gives the reactions of an albumose. The carbohydrates consist almost entirely of starch, which forms about 70 per cent. of wheat-flour.

Bread is made by moistening flour with water, so as to form dough. The dough is mixed with yeast and set in a warm place to 'rise.' By the action of the yeast on the starch, first dextrin and sugar, and then alcohol are formed, with the evolution of carbon dioxide, which forms little bubbles in the dough, so that this swells up. The raised dough is then baked. In the latter process the starch, exposed to a temperature of 200° C. to 270° C., becomes partly converted into dextrin, and is therefore rendered soluble in water.

Green vegetables are chiefly valuable in the human dietary owing to the large proportion of salts and cellulose they contain. Potatoes consist nearly entirely of starch, containing very little proteid. Hence to support life by this means alone enormous amounts must be taken. It must be remembered that starch-grains are enclosed in a series of cellulose envelopes, and are therefore indigestible when raw. On boiling, however, the starch-grains swell, rupturing these envelopes, and the opalescent semi-solution of starch thus formed is easily acted on by the digestive juices.

Ductless Glands

Under this title have been grouped a number of organs, the sole resemblance of which lies in the fact that we

know very little about them. Since, however, they seem to exert important though obscure influences on the nutrition of the body, they may be fitly discussed at the end of this chapter on metabolism. The ductless glands include the spleen, thyroid, thymus, and suprarenal capsules. The spleen has been already considered in its relationship to the blood in Chap. VI.

The thymus is a body situated in the anterior mediastinum; it is richly supplied with blood-vessels, and is composed of modified lymphoid tissue, which is peculiar in containing epithelial remnants known as Hassall's corpuscles, and derived from the epithelium of the branchial clefts of the embryo. It is only of importance in early life; it is relatively large in the fœtus, and increases in size during the first two years after birth. It afterwards atrophies, and in adult life is represented by a small collection of adipose tissue. Of its function we know nothing. It is supposed that it is of importance in the formation of blood in the young animal. From the thymus a body can be extracted (tissue-fibrinogen) which, injected into the veins of an animal, causes intravascular clotting. This fact, however, does not throw any light on the normal functions of the gland, since a similar body may be extracted from almost any organ that is rich in cells.

The thyroid was probably at one time in the history of the race a secreting gland in connection with the alimentary canal. In the developing animal it is formed, just like the pancreas and liver, as an outgrowth from the fore-part of the alimentary canal. Long before the end of fœtal life, however, its duct becomes obliterated, and each acinus becomes closed. The acini are filled with a peculiar hyaline material known as the colloid substance, and are lined with a single layer of epithelium.

Although its primitive function of secretion is lost, it is still of the utmost importance in the metabolism of the body. If the thyroid gland be totally extirpated in young

animals the operation is followed, after a short time, by severe symptoms, consisting of fibrillar twitchings and spasms of the muscles, attended with weakness and stupor. These effects usually terminate in the death of the animal. In man it has been shown that a disease (myxœdema) occurring in adult life is dependent on the atrophy of this gland. The main symptoms of this disease are generally stupidity and slowness of speech of the individual, slow pulse, subnormal temperature, and a thickening of the subcutaneous tissues, so that the patient at first sight looks dropsical.

Cretinism is also associated with absence of the thyroid gland. A cretin remains a childish idiot all his life, and preserves his childish appearance. In these cases small fatty tumours are often found on each side of the neck just above the clavicle. We are absolutely unable to explain the connection of these manifold symptoms with the absence of the thyroid gland.

It is interesting to note that the symptoms after extirpation or atrophy of the gland may be relieved by injection of an extract of the fresh gland, or by administration of the fresh or dried glands of sheep by the mouth.

The suprarenal capsules.—Here, again, pathology has taught us more than physiological research. The disorder known as Addison's disease, and distinguished by the three cardinal symptoms of extreme weakness, vomiting, and pigmentation of the skin (which acquires a bronzed colour), was recognised by its discoverer to be due to atrophy of the suprarenal capsules. The explanations which have been brought forward of the connection of these phenomena with the extirpation or destruction of these capsules may be classified into chemical and nervous. The suprarenals have a twofold origin, their medullary part being derived from the sympathetic nervous system, and their cortical part from the surrounding mesoblast. The supporters of the chemical theory base their views on the fact that derivatives of hæmoglobin are to be found in

these organs, and they therefore look upon them as chemical depôts for the removal or destruction of the waste pigmentary products. Retention of these in the blood gives rise to poisoning symptoms, and to deposition of pigment in the skin. As upholding the function of these bodies in influencing nutrition through the nervous system, widespread degenerations in the central nervous system have been described after their extirpation in animals. The facts at present do not permit of our deciding between the two theories.

From the medulla of the suprarenal glands a substance has recently been extracted which in minimal doses produces most marked effects. The chief results of the injection of this substance are marked rise of blood-pressure, due to constriction of all the arterioles of the body, and increased strength of the heart-beats. The nature of the active principle and the part it plays in the normal economy are as yet unknown.

CHAPTER XI

SPECIAL SENSES

We must now consider the means by which the individual is made aware of the events occurring in the outside world, the means by which his environment acts upon him. This subject is comprised in the physiology of the special senses.

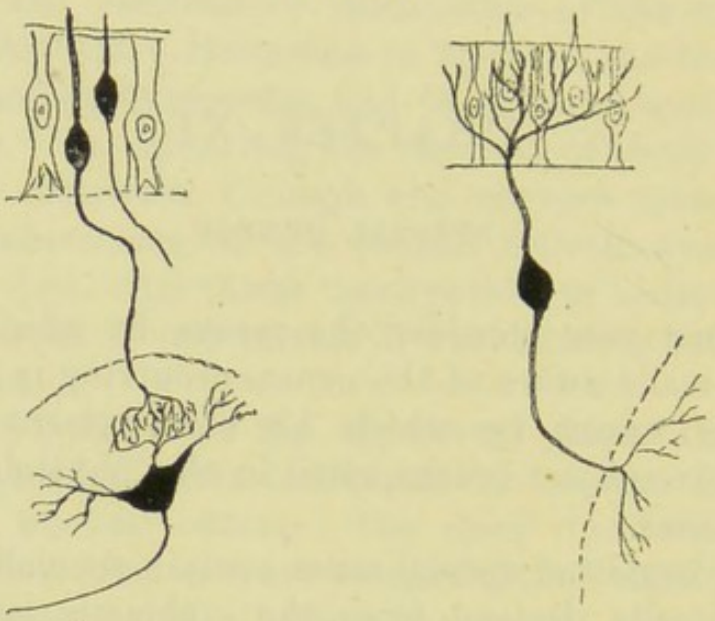
All the organs of special sense contain specially modified epithelial cells, derived from the epiblastic layer of the embryo, or processes of these cells. From the deeper side of these cells, processes or nerve-fibres grow into the central nervous system, and these break up into fine arborisations of fibres which come into close contact with other cells or fibres, and so make functional connection with the nerve-tracts which serve as paths to the higher centres, or to the cells which preside over the movements of certain muscles.

In some cases, such as the olfactory mucous membrane (Fig. 90, A), the sensory cell lies close to the periphery, and is the immediate recipient of the physical stimulus which it has to transmute into a physiological nerve impulse.

In the auditory organ the special sense-cell seems to be represented by the bipolar cells of the spiral ganglion. These (Fig. 90, B) send one process towards the organ of Corti, where it terminates in fine filaments among the hair-cells, and one running in the auditory nerve towards the medulla.

In other cases the sensory cell may lie still further away from the sensory surface. Thus, in the skin, the sensory filaments ramifying in the epidermis represent the terminal

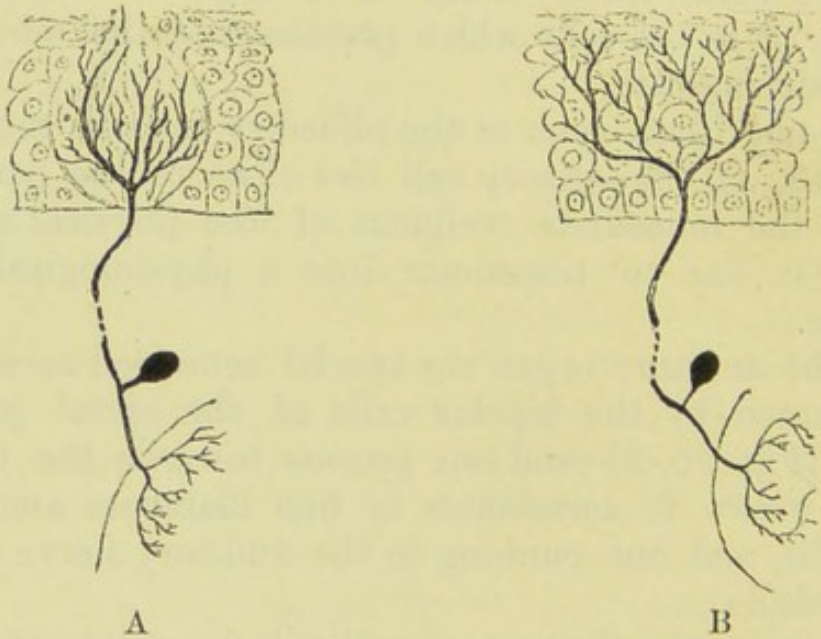
FIG. 90.



A B

A. Connections of olfactory cells with olfactory lobe.
B. Auditory sense-organs.

FIG. 91.



A B

A. Connections of gustatory fibres. (Taste-bud.)
B. Nerve-ending in skin or corneal epithelium (probably pain-fibres).

arborisation of the process of a cell in a posterior root ganglion. This process joins by a T-shaped junction with another process which runs centralwards and terminates in fine filaments in the grey matter of the spinal cord and medulla (Fig. 91, A).

The peripheral terminal filaments of these nerve-cells may either end freely among ordinary undifferentiated epithelial cells (as in Fig. 91, B), or may be closely applied to specially modified epithelial cells. Such special sensory epithelium is found in the taste-buds (Fig. 91, A) and in many parts of the skin (tactile corpuscles).

In every case a sensation, whether of heat, light, sound, or touch, is caused by some movement of molecules or masses occurring in the outside world, and the function of the special sense-organs is to be acted on by these movements and to convert them into a nerve impulse, which ascends an afferent nerve towards the spinal cord or brain. Arrived here, it gives rise to some form of reflex action, which may be unconscious or conscious. In the latter case we become aware of a *sensation* of light, heat, or sound, &c. Now it is found that if the nerve-fibres coming from a special sense-organ be stimulated artificially by electric shocks, or in any other way, we get a sensation similar in kind to that which would occur if the sense-organ itself were stimulated in the normal way. Thus stimulation of the optic nerve gives rise to the sensation of light; of the auditory nerve, to one of sound; of the nerves of smell or taste, to these respective sensations. This fact, which has not been proved experimentally for all sensory nerves, is yet so general that it has been formulated as a law, known as Müller's law of specific irritability. This law merely states that every sensory nerve reacts to one form of stimulus and gives rise to one form of sensation only; that every sensory nerve, in fact, minds its own business.

Most important in connection with the physiology of the senses is the fact that in some cases we are able to

project the stimulus, and recognise it as coming from an object at some distance from us. We can also *localise* the stimulus, and recognise what part of the body is being stimulated, or the position of the body in space from which the stimulus arises.

There is a certain proportionality between the strength of the stimulus and the intensity of the sensation produced; that is to say, a stronger stimulus will produce a stronger sensation. As the stimulus is increased, the amount of additional stimulus required to produce any appreciable increase of sensation is also increased. Thus we can distinguish the heavier of two weights—one of 39 oz., the other of 40 oz.; we cannot, however, between 39 lbs. and 39 lbs. 1 oz., but must add a whole pound to the 39 lbs. in order to appreciate a distinct difference. This fact is known as Weber's law, which runs thus:—*The increase of stimulus which is required to produce distinct increase of sensation always bears the same ratio to the whole stimulus.* In the example above given this ratio is 1 to 40 (muscular sense). In the case of the pressure or tactile sense the ratio is 1 to 30. This law only holds good within certain limits, and fails when the stimuli are very strong.

Besides the five senses that are commonly recognised—of sight, hearing, touch, taste, and smell—physiologists reckon the senses of heat and cold, pain, and the muscular sense. The indefinite sensations of hunger, thirst, weariness, &c., defy accurate physiological analysis.

Cutaneous Sensations

The whole surface of the body is susceptible to stimuli, which may give rise to sensations of touch, heat, cold, or pain; and it seems probable that these different kinds of sensation are served by four different sets of nerve-fibres.

The *tactile* or *pressure sense* seems to be dependent on the presence in the skin of certain end-organs which are

called touch-corpuscles. By means of this sense we are able to judge of the shape, consistence, and size of bodies in contact with the skin. We are also able to *localise* the exact point at which the skin is stimulated, but the accuracy of this localisation varies at different parts of the body. Thus if two points tipped with cork, a quarter of an inch apart, be applied to the tongue, they are perceived as two points; applied to the skin of the back they give rise only to one sensation. The following table shows the distances which two points must be apart in order to give rise to two distinct sensations:

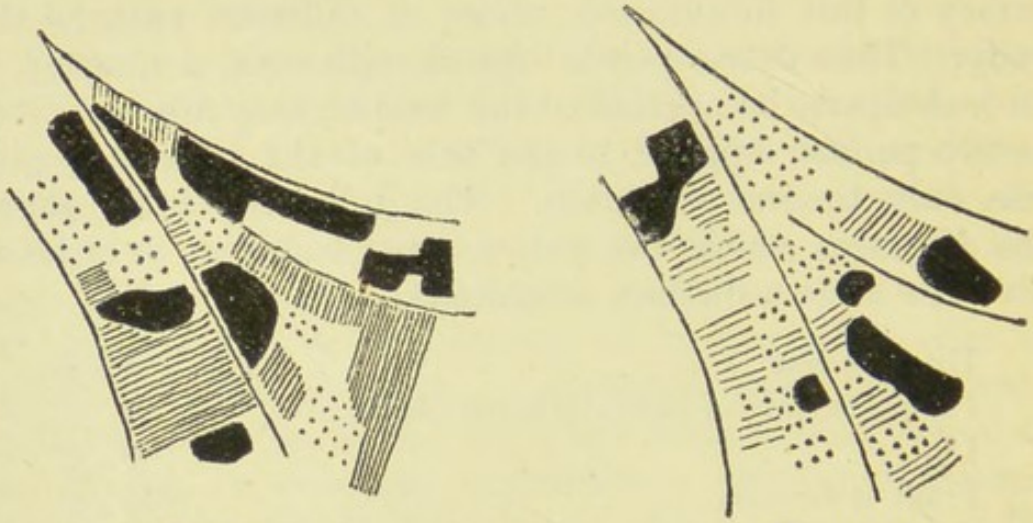
Tip of tongue	1 mm.
Palmar surface of hand, terminal phalanx	2 „
Lip	9 „
Front of forearm	15 „
Forehead	23 „
Back of hand	30 „
Neck, back, arm, and thigh	50—70 „

As we shall see later, tactile sensations are of immense importance in the reflex maintenance of equilibrium and the performance of co-ordinated movements.

Temperature sense.—Our subjective feeling of warmth or cold depends not on the temperature of the body itself, but on the temperature of the skin, where the special sense-organs are situated. It has been shown that there are two kinds of nerve-endings for temperature in the skin, which are respectively excited by heat or cold. Thus if a small metallic pencil, kept at body temperature by a stream of warm water through it, be moved gently over the skin, and the attention be directed on the sensations evoked, it will be found that while at some points the sensations are indifferent or merely tactile, at certain points the pencil may feel uncomfortably hot. The points where this is found to be the case are mapped out as heat-spots. By using a cool pencil a series of cold-spots may be mapped out in the same way, and it is found that this

series does not coincide with the first. Fig. 92 shows the distribution of the heat and cold spots.

FIG. 92.



Cold-spots. Heat-spots.

Heat and cold spots on part of palm of right hand. The sensitive points are shaded, the black being more sensitive than the lined and than the dotted parts. The unshaded parts correspond to those points where no special sensation was evoked. (Goldscheider.)

Over-excitation of the nerves of the skin, whether by cutting, electrical stimuli, excessive heat or cold, produces a sensation of pain. Hence it has been thought that pain is merely a hypertrophied tactile or temperature sensation ; but there are arguments which tend to show that pain is a distinct sense, and subserved by a distinct set of nerve-fibres. Many cases of disease occur in which the patient can feel the slightest touch, but is quite insensitive to pain. In other cases, in which the tactile sense is deficient, the pain sense may be exalted. We can, moreover, map out on the surface of the skin pain-spots similar to the heat and cold spots mentioned above.

Direct stimulation of the trunk of a nerve going to the skin only gives rise to a sensation of pain, whatever may be the nature of the stimulus. Thus plunging the elbow

into a freezing mixture excites the ulnar nerve, and gives rise to a sensation of pain which is referred to the ring and little fingers.

Muscular sense.—This term is applied to those sensations by which we know the position of our limbs, the extent to, and the force with which they have been moved. They are very complex in their nature, being made up of sensations from skin, joints, tendons, and muscles. That the muscles have afferent nerves distributed to them is shown by the fact that, if we cut the nerve going to a muscle, stimulation of its central end gives rise to reflex movements. We use this sense in judging of weights and differences of weights. It is thought by many that this sense is largely, if not entirely due to what is called a sense of innervation; that is to say, when we raise a weight, we know the strength of the impulse that starts from the motor cells in our brain, and tell the weight, not by the amount of stretching of the muscle or pressure on sensory nerves in the muscle, but by the amount of force we voluntarily put forward to raise the weight. The fact, however, that we can judge of weights when the muscles are made to contract by electrical stimuli, and not by voluntary impulses, shows that this sense is in large part, at any rate, peripheral.

Taste

The end-organs of the taste-nerves are represented by the taste-buds, which are oval bodies consisting of medullary and cortical parts, the former being composed of columnar cells, the latter of thin fusiform cells, among which ramify the terminal fibres of the gustatory nerves. These occur scattered over the tongue and soft palate, but are especially numerous in the trenches round the circumvallate papillæ. A sapid substance to stimulate these organs must be in solution; hence quinine in powder is almost tasteless, owing to its slight solubility in neutral or

alkaline fluids. We distinguish four primitive taste sensations, sweet, sour, bitter, and salt, and it is supposed that there are different nerve-fibres for each of these tastes. Most of our so-called tastes are really dependent on the sense of smell. Without this sense there would be very little difference between an onion and an apple. The epicure with a fine palate has really educated his sense of smell rather than of taste.

The nerves of taste are the glosso-pharyngeal, which supplies the back part of the tongue, and the lingual branch of the fifth nerve and the chorda tympani, which supply the front part.

Smell

The organ of smell is situated at the upper part of the nasal cavities. Here the mucous membrane covering the superior and middle turbinate bones and the corresponding part of the septum is different from that covering the rest of the nasal passages, which is ciliated columnar epithelium. The olfactory mucous membrane has no cilia, and consists of columnar cells and spindle-shaped cells, to the lower ends of which terminal branches of the olfactory nerve have been traced. A substance to excite a sense of smell must be in a gaseous condition. If the nasal cavities be filled with rose water, not only is no smell perceived, but the sense is paralysed for some time afterwards. It is impossible to give any classification of smells; their name is legion.

Hearing

Sound is a sensation produced in our ears by vibrations occurring in surrounding bodies, and transmitted to them by the atmosphere.

Sound produced by a regular series of vibrations is a musical tone: if the vibrations are quite irregular the effect is a noise. In a musical

tone we can distinguish three qualities, according to the character of the vibrations; these are pitch, loudness, and timbre or quality. The pitch of a note depends on the number of vibrations per second. A note of 400 vibrations is an octave higher than a note of 200 vibrations. The loudness of a sound depends on the amplitude of vibration. The timbre or quality is dependent on the presence with the fundamental tone of certain overtones or harmonics. Thus if we strike a piano string, the fundamental note of which is 100 vibrations, we get superposed on this tone a series of notes whose vibration frequencies are 2, 3, 4, 5, 6, 7 hundred. It is on the varying predominance of these overtones that the differences between a given note sounded by the organ, piano, trumpet, or violin depend.

If we raise the damper of a piano and sing into it, it will be noticed that a large number of the strings go on vibrating. This is due to the fact that every note in our voice is accompanied by overtones, and the piano strings pick out those overtones which correspond to them in vibration frequency (pitch); they are said to resonate. Instead of piano strings we may use cylinders of different lengths as resonators, and by employing a battery of these resonators it is possible to analyse all manner of compound sounds.

The organ of hearing may be considered as consisting of an accessory part and an essential part. The essential part is formed by the terminal expansion of the auditory nerve; the accessory part is constructed so as to bring the waves of sound to act on the end-organs.

The ear is divided anatomically into three parts; the external ear with the auditory meatus, the tympanum, and the internal ear. The external ear in the lower animals is fashioned so as to collect sound-waves from different directions; and to this end it is provided with muscles, and is very moveable. This function in man is rudimentary, so that he can hear almost as well with his ear cut off as normally. The meatus is separated from the tympanum by the drum of the ear, or membrana tympani. This is formed by a thin layer of fibrous tissue, covered with skin externally, and with mucous membrane of the tympanum internally. Attached to the point of its

inner surface, and dragging it inwards, is the handle of the malleus. The attachment of this to the membrane is eccentric—an arrangement which is of great importance, since the membrane in this way is rendered aperiodic, *i. e.* it will vibrate with equal facility to any number of vibrations, and not pick out a particular note, as a drum that was equally stretched all round would do.

The cavity of the tympanum is connected in front with the pharynx by means of the Eustachian tube. This is opened by each movement of swallowing, so that the pressure in the tympanum is kept equal to that of the outside air. If the Eustachian tube be blocked by disease, the cavity of the tympanum becomes distended, and the

FIG. 93.

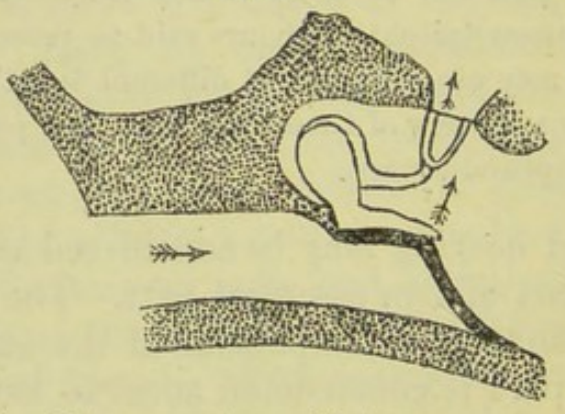


Diagram of auditory meatus, with tympanum and auditory ossicles.

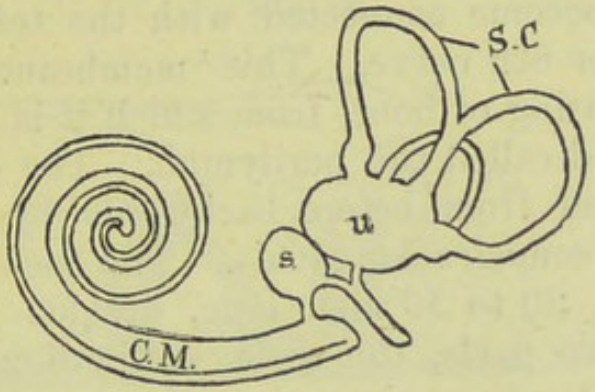
patient becomes deaf on that side. Stretching across the tympanum, from the membrana tympani to the outer wall of the internal ear, is a chain of ossicles, the malleus, incus, and stapes. The base of the stapes is inserted into the foramen ovale, being joined to its margins by a membrane. This chain of bones acts as a system of levers, by which the vibrations of the tympanic membrane are transmitted to the fluid in the internal ear.

The excursion at the end of the lever formed by the stapes is only two thirds of the excursion of the handle of

the malleus, so that, in their transmission through the ossicles, the vibrations are diminished in extent but increased in force.

The tensor tympani muscle, which is attached to the handle of the malleus, serves by its contraction to draw

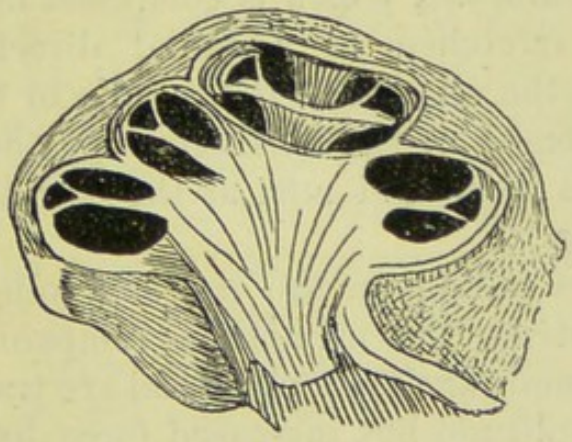
FIG. 94.



The membranous labyrinth. C.M. Canalis media of the cochlea. S. Saccule. U. Utricle. S.C. Semicircular canals.

this in, and to render the membrane more tense, and therefore more easily affected by high notes. The stape-

FIG. 95.



Vertical section through the cochlea.

dius muscle, when it contracts, tilts the stapes backwards. Its use is unknown.

The internal ear consists essentially of a membranous

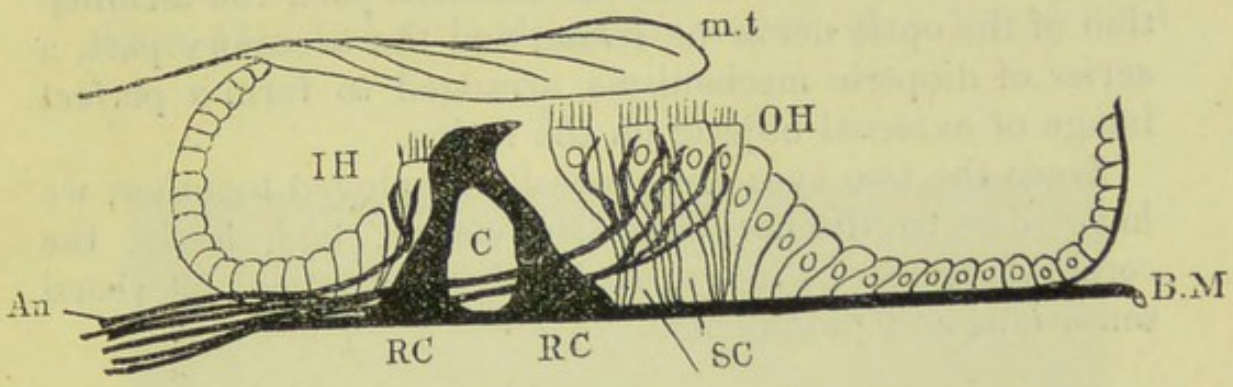
sac, which is formed by an involution of the epithelium covering the surface of the embryo. In the course of development the sac, which is filled with a fluid called endolymph, becomes much modified in shape, forming from before backwards the scala media of the cochlea, the saccule, the utricle, and the three semicircular canals. At certain parts of its inner surface thickenings of the epithelium occur, which become connected with the terminations of the auditory or 8th nerve. This 'membranous labyrinth' lies inside a casing of bone, from which it is separated by a layer of fluid called the perilymph. The osseous labyrinth is formed from before backwards by the cochlea, vestibule, and semicircular canals. The cochlea is a spiral tube of bone, 20 to 30 mm. long, divided by the scala media into two parts, the scala vestibuli and the scala tympani, which are continuous at the apex of the spiral (helicotrema). The scala media contains the essential part of the organ of hearing, which is called the organ of Corti (Fig. 96). This consists of a double row of stiff cells—the inner and outer rods of Corti, supporting on each side one or three rows of *hair-cells*, which are continuous with the terminations of the auditory nerve. The organ rests on the basilar membrane, which is composed of a number of elastic fibrils stretched in a radial direction from the central axis of the cochlea to the middle of the wall of the spiral. The length of the fibrils forming the basilar membrane increases from ·041 mm. at the base to ·495 mm. at the helicotrema.

Sound-waves falling on the ear are collected into the meatus, and strike the membrana tympani. The vibrations of the membrane thus produced are transmitted with diminished amplitude but increased force by the chain of ossicles to the foramen ovale, where they are communicated to the perilymph. The vibrations travel in the perilymph from the vestibule to scala vestibuli and scala tympani, and end on the membrane closing in the foramen rotundum, a small opening in the inner wall of the tym-

panum at the base of the scala tympani. In their course the vibrations set the basilar membrane of the scala media into vibration, and in this way affect the hair-cells and the terminations of the auditory nerve.

The fact that we are in many cases able to resolve the compound sound into its simpler components, that a

FIG. 96.



Section through the end-organ of the auditory nerve in the cochlea (organ of Corti). B.M. Basilar membrane. C. Canal of Corti. RC. Rods of Corti. IH and OH. Inner and outer hair-cells. S.C. Sustentacular cells. An. Auditory nerve. m.t. Membrana tectori.

musician can name the notes forming a chord struck on the piano, shows that there must be some mechanism in the ear by which the sounds are analysed. This mechanism is supposed to be furnished by the basilar membrane. It is thought that the longer fibres near the apex of the cochlea vibrate only to low notes, and that the shorter fibres near the base of the cochlea vibrate only to high notes, and that when a chord is struck it sets into vibration fibres of the basilar membrane at different parts of the cochlea, each of which excites the hair-cells and auditory nerve-endings lying immediately on it, giving rise to a series of simple sensations.

The rate of vibration frequency, within which an audible note is produced, may extend from 16 to 40,000 vibrations per second, although in most people no sound is produced

by vibration frequencies below 30 or above 30,000. According to Exner, two sounds following one another are perceived as distinct if the interval between them is not less than ·002 second.

Vision

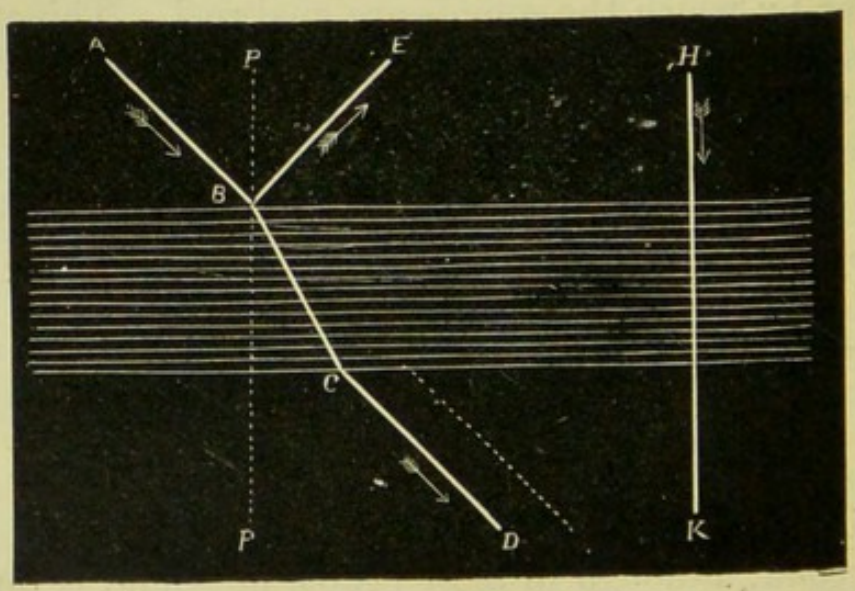
In treating of the functions of the eye, the organ of vision, we have to consider the essential part, the termination of the optic nerve or *retina*, and the accessory part, a series of dioptric mechanisms, arranged to form a perfect image of external objects on the retina.

Since the two eyes are generally employed together, we have also to discuss binocular vision; and, lastly, the cerebral processes engaged in the formation of visual sensations and judgments.

The Manner in which a Distinct Image of External Objects is formed on the Retina

The eye may be compared to a photographic camera, the lens being represented by several refracting surfaces, the

Fig. 97 A.

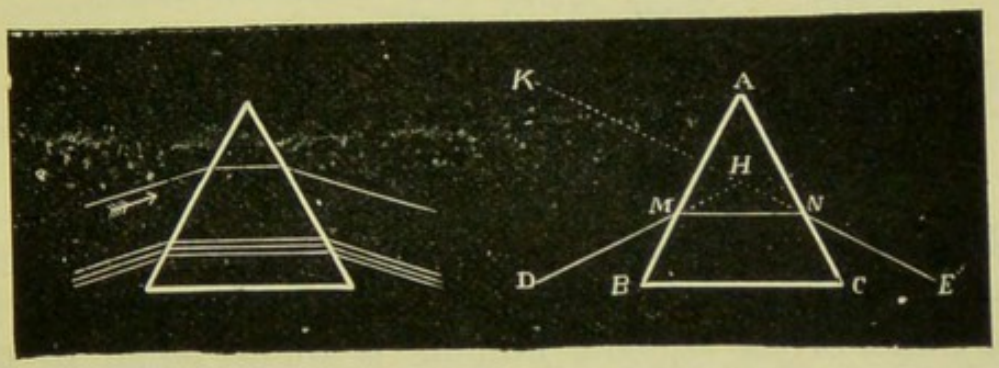


cornea, lens, and vitreous, and the sensitive plate on which the image is formed by the retina.

A ray of light when passing obliquely from a medium of low density (such as the air) to a medium of high density (such as water or glass) changes its course, being bent towards the perpendicular drawn to the surface separating the two media. On leaving the dense for a rarer medium it is bent once more away from the perpendicular.

Figs. 97 A and B represent the course of a ray of light

FIG. 97 B.



in passing through a plate of glass with parallel sides, and through a prism.

By means of a convex lens the rays of light from any one source may be all refracted so as to meet at a point. The point at which parallel rays of light (such as the sun's rays) meet is called the principal focus of the lens (Fig. 98).

FIG. 98.

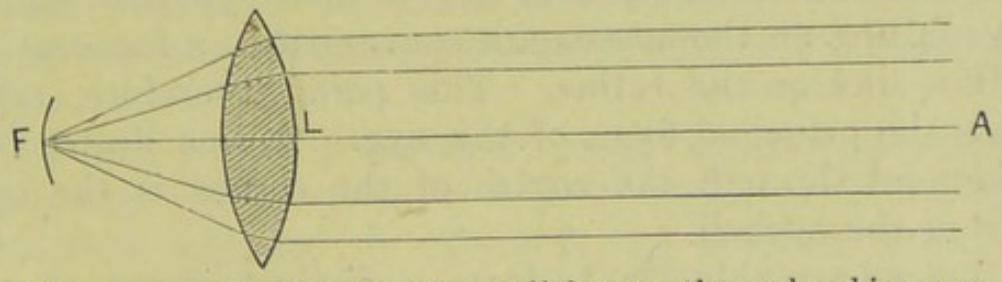
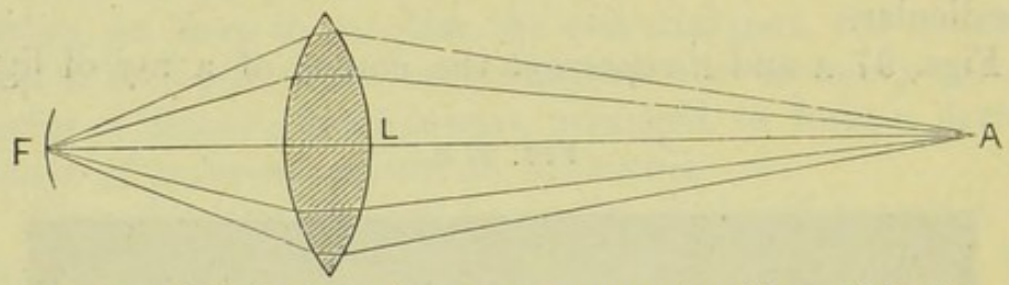


Diagram of the course of parallel rays through a biconvex lens, by which they are converged to the principal focus, F.

If the origin of the rays be a point of light near the lens, so that the rays are not parallel, they are converged by the lens to a point (secondary focus) situated further away from the lens than the principal focus. The two points, the point whence the rays of light diverge and the point to which they converge, are called *conjugate foci* (Fig. 99).

FIG. 99.



The rays of light from A converge on passing through the lens to the secondary focus, F. F and A are conjugate foci.

In the eye there are several surfaces separating different media where refraction takes place. Since the refractive index of the aqueous humour is almost equal to that of the cornea, we may reduce the refracting surfaces to three, viz.—

Anterior surface of cornea,
Anterior surface of lens,
Posterior surface of lens;

and the refracting media to three—

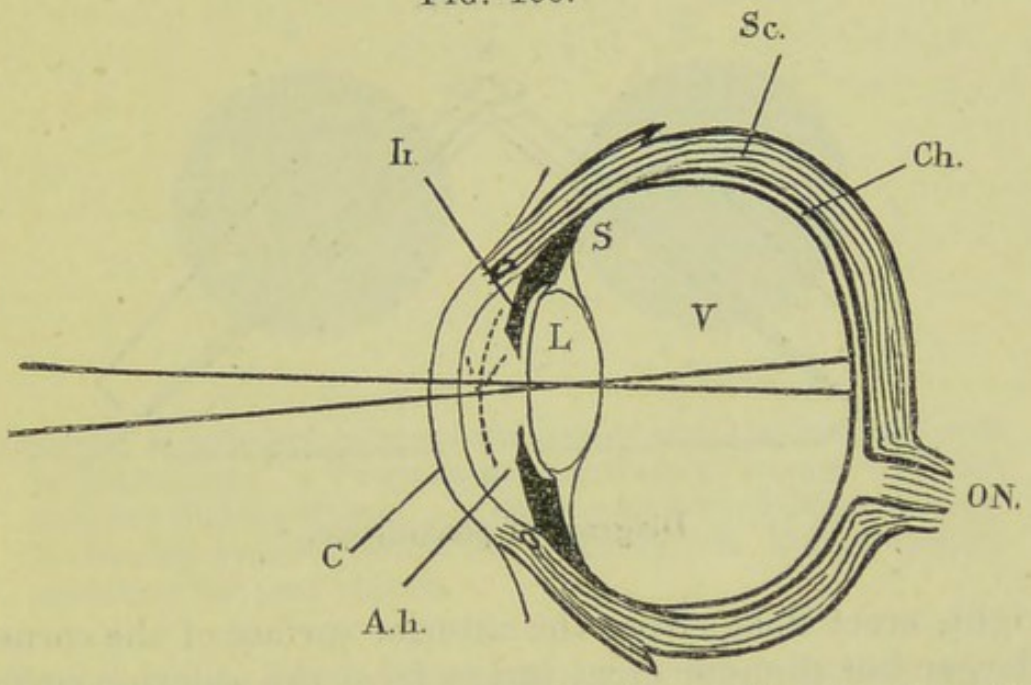
Aqueous humour (or cornea),
Lens,
Vitreous humour.

These are so adapted in the normal eye that parallel rays falling on the cornea are converged to a focus at the yellow spot on the retina. This point, therefore, represents the principal focus of the eye. A line drawn from this point through the centre of the cornea is the optic axis of the eyeball.

But we are able also to form a distinct image of near objects on the retina, and we notice that, when we

turn our gaze from far to near objects, there is a distinct feeling of muscular effort in the eyes. There must, then,

FIG. 100.



Section through eyeball to show refractive media. Sc. Sclerotic coat. Ch. Choroid coat. V. Vitreous humour. L. Lens. S. Suspensory ligament of lens. ON. Optic nerve. C. Cornea. A.h. Aqueous humour. Ir. Iris.

be some means by which the eye can be altered and arranged for focussing near objects. In a photographic camera the focus may be altered either by changing the lenses, putting in a lens of greater or less curvature, or by altering the distance of the screen from the lens. The last method is obviously impracticable in the rigid eyeball, and we find that the act of focussing (or accommodating) for near objects is associated with a change in the curvature of the lens, which becomes more convex on its anterior surface.

This may be easily shown by means of the phakoscope (Fig. 101). This is simply a box, blackened inside, with holes at a, b, c, and d. At a is the observer's eye; at b the observed eye. Across the middle of d a wire is stretched.

A candle is placed at c. The observer at a then sees three reflections of the candle from the eye at b : a

FIG. 101.

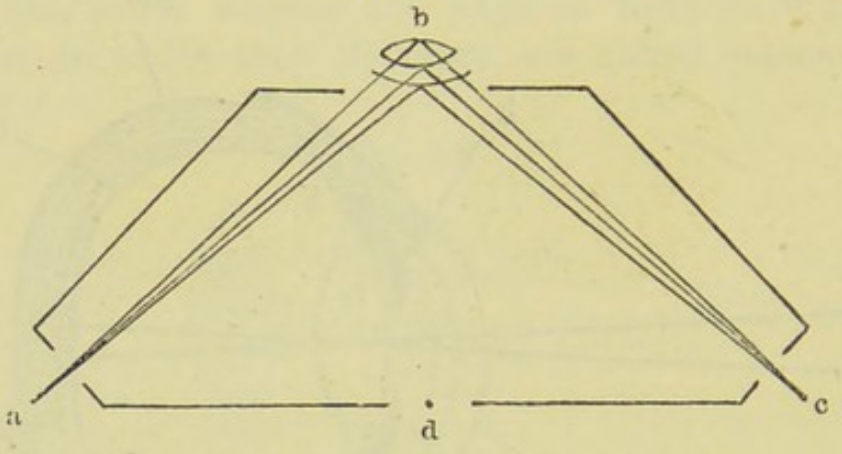


Diagram of phakoscope.

bright, erect image from the anterior surface of the cornea ; a larger but dimmer erect image from the anterior surface of the lens ; and a small, very dim inverted image from the posterior surface of the lens. These images must be observed first when the eye at b is accommodated for a distant object, and then when it is accommodated for the wire stretched across the opening d. It will be noticed that the change of accommodation from far to near objects is accompanied with a change in the second image (that from the anterior surface of the lens), which becomes smaller. The change in this image is more easily seen if the candle be made to throw the images on the eye by interposing a double prism at c. Then, as the lens becomes more convex to accommodate for near objects, the two images of the candle reflected from its anterior surface approach one another (Fig. 102).

We must now inquire how this change in the shape of the lens is brought about.

By measuring the size of the image of the candle produced by the anterior surface of the lens, and knowing the size of the candle itself and the distance from the observed

eye, it is possible to calculate the curvature of the lens in the living body. If the lens be now cut out of the eye, it

FIG. 102.

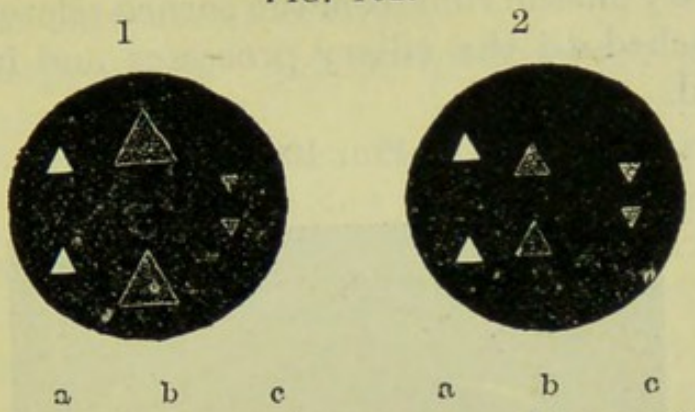


Diagram of reflected images from cornea and lens surfaces seen in phakoscope. a. From anterior surface of cornea. b. From anterior surface of lens. c. From posterior surface of lens. 1. During accommodation for distance. 2. During accommodation for near objects.

is found when freed from its supporting structures that the curvature of its anterior surface is much greater than it was before. It is evident, then, that a pressure is normally exerted by some structure on the anterior surface of the lens, repressing its natural tendency to become convex. If we examine sections through the eye we find that this structure is the suspensory ligament of the lens.

The membrana hyaloidea of the vitreous is thickened in front and closely adherent to the ciliary processes. At the margin of the lens it divides, sending a thick tough expansion forwards to cover the anterior surface of the lens, and a thin expansion behind which separates the lens from the vitreous. The part of the membrane extending from the edge of the lens to the ciliary processes is the suspensory ligament.

This ligament is normally on the stretch, and keeps the anterior surface of the lens nearly flat, so that the eye is accommodated for infinite distance.

When the eye is to be accommodated for near objects the ciliary processes are pulled forwards and inwards by

the contraction of the ciliary muscle, and so the suspensory ligament is relaxed and the front of the lens allowed to bulge forward.

The ciliary muscle runs from the corneo-sclerotic junction, to be attached to the ciliary processes and front part of the choroid.

Fig. 103.

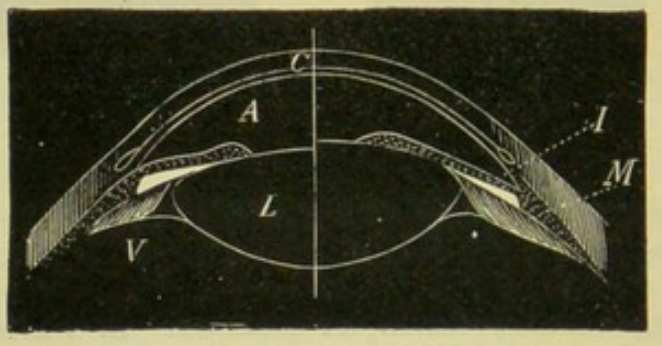


Diagram showing change in lens during accommodation. *M.* Ciliary muscle. *I.* Iris. *L.* Lens. *V.* Vitreous humour. *A.* Aqueous humour. *C.* Cornea.

Accommodation is a voluntary action, although the ciliary muscle consists of unstriated fibres. Contraction is brought about through the intervention of the short ciliary nerves, which are derived from the third nerve. The nucleus of the third nerve is situated in the extreme hinder part of the third ventricle and the anterior part of the iter of Sylvius. The centre presiding over the movement of accommodation occupies the most anterior part of this nucleus.

Accommodation for near objects is always associated with contraction of the iris, the function of which we must now consider. In an ordinary spherical biconvex lens the rays of light passing through the periphery of the lens come to a focus at a nearer point than the rays passing through the central parts. In this way a certain amount of blurring of an image is produced, which is spoken of as spherical aberration. This spherical aberration may be corrected in three possible ways.

1. By making the refractive index of the lens higher at its centre than at its circumference.

2. By making the curvature of the lens less near its circumference than at the centre.

3. By 'stopping out' the peripheral rays of light by means of a diaphragm.

The two latter methods are the ones used in most optical instruments. In the eye there is an attempt at all three, but the most important means is the third, the diaphragm being formed by the iris. This is a circular curtain with a hole in the middle, lying just on the anterior surface of the lens. Pigmented cells in it effectually stop out peripheral rays of light, and the size of the opening in it, the pupil, is controlled by the contraction or relaxation of a ring of unstriated muscular fibres situated near the margin of the pupil.

The iris has a twofold nerve-supply from the third nerve through the short ciliary nerves, and from the cervical sympathetic through the Gasserian ganglion, ophthalmic branch of the fifth and long ciliary nerves. Stimulation of the third nerve causes contraction of the pupil. The centre for this movement is in the anterior part of the floor of the Sylvian iter, just behind the centre for accommodation. Stimulation of the cervical sympathetic produces dilatation of the pupil. The fibres serving this action leave the spinal cord by the second dorsal nerve, and pass up through the stellate ganglion into the cervical sympathetic.

Contraction of the pupil occurs under the following conditions:

1. Stimulation of the optic nerve by exposure of the eye to light, or by artificial means. In the higher mammals this is a crossed reflex, exposure of one eye to light causing contraction of both pupils.

2. Associated with movements of accommodation and convergence of the optic axes.

3. Various poisons, especially opium and physostigmin.

FIG. 104.

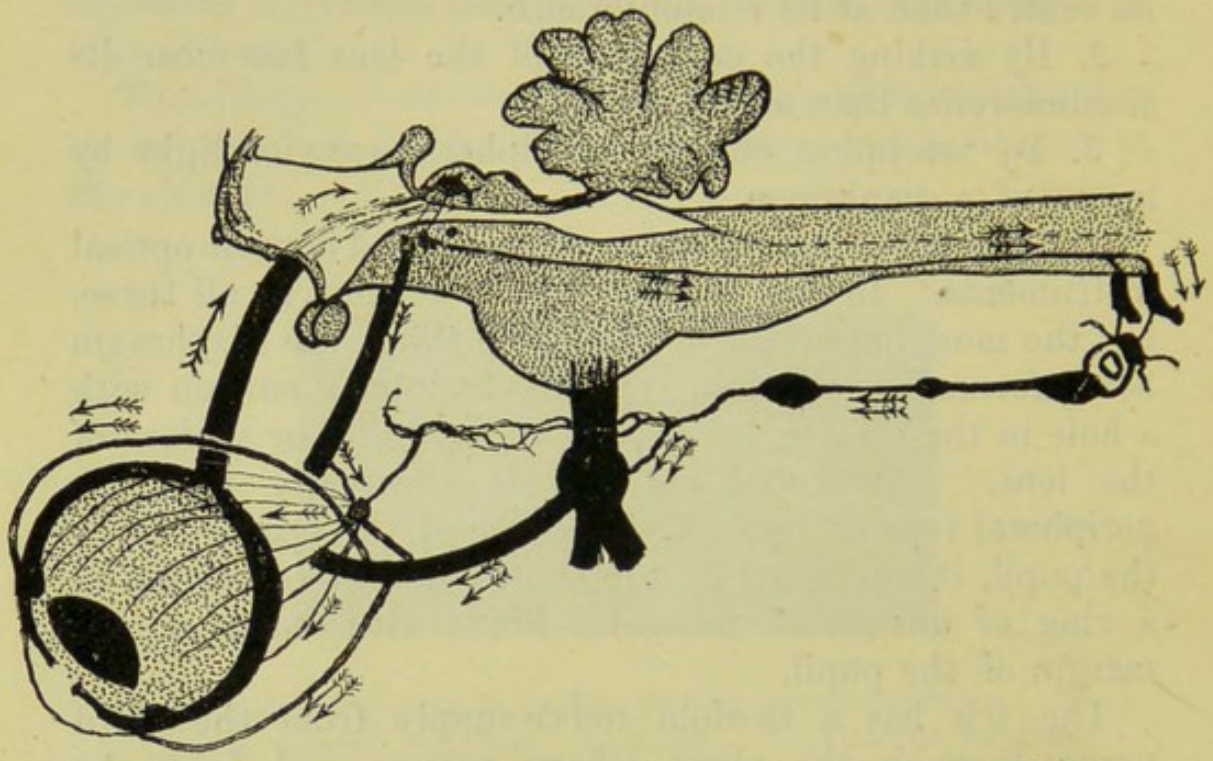


Diagram to show course of the impulses in the light reflex (shown by single arrows), and of those which, starting from the oculo-motor nucleus, cause dilatation of the pupil (double arrows).

The latter drug exerts a local influence on the iris, and can cause contraction of the pupil when all nerves to the eyeball are cut.

4. In sleep.

The pupil is dilated—

1. When the eye is removed from light.

2. Reflexly by strong stimulation of any sensory surface.

3. When accommodation is relaxed.

4. Under the influence of emotion, such as fear.

5. In the last stage of asphyxia.

6. In deep chloroform narcosis, and under the influence of atropin and other alkaloids derived from the solanaceous family. Atropin exerts a strong local influence on the iris. Stimulation of the third nerve has no power to constrict a pupil that is dilated fully by atropin.

Optical Defects of the Eye

Chromatic aberration.—Since blue rays are more refrangible than red rays, they are brought to a focus at a point nearer the lens than the red rays. This is the reason why with an ordinary magnifying glass we see a coloured fringe round the margins of the object. Chromatic aberration is corrected in optical instruments by using two different kinds of glass. In the eye it is uncorrected. Hence it is that a blue light and a red light at the same distance from the eye appear to be unequally distant; the red light, requiring greater accommodation than the blue, appears to be the nearer of the two. The error in most cases is so slight that we do not notice the chromatic fringes under normal circumstances.

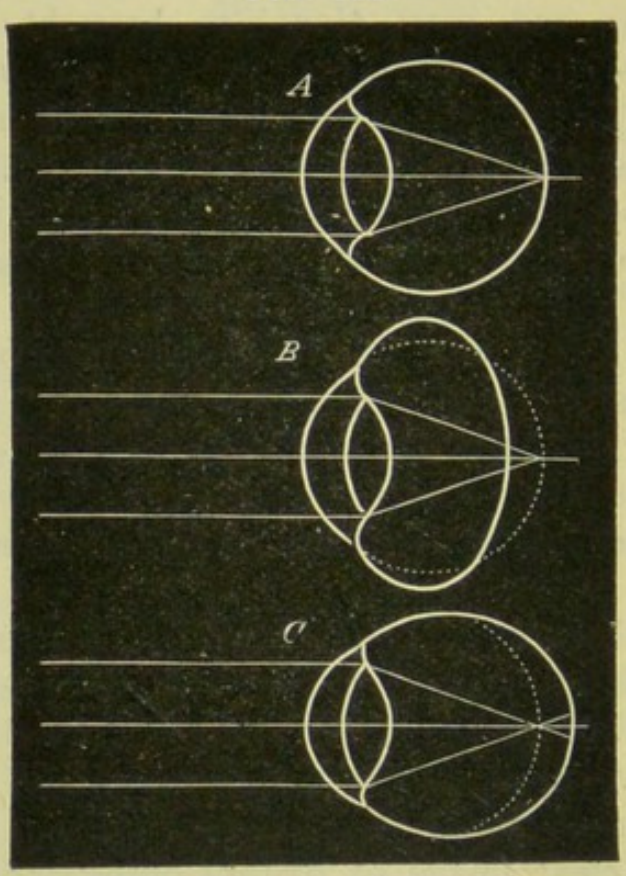
The normal or emmetropic eye is so constructed that, when the ciliary muscle is relaxed, parallel rays are focussed on the retina. If the eyeball be longer than usual, it is evident that the parallel rays will come to a focus rather in front of the retina, so that it will be impossible for a clear image of distant objects to be formed on the retina. Objects at a certain small distance from the eye will be focussed on the retina without any effort of accommodation. People with eyes of this description are said to be myopic or short-sighted. Under these circumstances concave spectacles are necessary, in order to form a distinct retinal image of distant objects.

If, on the other hand, the eyeball be too short in its antero-posterior diameter, the parallel rays entering the eye will come to a focus at a point behind the retina. In order that a distinct image may be formed, even of distant objects, it will be necessary to increase the curvature of the lens by contracting the ciliary muscle. Such eyes are hypermetropic or long-sighted.

As old age comes on the lens becomes more rigid, and

loses more or less its tendency to become convex. Hence the near limit of accommodation gets further and further

FIG. 105.



Diagrams of course taken by parallel rays in entering normal (emmetropic) eye (*A*), hypermetropic eye (*B*), and myopic eye (*C*).

with advancing age. Such a condition is not to be confused with long-sightedness; it is merely a defect in the power of accommodation, and not dependent on a structural defect of the eyeball. It is spoken of as presbyopia.

Astigmatism.—The curvature of the vertical meridian of the cornea is usually greater than that of the horizontal meridian. The difference may be so great as to make it impossible for a definite image of a point of light to be formed on the retina, the rays diverging from the luminous point in the vertical plane (greater curvature) being brought to a focus sooner than those in a horizontal

plane. To correct this defect it is necessary to use cylindrical glasses to make up for the lesser curvature of the cornea in this direction.

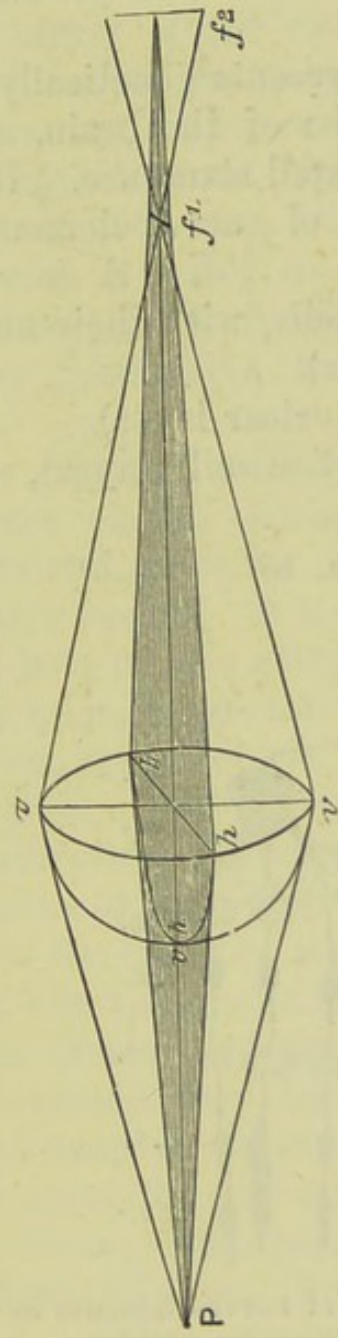


FIG. 106.

Diagram showing course of rays in an astigmatic eye (Waller). The curvature of the cornea is greater in the vertical meridian *v v v* than in the horizontal meridian *h h h*. Hence the rays of light coming from the point P and passing through the vertical meridian come to a focus at f^1, while those through the horizontal meridian come to a focus at f^2. There is, therefore, no point behind the cornea at which all the rays from P will come to a focus, and the image of the point must be blurred, being elongated in a horizontal direction at f^1, and in a vertical direction at f^2.

Retinal Changes involved in Vision

We have seen that, in nearly all sense-organs, the essential constituent is a bipolar nerve-cell having a peri-

pheral process extending towards the surface and ending between the epithelial cells covering that surface, and a central process which runs towards the central nervous system, where it terminates in close contact with other nerve-cells.

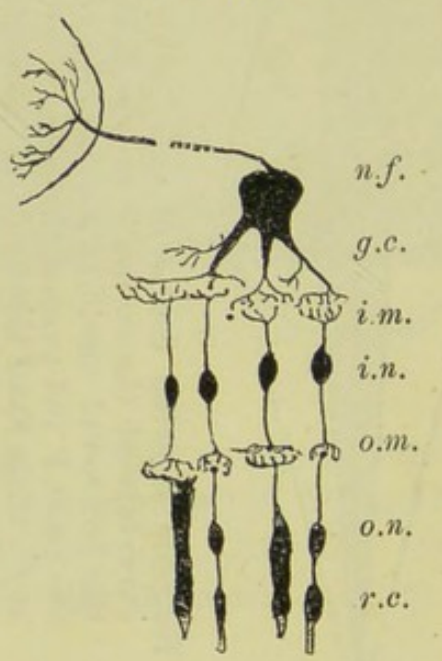
The retina, however, represents genetically not a simple sense-organ, but a whole lobe of the brain, and has therefore a much more complicated structure. It is composed of three separate relays of nerve-elements (neurons). These are—

(1) The rod and cone cells, with their nuclei (rod and cone and outer nuclear layer).

(2) Bipolar cells (inner nuclear layer).

(3) Ganglion-cells (ganglion-cell layer), from which

FIG. 107.



To show arrangement of the chief nerve-elements in the retina. *n.f.* Nerve-fibre layer. *g.c.* Ganglion-cell layer. *i.m.* Inner molecular. *i.n.* Inner nuclear. *o.m.* Outer molecular. *o.n.* Outer nuclear layer. *r.c.* Layer of rods and cones.

spring the axis-cylinders joining the nerve-fibre layer, and which run along the optic nerves and tracts to terminate

in the region of the anterior corpus quadrigeminum. The functional connection between the processes of these three sets of nerve-cells takes place in the outer and inner molecular layers.

Of these layers of the retina, the hindmost, the layer of rods and cones, represents the end-organ of vision; and therefore, for distinct vision to take place, the image of external objects must be formed on this layer. This is shown by the following facts.

a. The point of entry of the optic nerve, where the whole thickness of the retina is composed of nerve-fibres, is absolutely insensitive to light, and constitutes the 'blind spot.'

b. At the macula lutea, where vision is most distinct, all the layers of the retina are diminished except the layer of rods and cones.

c. Purkinje's figures. If a strong light be focussed by means of a lens on the sclerotic just outside the cornea, and the eye be made to stare fixedly at a dull background, an arborescent image of the retinal vessels will appear on the background. On moving the illumination the image of the vessels will move in the same direction. Knowing the dimensions of the eyeball and the distance of the background from the eye, the angle through which the light is moved, and the apparent displacement of the image of the vessels, the distance of the principal part of the retina behind the vessels may be calculated. This distance is found to correspond with the distance of the rod and cone layer from the retinal vessels, and hence this layer is taken to be the end-organ of vision.

When light falls on the retina certain chemical and physical changes take place, which either originate or accompany the transmutation of the ether vibrations into nerve-impulses, which may ascend the optic nerve. If a frog that has been in the dark for some time be killed, an eye taken out, bisected, and the retina removed and examined by a weak light, it will be found that this latter

has a purplish-red colour. On microscopical examination this colour is seen to be confined to the outer limbs of the

FIG. 108.

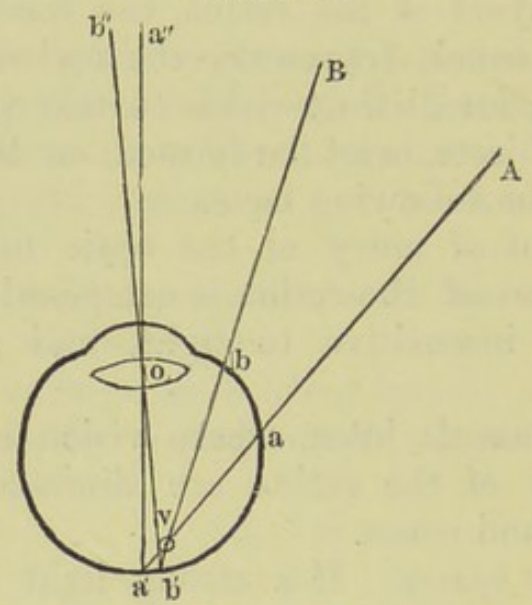


Diagram of the path of the rays of light in the formation of Purkinje's figures. v represents a retinal vessel. When this is illuminated from A, a shadow is formed on the hinder layers of the retina at a′. This is projected along a line passing through the optic axis, and appears to come from a point a″ on the wall. On moving the light from A to B, the image of the vessel appears to move from a″ to b″.

rods. After a very short exposure to diffuse daylight the colour disappears. The colouring matter (*rhodopsin*) may be dissolved out by means of a solution of bile salts. The purple-red solution thus formed also bleaches rapidly on exposure to light. It is evident that, by means of this rhodopsin, photographs or 'optograms' of external objects may be taken on the retina. The frog's eye which is cut out is placed in front of a window. After some time the eye is bisected and plunged into a 4 per cent. solution of alum, which fixes the optogram, and a permanent inverted picture of the window with its cross-bars is obtained on the retina.

If a retina which has been bleached by exposure to light

be replaced on the pigment layer lining the choroid, in a short time the colour will be restored. On examining sections through the retinæ it is found that, in those which have been exposed to light, the cells of the layer of pigmented epithelium send up fine processes full of pigmented granules between the outer limbs of the rods. In an eye which has been kept in the dark, on the other hand, the cells of the pigment layer are quite flat, so that the front part of the retina, including the rods and cones, can be removed without any difficulty. We see, then, that the function of the pigmented epithelium is to supply visual purple to the outer limbs of the rods as fast as the pigment already there is bleached by light. It might be thought that this chemical change was the active agent in producing excitation of the optic nerve-fibres. But the facts that in the fovea centralis, the region of most distinct vision, we find only cones which contain no visual purple, and that in certain birds there are no rods and no visual purple in the whole retina, show that this chemical process, interesting though it may be, is not essential for the conversion of light-waves into a nervous impulse.

When light falls upon the retina the cones are retracted, and lie close upon the external limiting membrane; whereas in an eye that has been kept in the dark they extend down between the rods as far as the pigmented layer.

The falling of light on the retina is also accompanied by an electrical change, which may be regarded as analogous to the current of action in muscles.

Binocular Vision

Under normal circumstances we use both eyes in seeing. Since, however, the visual impression produced by the two retinal images is not double, but single, there must be a series of points in each retina which, stimulated simultaneously, give rise to a single impression. These

points are called 'corresponding' points. Thus, when we look at a spot, the axes of the eyes are so directed that an

Fig. 109.

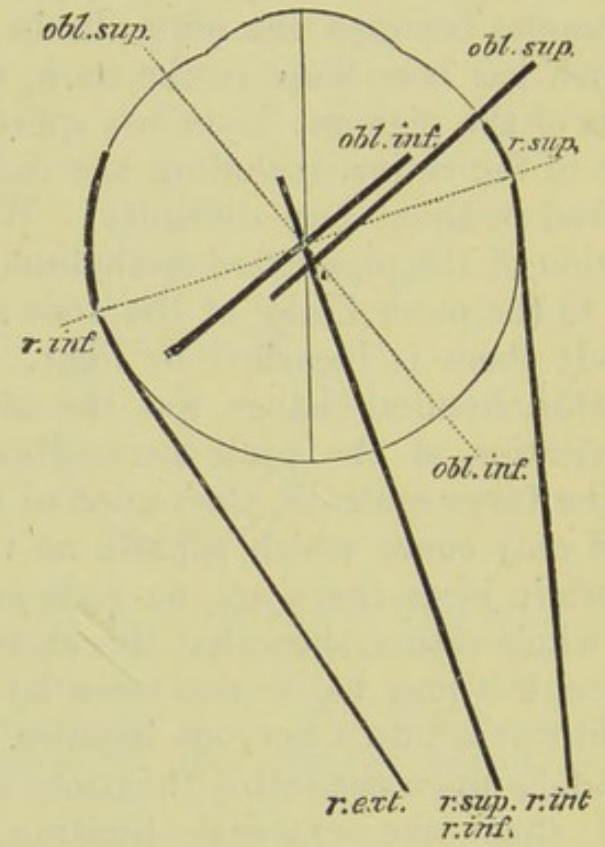


Diagram to show points of attachment and lines of action of extrinsic ocular muscles.

image of it falls on the yellow spots of the two retinæ. The images of all points to the right of this spot will fall on the nasal side of the right retina and on the temporal side of the left retina, and *vice versâ*. So if the right retina were cut out and placed on the left, the corresponding points in the two retinæ would be exactly over one another. In order that we may have single vision it is necessary that the images of external objects should fall on corresponding points of the two retinæ. This is effected by the harmonious co-operation of the muscles of the eyeball. These are six in number: superior, inferior,

external, and internal recti, superior and inferior oblique. The action of these muscles is as follows :

Superior rectus	moves	the centre of the cornea		upwards and inwards.
Inferior	,,	,,	,,	downwards and inwards.
Internal	,,	,,	,,	directly inwards.
External	,,	,,	,,	directly outwards.
Superior oblique	,,	,,	,,	downwards and outwards.
Inferior	,,	,,	,,	upwards and outwards.

FIG. 110.

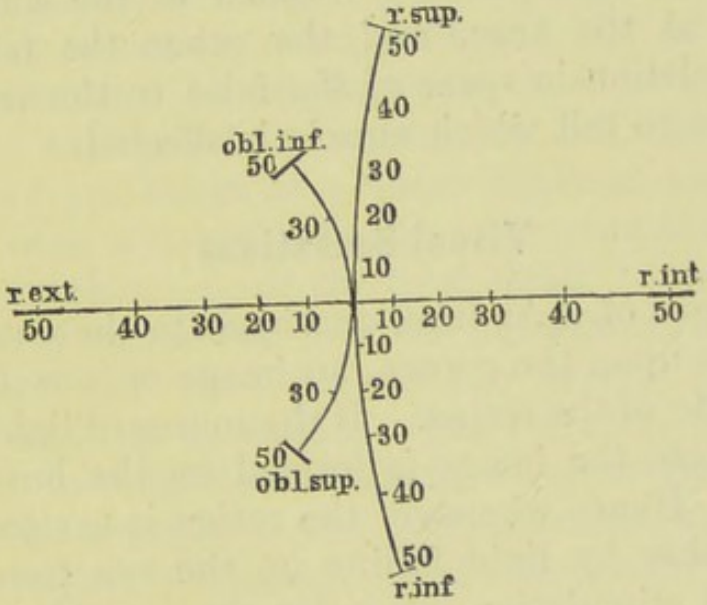


Diagram to show direction in which pupil will move under the action of the various ocular muscles.

So the muscles required for the following movements will be—

Looking upwards, superior recti and inferior oblique muscles.
,, downwards, inferior recti and superior oblique muscles.
,, inwards (convergence of eyes), the two internal recti.
,, to the right, the right external rectus and the left internal rectus.
,, to the left, the left external rectus and the right internal rectus.

These movements of the eyes to one side or the other are spoken of as conjugate deviation. The centres of most of these movements are situated in the floor of the iter of Sylvius. The movements which involve the external recti are carried out by the nucleus of the sixth nerve, which is functionally connected with nuclei in the floor of the iter by the posterior longitudinal bundle.

If from weakness of one of the ocular muscles the optic axes cannot be made to converge to any point in the field of vision, so that the images of external objects do not fall upon corresponding points of the two retinæ, double vision results, and the patient is said to suffer from a squint. In this case the image which is formed in the sound eye is spoken of as the true, and the other the false image. From the relation in space of the false to the true image, it is possible to tell which muscle is affected.

Visual Sensations

When a ray of light from an object to the outer side of the eye falls upon the cornea, an image of it is formed on the nasal side of the retina. If the source of light be above the visual axis, the image is formed on the lower half of the retina. Hence whenever the retina is excited at these points, whether by light falling on the eye from without or by direct stimulation, we refer the sensation produced to some position in the outside world which the experience gained by all our other senses points out.

Thus if the right eye be turned inwards, and pressure with the finger made on the outside of the sclerotic near the outer angle of the eyelids, we have a sensation of a ring of light produced by the direct excitation of the outer part of the retina, which we refer or 'project' to a point on the extreme inner side of the eye. It was often discussed how it is that we see external objects erect when the retinal image is inverted. But we do not look at the image on the retina. The stimulation of the retina at a

point on the nasal side merely gives rise to sensations which experience has taught us to recognise as coming from an object to the outer side of the visual axis.

Atrophy of the nasal half of the right retina, therefore, would give rise to blindness to the outer side of that eye, which would probably only be recognised when the left eye was closed.

Intensity of stimulus.—Weber's law, that the increase of stimulus necessary to cause an increase of sensation always bears the same ratio to the whole stimulus, holds good also for visual sensations.

This ratio in the case of the eye is about $\frac{1}{100}$. We can thus distinguish between two lights of 20 and $20\frac{1}{5}$ candle-power, or between two of 99 and 100 candle-power. If the illumination be excessive the law no longer holds good; and we should be unable to tell the difference between two arc lamps at a short distance, although one might be much stronger than the other, and the difference much greater than $\frac{1}{100}$ of the total light.

Duration of stimulus.—We do not know how long a stimulus of light must act on the retina in order to produce a definite sensation. The duration is, however, very short, since an electric spark, which is almost instantaneous in its appearance and disappearance, may excite a strong sensation of light. This momentary stimulus, however, as in the case of muscle, excites a condition of activity and change in the retina which lasts a measurable period.

The sensation produced by a momentary stimulus rises sharply to a maximum and then sinks, first quickly and then more gradually. The first part of the fall, after the attainment of the maximum sensation, is more rapid in the case of strong than of weak stimuli.

This duration of the sensation after the stimulus has ceased may be so pronounced, when the stimulus is very strong, as to give rise to a definite 'after-image.' After looking at the sun for some time and then turning away,

we may see an after-image that may last several seconds or minutes.

If one stimulus follows another at a very short interval we get a summation of stimuli, and the two sensations are fused into one. The interval which must intervene between two stimuli, in order that two distinct sensations may be produced, is greater when the stimuli are small than when they are intense.

This interval may be determined by causing a disc, on which alternate sectors of black and white are painted, to revolve at known rates, and noticing the time that a white sector takes to pass a given point (in the visual axis) when the sensations are just fused. If the illumination of the disc be feeble, this time will be found to be about $\frac{1}{10}$ second. If now the illumination be increased, the grey disappears, and we observe a flickering of the disc due to imperfect fusion of the separate visual sensations (cf. imperfect tetanus of muscle).

In the latter case the time between two successive stimuli may be reduced to $\frac{1}{40}$ or $\frac{1}{50}$ second before apparent fusion of the discs takes place.

The production of a circle of light when a stick with a glowing end is rapidly whirled round, and all the effects of pyrotechny, are dependent on this persistence of retinal activity after the stimulus calling it forth has ceased.

Colour Vision

If a ray of white light be passed through a prism it is unequally refracted, so that it is widened out into a broad band or spectrum, which is variously coloured, the red rays at one end being less refrangible than the blue rays at the other. We may divide the colours of the spectrum into seven—red, orange, yellow, green, blue, indigo, violet; but the division is quite arbitrary, the colours shading so gradually into one another that no two observers would

agree exactly on the limits between them. This spectrum can be recomposed by another prism in the reverse direction with the formation of white light, so that we say white light is composed of all these different colours. It might at first be thought that the retina could respond with a simple sensation to stimulation by any part of the spectrum, a low number of ether vibrations per second producing a sensation of red, a number rather higher a sensation of orange; so that the sensation produced by any part of the spectrum would be a simple colour sensation, of which there would in this case be an infinite number. But a simple analysis of our own sensations seems to show that some of the spectral colours are mixed sensations. Thus most people will say at once that orange is a mixture of red and yellow, and, as a matter of fact, we find on mixing rays from the red with others from the yellow part of the spectrum we do get a sensation of orange. The stimulus obtained by mixing red and yellow rays is not the same as a stimulus caused by rays from the orange part of the spectrum. In the former case compound waves made up of the two wave-lengths, 656 λ and 564 λ, are falling on the retina; in the latter case a simple wave, with length 608 λ; and yet the sensations produced are identical.

In order to recompose the white light it is not necessary to mix all the spectral colours. We may take a pair of colours, situated a certain distance apart in the spectrum, and by combining these form a white light. Thus red with green, or blue with yellow, will give white light. Any pair of colours, which together give rise to a sensation of white, are called *complementary*. By taking three colours, such as red, green, and violet, it is possible by mixing them in various proportions to form either white light or any colour of the spectrum. The colours so formed differ from the spectral colours in being less *saturated*, *i. e.* they contain, besides the pure colour, white light.

These experiments on mixing colours can be performed in various ways.

A. Sectors of the different colours are painted on a disc, and the colour sensations are fused by rapid rotation of the disc (Maxwell's colour-top).

B. Two small coloured discs are placed on the table, with a vertical glass plate between them. It is possible so to arrange the direction of vision that the reflected image of the disc from the glass plate coincides in position with the other disc seen through the plate.

C. These methods with painted discs are open to the objection that no pigments give perfectly pure colour sensations. It is therefore better to use the pure colours of the spectrum itself, combining any two bits of the spectrum by means of reflectors or prisms. A less perfect method is to cause light from two sources, coloured by different coloured glass, to fall on the same surface.

These facts show that in all probability the primitive colour sensations are few in number, and that the various colour sensations of a spectrum are not pure, but mixtures of these primary sensations. There are two theories of colour vision—the Young-Helmholtz and Hering's.

According to the former, there are three primary colour sensations—red, green, and violet,—each of which is represented by a separate set of nerve-fibrils. One set of fibres is most sensitive to red rays, and only slightly sensitive to the green and blue parts of the spectrum; the second set is most sensitive to the middle, and the third set to the blue end of the spectrum. White light is produced by an equal stimulation of the three sets.

Hering distinguishes four primary colour sensations—red, yellow, green, and blue,—and also considers the sensations of white and black as primary visual sensations. These sensations are placed in three groups, red and green, yellow and blue, white and black. For each pair of sensations he considers that there is a special substance in the retina, dissimilation or katabolism of which gives rise to one colour sensation; anabolism or assimilation to the

other. Thus if white light falls on the retina, it causes a breaking down or katabolism of the white-black substance. This breaking down excites certain fibres of the optic nerve, and produces in consciousness a sensation of white. If the light be now removed this breaking down gives place to anabolism or building up of the white-black substance, which excites the same nerve-fibrils in a different way, giving rise to a sensation of black. The white-black substance is affected not only by white light, but also by the colours red, green, yellow, blue, and their mixtures. The other two visual substances are only affected by red and green or by yellow and blue respectively. Hence even the spectral colours do not give rise to pure sensations, there being always some mixture of a sensation of white with the proper colour sensation.

The phenomena of colour vision that we have mentioned above can be equally well explained on either theory. Thus the fact that blue and yellow together give rise to a sensation of white may be explained on the Young-Helmholtz theory by saying that the stimulation of all three sets of fibrils is equal—as will be seen by adding together the ordinates of each curve in Fig. 111 at yellow and at blue.

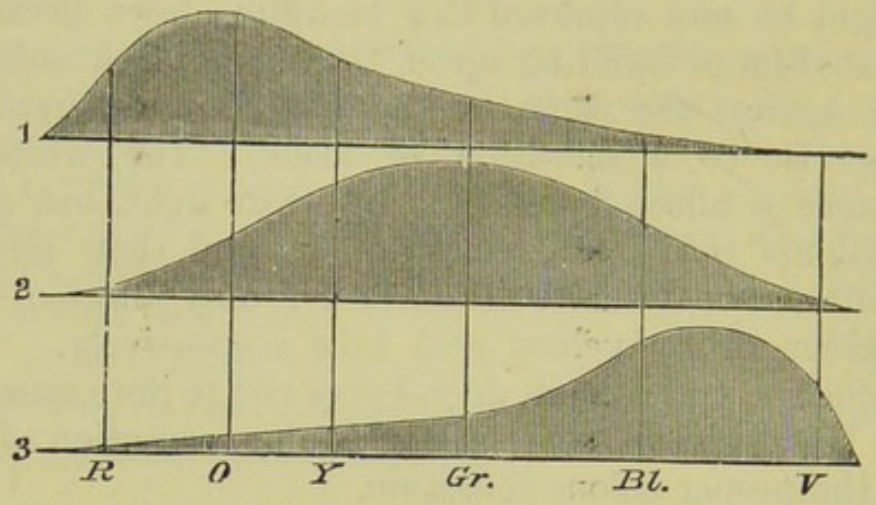
Adopting Hering's hypothesis, we may say that anabolism and katabolism being equally excited in the yellow-blue substance no change in it takes place, and the sole sensation is that produced by the stimulation of the white-black substance.

The fact that any coloured light, if very dim, or if falling on only a minute part of the retina, produces only a sensation of white, is more readily explicable on Hering's than on the Young-Helmholtz theory.

Cases are not rare in which a person is unable to distinguish between red and green, so that he can only tell a cherry from the leaves on the tree by its shape. Such cases may be explained on either theory. Hering's theory, however, seems necessary to account for the cases of

complete colour-blindness which are said to occur. In these the only sensations are of light and shade, and we

FIG. 111.



Curves showing sensitiveness of the three varieties of nerve-fibres to different parts of the spectrum. 1. Red fibres. 2. Green fibres. 3. Violet fibres.

may suppose that the red-green and blue-yellow substances are lacking in the retina.

Contrast phenomena.—If a grey disc be placed on a piece of red paper, and the whole covered with tissue-paper, the disc will take on a greenish tinge. If the ground colour be green, the disc will appear red; if blue, the disc will appear yellow; in fine, whatever be the ground colour, the colour of the disc will be complementary to it. These effects are spoken of as simultaneous contrast.

If, after gazing steadily for some time at a red disc on a white surface, the eyes be turned towards a plain white surface, a negative after-image of the disc is seen on the paper, coloured green,—that is, the complementary colour of the red disc. Surrounding this the paper appears red. If we look at the sun for some time, and then turn our eyes away, there is at first a positive after-image, and we see a bright sun wherever we look. In a short time this disappears and gives way to a black sun (a negative after-image). Thus we may say that stimulation of any part

of the retina with any colour is followed by a colour sensation, referred to the same part of the visual field, and complementary to the first.

It has been much discussed whether these phenomena are simply effects of judgment, or whether they are produced by definite changes taking place in the retina.

Helmholtz explains them by the first hypothesis, and looks upon them as cerebral processes.

Hering, on the other hand, has extended his theory so as to embrace these phenomena, and ascribes them to definite changes in the retina, or at any rate in the peripheral part of the visual mechanism.

A corollary to his theory that we mentioned above is, that if dissimilation of a visual substance be excited at any point of the retina, assimilation of the same substance is set up in the parts of the retina immediately adjoining that point. In this way the phenomena of simultaneous contrast may be explained.

Thus if a ray of red light falls on any spot, it may be supposed to excite dissimilation of the red-green substance at this spot. This sets up assimilation of the same substance in the adjoining parts of the retina, and the red object is therefore surrounded with a green halo, which at once becomes evident if we increase our appreciation for slight colour-tones by diminishing the total amount of light by means of tissue-paper.

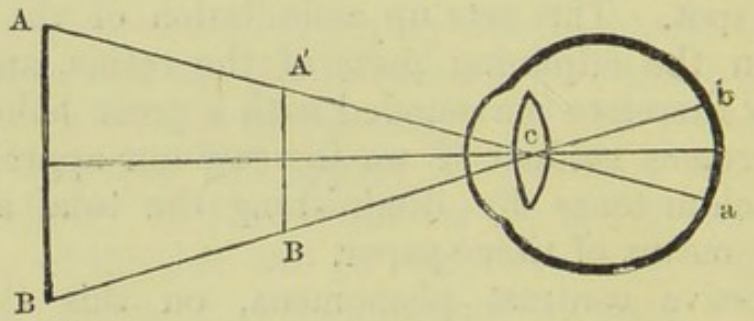
Successive contrast phenomena, on this theory, are exactly analogous to what we have seen take place in other tissues. If extensive breaking down of the visual stuff has been occurring, when the stimulus is removed there will be a swing back of the condition of the protoplasm of the nerve-endings in the opposite direction, and the katabolic will be replaced by anabolic changes ; just as, on breaking a constant current that has been flowing through a nerve, the condition of raised irritability at the kathode gives place to a condition in which the irritability is depressed below the normal.

The improving effect on the heart of stimulation of the vagus is also exactly analogous to a successive contrast effect. During stimulation of the vagus the breaking down of the contractile substance is stopped or checked, so that building up or anabolism can go on without interruption. When the excitation of the vagus ceases there is an extra store of contractile material in the muscle cells. This causes the beat to be more vigorous, and we may say that the increased anabolism has been followed by a period of increased katabolism, just as strong stimulation of a part of the retina with green (anabolism) gives rise to a red after-image (katabolism).

Visual Judgments

Size.—The apparent size of an object is determined by the magnitude of its image formed on the retina. As will

FIG. 112.



be evident from the diagram (Fig. 112), the apparent size of any given object is inversely proportional to the distance. Thus the size of the image on the retina of an object two inches long at a distance of a foot is equal to the image of an object four inches long at a distance of two feet.

An object can be seen if the visual angle subtended by it (the angle A c B in Fig. 112) is not less than sixty seconds. This is equivalent to an image on the fovea

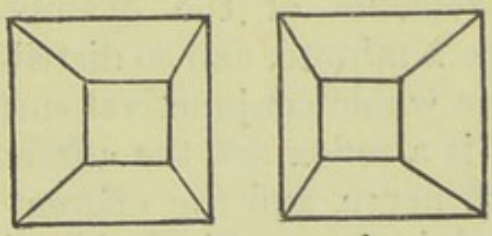
centralis of the retina about 4 μ* across, which corresponds to the diameter of a cone.

Estimation of distance depends partly on muscular sensations from the degree of convergence of the optic axes and of accommodation, partly on comparisons of the apparent size of the object with that of a neighbouring object (such as a man) the real size of which is known, and partly on the amount of blurring of the outlines of the object due to the haziness of the atmosphere. The latter factor is of great importance when the object is too large and remote to be compared with others of a known size. After a storm of rain distant mountains may seem to be many miles nearer than they did before.

Judgment of Solidity—Stereoscopic Vision

If we look at a solid object, such as a cube, with both eyes, the images formed on the corresponding points of the two retinæ are not identical, the one in the right eye

FIG. 113.



representing more of the right side of the cube, and in the left eye more of the left side (Fig. 113).

If the two images a and b be so arranged that they fall on corresponding points of the two retinæ, the resulting impression is that of a solid body, in the form of a cube. This is the principle involved in the stereoscope. When only one eye is used, the external world has a much flatter

* μ = ·001 millimetre.

appearance, although some idea of solidity is still gained from the fact that the accommodation has to be altered in order to bring different parts of the solid body into focus. The effects of light and shade also aid in the judgment of solidity.

Accessory Parts of the Eye

The eyeball is protected in front by the eyelids. These are lined internally with a delicate mucous membrane, continuous with the conjunctiva covering the anterior surface of the eyeball. This membrane is kept constantly moist by the secretion of the lachrymal gland, a small acino-tubular gland built up on the type of a serous gland, situated at the upper and inner angle of the orbit. The excess of fluid is drained off by the nasal duct, which leads from the conjunctival sac to the nasal cavity on the same side. If the eyes be kept open for some minutes, the conjunctiva covering the eyeball becomes dry, and irritation is set up. Normally the membrane, and especially that over the cornea, is kept moist and transparent by involuntary movements of the eyelids, which close or blink about twice a minute, and so distribute the lachrymal secretion over the whole conjunctival surface.

This blinking is a reflex act, the afferent channels being fibres of the fifth nerve, and the efferent the fibres of the facial nerve supplying the orbicularis palpebrarum. It is spoken of as the 'conjunctival reflex,' and is one of the last to disappear in chloroform or ether narcosis.

CHAPTER XII

THE SPINAL CORD

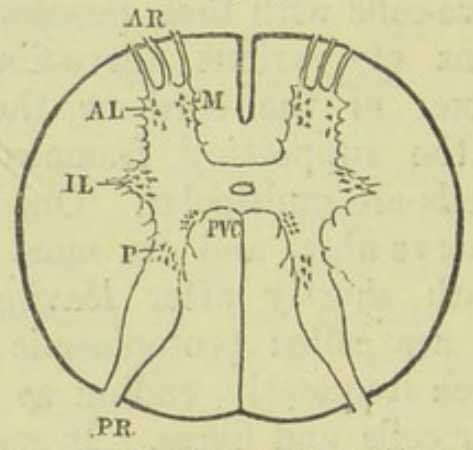
The spinal cord and bulb may be regarded in two lights, as a centre presiding over reflex actions and as a channel of communication between the periphery and the brain. Its structure corresponds, roughly speaking, to this twofold action, consisting as it does of a tube of grey matter internally, which may be looked upon as a collection of reflex centres, surrounded externally by a layer of white matter, composed of medullated nerve-fibres, and serving as simple conducting tissue. The grey matter consists of nerve-cells with their processes, of the branching terminations of various nerve-fibres derived from the white matter of the cord or the posterior nerve-roots, and of the supporting framework or neuroglia. All the nerve-cells are multipolar. One of their processes represents a nerve-fibre, and in most cases acquires a medullary sheath shortly after leaving the cell. The other processes are called protoplasmic processes or *dendrites*, and branch frequently, ending as fine arborisations among the other cells and fibres. It seems probable that in all cases, where a distinction between dendrites and axis-cylinder processes is to be made out, the nerve impulse is conducted from dendrites to cell, and from the cell along the axis-cylinder or nerve-fibre process. It is interesting to note that in no case has any anatomical continuity been observed between the processes of different nerve-cells. Each nerve-cell with its protoplasmic and axis-cylinder processes seems to form an anatomical unit—the propagation of impulses from one to another being carried out by simple contact (cf. Fig. 11). The grey matter is more richly supplied with blood than the white matter, and hence has a pinkish-grey appearance when alive. The

cells of the grey matter are arranged in definite groups or columns, some of which extend throughout the whole length of the cord, whilst others are confined to certain regions. These columns are—

1. In the anterior cornu, two sets of cells, the anterior and the external groups. These cells are the largest in the cord; they have many processes, one process being continued into the medullated nerve-fibre of an anterior root, the other processes (dendrites) breaking up into a fine meshwork of non-medullated fibrils, which become lost in the meshwork of the grey matter.

2. The lateral column or intermedio-lateral tract, confined to the dorsal and upper part of the lumbar spinal cord.

FIG. 114.



Arrangement of nerve-cells in grey matter of spinal cord. AL. Antero-lateral group of cells. M. Medial group. IL. Intermedio-lateral tract. PVC. Posterior vesicular column. P. Cells in posterior horn. AR. Anterior nerve-roots. PR. Posterior nerve-roots.

3. The cells of the posterior horn, small multipolar cells.

4. Clarke's column or posterior vesicular column, reaching from the seventh or eighth cervical nerve to the third lumbar nerve, and represented opposite the second and third cervical nerves by a small group of cells, and possibly also in the sacral region by a group known as Stilling's nucleus. The cells composing this column are large and fusiform, with their long axes parallel to that of the cord,

so that in cross-section they have the appearance of small round cells.

More useful, however, than this purely anatomical classification is the classification of the nerve-cells which is based on the destination of their nerve-fibre processes. In this way we may distinguish—

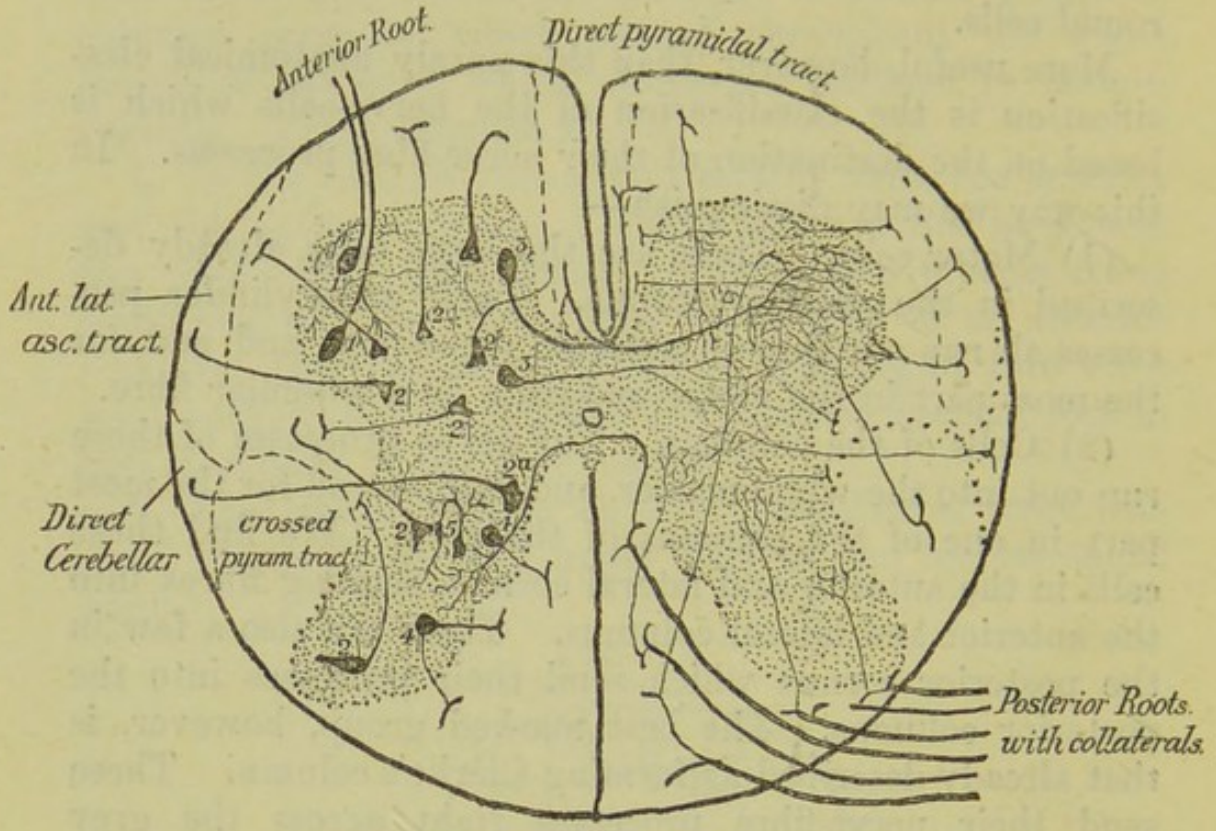
(1) Motor cells. These are the large cells already described in the anterior cornua. Their axis-cylinder processes all run out into an anterior nerve-root, and end for the most part in the motor end-plate on a muscular fibre.

(2) Cells of the columns. The nerve processes of these run out into the white matter, and then ascend for the most part in one of the columns of the cord. We find these cells in the anterior and lateral cornua, sending fibres into the anterior and lateral columns. There are also a few in the posterior cornua which send their processes into the posterior columns. The best marked group, however, is that already described as forming Clarke's column. These send their nerve-fibre processes right across the grey matter into the lateral column of the same side, where they turn upwards, forming a distinct tract of fibres—the direct or posterior cerebellar tract.

(3) Commissural cells. This class embraces a number of cells of different sizes and shapes. Their processes either end in the grey matter of the same side, or pass across the cord to form connections with the grey matter of the other side. Many of these fibres pass through the anterior white commissure.

Each nerve of the thirty-one pairs that arise from the spinal cord has two roots, anterior and posterior. The anterior root arises by several bundles from the antero-lateral part of the cord ; the posterior root arises as a single bundle, emerging from the spinal cord opposite the posterior horn of grey matter. The two roots join to form the trunk of the spinal nerve. On the posterior root, just before it joins the anterior root, is situated a ganglion, the posterior root ganglion.

FIG. 115.



Spinal cord (after Lenhossek).

On left side of figure are shown the nerve-cells with their axis-cylinder processes. On the right side the distribution of the chief collaterals. 1. Motor cells. 2. Cells of the columns. 2*a*. Cells of Clarke's column, sending processes across into direct cerebellar tract. 3, 4, and 5. Commissural cells.

We have already stated that the anterior root is motor or efferent, and the posterior root sensory or afferent. The evidence for this is as follows:—If the anterior root be divided, the muscles supplied by the nerve are paralysed. Excitation of the peripheral end of the anterior root will cause them to contract. Excitation of its central end has no effect.

Section of the posterior root causes loss of sensation in its area of distribution. Stimulation of its peripheral end has no effect. Stimulation of its central end causes marked signs of pain, such as struggling, crying out, or, in a curarised animal, rise of blood-pressure.

In some cases we may find that stimulation of the peri-

pheral end of the anterior root gives rise to evidence of pain. This is spoken of as *recurrent sensibility*, and is due to stimulation of fibres which leave the cord by the posterior roots, and after travelling some distance towards the periphery turn back and run up in the anterior root. Recurrent sensibility is abolished, as would be expected, by division of the posterior root.

Tracts in the white matter of the cord.—Coarse anatomical investigation teaches us little concerning the tracts in the white matter. By the anterior and posterior nerve-roots each side of the cord may be divided into anterior, lateral, and posterior columns; and the posterior column is further subdivided by a small fissure into the postero-median column (Goll's column), and the postero-external column or posterior root-zone (column of Burdach). But in this investigation other methods have come to our assistance.

(*a*) Of these the most important is the Wallerian method. We have already seen that section of a peripheral nerve gives rise to a gradual fall of irritability, after a small initial rise, in the part of the nerve below the section. This goes on to complete loss of irritability, and on microscopic investigation it is found that the physiological change is accompanied by definite progressive structural changes.

About four days after the section (in mammals) the myelin forming the medullary sheath of the nerve-fibres in the peripheral part of the nerve becomes segmented, and breaks up into drops of various size. A little later the axis-cylinder is also broken across, so that there is no longer any physiological continuity in the nerve-fibre. This is followed by enlargement and proliferation of the internodal nuclei; the protoplasm within the primitive sheath increases in quantity, and the drops of myelin are gradually absorbed and disappear. Finally, about the twenty-first day or later, the original structure of the nerve-fibres has entirely disappeared, and they consist of merely a tubular sheath, containing nuclei and structureless

protoplasm. If no regeneration can take place these structures also disappear, giving place to simple connective tissue. If however, after the section, the two ends of the nerve have been kept in close apposition by means of sutures, regeneration of the peripheral part of the nerve takes place. New axis-cylinders grow out from the old axis-cylinders of the central part of the nerve at the node of Ranvier just above the point of division, and these grow down into the structureless protoplasm, filling the sheaths of the peripheral nerve-fibres, thus restoring functional continuity. The myelin sheaths of the regenerated nerve-fibres make their appearance rather later. Nerve-fibres have already been spoken of as being enormously elongated cell-processes, and it seems that a fibre degenerates whenever it is separated from the cell of which it is an outgrowth, and must be regenerated by a renewed outgrowth from this cell. We may look upon the nerve-cells as presiding over the nutrition of the fibres which spring from them; and they are therefore called the 'trophic centres' of these fibres. If a nerve be divided, only that half which is separated from its trophic centre will degenerate. This fact was first pointed out clearly by Waller, and hence the method of diagnosing the course of tracts in the central nervous system is named the Wallerian method.

A large majority of the white fibres of the spinal cord are dependent for their nutrition upon their continuity with a nerve-cell, and if this be abolished the part of the nerve-fibre severed from the cell degenerates. If the anterior root be divided the part attached to the cord remains intact, but the whole peripheral part of the fibres degenerates, so that in a section of the mixed nerve the degenerated motor fibres can be identified.

If the posterior root be divided between the ganglion and its junction with the anterior root, all the sensory fibres in the mixed nerve below the junction degenerate. If, however, it be divided between the ganglion and the

cord, the sensory fibres in the mixed nerve remain intact, but the central parts of the fibres degenerate right up into the cord, and may be traced in the cord as far up as the medulla.

If the cord be cut across transversely, some tracts of white matter are found degenerated in the cord above the lesion (ascending degeneration), whilst other tracts degenerate in the cord below the lesion (descending degeneration), and in this way the white matter may be divided into ascending and descending tracts.*

(*b*) Developmental method (Flechsig). This method is founded on the fact that when the nerve-fibres are first formed in the fœtal cord they are non-medullated, and the different tracts of the cord acquire a medullary sheath at different intervals, the pyramidal tracts being latest of all in acquiring their sheath.

(*c*) Electrical method. The passage of a nerve-impulse along the cord, as along a nerve, is accompanied by an electrical change (current of action). It is possible to find out by what path the electrical change travels, and thereby to determine the path of the impulse of which the electrical change is the concomitant (Gotch and Horsley).

(*d*) Experimental method. Different parts of the white columns may be cut through, and the effects that are produced in this way observed on the conduction of motor or sensory impulses. Evidence in this direction is also furnished by the effects that are observed clinically of lesions of various parts of the cord.

By a combination of these methods the following conclusions have been arrived at. The white matter of the cord may be divided into ascending and descending tracts.

* A caution is here necessary. It is often assumed that a tract which degenerates upwards is necessarily afferent in function, and *vice versâ*. But the result of section of a peripheral nerve, after which sensory as well as motor fibres degenerate below the section, shows that the direction of degeneration is not necessarily the same as the direction of conduction.

A. *Descending tracts.* — If the spinal cord be divided in the cervical region, degeneration of two distinct tracts in the anterior and postero-lateral columns is produced. These are the anterior or direct and the crossed pyramidal tracts. The fibres composing these tracts are derived from the pyramidal cells in the motor area of the cerebral cortex, and are therefore found degenerated if the motor area of the cortex is destroyed. They end in the spinal cord by turning into the grey matter, and there breaking up into a fine bunch of fibrils in close connection with the motor cells of the anterior cornua. On their way down the cord they give off fine side branches or 'collaterals,' which run into the anterior cornu and there terminate, thus establishing connections between one cortical cell and the anterior cornual cells of several different segments of the spinal cord. It is, therefore, concluded that they carry motor

FIG. 116.

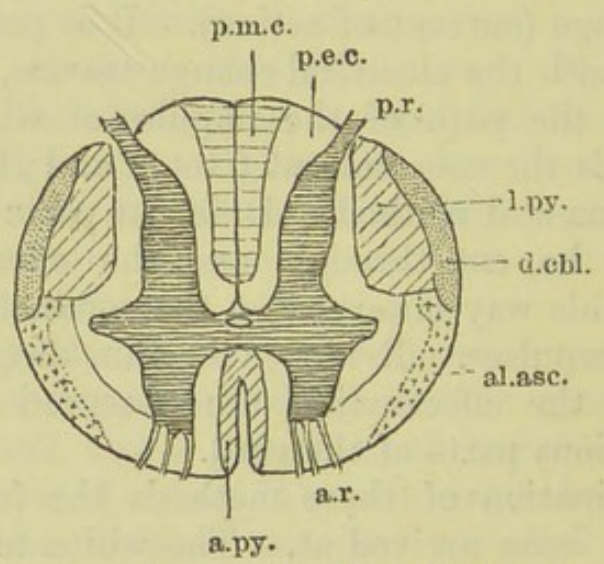


Diagram of spinal cord. a.r. Anterior spinal nerve-roots. p.r. Posterior root. a.py. Anterior pyramidal tract. l.py. Lateral pyramidal tract. d.cbl. Direct cerebellar tract. p.m.c. Posterior median column. p.e.c. Posterior external column. al.asc. Antero-lateral ascending tract.

impulses from the cerebral cortex to the ganglion-cells of the cord. Destruction of these columns by disease or

otherwise causes the abolition of voluntary control over the muscles.

There are also some scattered fibres in the antero-lateral column, which degenerate in the downward direction. These are supposed to be derived from the cerebellum of the same side.

B. *Ascending tracts.*—The tracts which degenerate in the cord above a transverse section are four in number :

1. The postero-median, as far up as the nucleus gracilis in the medulla.

2. The posterior root-zone for one or two segments above the lesion.

3. The direct or posterior cerebellar tract as far as the cerebellum.

4. The antero-lateral ascending tract or anterior cerebellar tract. The fibres of this tract also end in the cerebellum near those of No. 3, but take a more circuitous path than those of the latter tract.

Division of all the posterior roots on one side causes degeneration of the posterior root-zone and postero-median column on the same side. Hence the fibres of these columns have their trophic centres on the ganglia of the posterior roots. The other two ascending tracts do not degenerate after section of the posterior roots, and must therefore have their trophic centres in the cells of the grey matter of the cord. We have already mentioned that the direct cerebellar tract is derived from the cells of the posterior vesicular column of Clarke. All these tracts send off branches or collaterals on their way up the cord, which terminate round the cells of the grey matter in the different segments of the cord. Some of these run from the posterior root-fibres directly across to the anterior cornu of the same side, and thus subserve the simplest forms of reflex action (cf. Figs. 115 and 117).

Besides these special tracts there is a large number of fibres in the white matter which do not degenerate either above or below a transverse section of the cord. These

are supposed to be commissural, serving to connect one segment of the cord with the other.

FIG. 117.

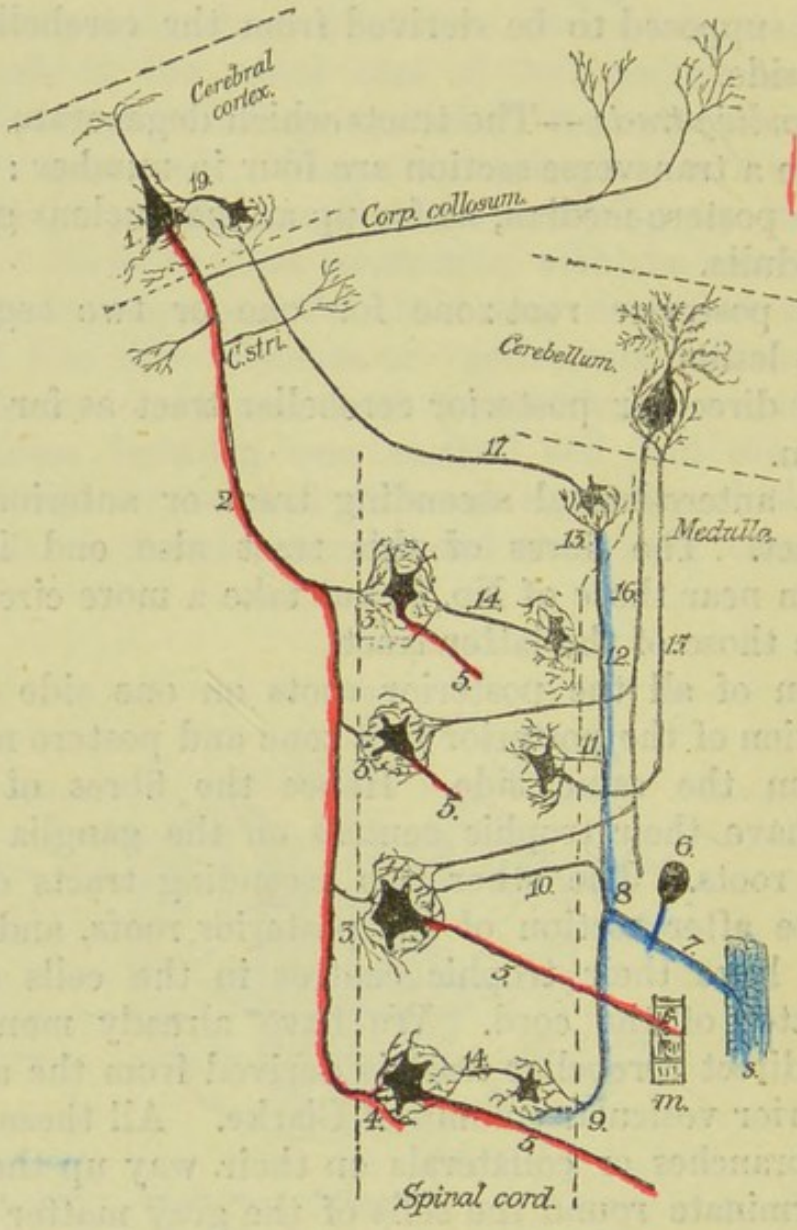


Diagram showing the probable relations of some of the principal cells of the cerebro-spinal system to one another (Schäfer).

1, a cell of the cortex cerebri; 2, its axis-cylinder or nerve-process passing down in the pyramidal tract, and giving off collaterals, some of which, 3, 3, end in arborisations around cells of the anterior horn of the spinal cord, the main fibre having a similar ending at 4; *Corp. collosum*, a collateral passing to the corpus callosum; *C. stri.*, another passing to the corpus striatum; 5, axis-cylinder process of anterior

Paths of impulses in the cord.—It is supposed that some or all of the ascending tracts convey afferent impulses from the posterior roots to the brain, although evidence as to the part taken by each tract is very conflicting. We have pathological evidence that the path for pain impulses is different from that for touch or temperature. Cases have been recorded (Gowers) which seem to show that tactile impulses travel up the posterior column, and pain impulses in the lateral columns. It is more probable, however, that the pain impulses are conducted upwards through the grey matter. In certain cases in which the grey matter is entirely destroyed (syringomyelia) sensations of pain are absent, although those for touch may be perfectly preserved. But the only thing definitely proved is that sensory impulses from one side of the body travel up the spinal cord on the same side, crossing at the upper part of the medulla on the same side to the other side by the

cornu-cell passing to form a terminal arborisation in the end-plate of a muscle-fibre, *m*.

6, a cell of one of the spinal ganglia. Its axis-cylinder process bifurcates, and one branch, 7, passes to the periphery to end in an arborisation in the sensory surface, *s*. The other (central) branch bifurcates after entering the cord (at 8), and its divisions pass upwards and downwards (the latter for a short distance only); 9, ending of the descending branch in a terminal arborisation around a cell of the posterior horn, the axis-cylinder process of which, again, ends in a similar arborisation around a cell of the anterior horn; 10, a collateral passing from the ascending division directly to envelop a cell of the anterior horn; 11, one passing to envelop a cell of Clarke's column; 12, a collateral having connections like those of 9; 13, ending of the ascending division of the posterior root-fibre around one of the cells of the posterior columns of the bulb; 14, 14, axis-cylinder processes of cells of the posterior horn passing to form an arborisation around the motor cells; 15, a fibre of the ascending cerebellar tract passing up to form an arborisation around a cell of the cerebellum; 16, axis-cylinder process of this cell passing down the bulb and cord, and giving off collaterals to envelop the cells of the anterior horn; 17, axis-cylinder process of one of the cells of the posterior column of the bulb passing as a fibre of the fillet to the cerebrum, and forming a terminal arborisation around one of the smaller cerebral cells; 19, axis-cylinder process of this cell, forming an arborisation around the pyramidal cell, 1.

superior pyramidal decussation, and from here are conveyed to the cortex of the opposite side.

Motor impulses, too, which start from the cerebral cortex at one side, pass down that side till they reach the lower part of the medulla. Here the greater number of the fibres pass over in the pyramidal decussation to run down in the crossed pyramidal tract in the other side of the cord. The few fibres which do not cross over in the pyramidal decussation are continued as the direct or anterior pyramidal tract. These, however, also cross to the other side in their passage down the cord before becoming connected with the anterior cornual cells. Hemisection, therefore, of the spinal cord in the dorsal region will produce paralysis of motion and loss of or impaired sensation in the parts supplied by the nerves on the same side below the lesion.*

A great part of the white matter of the cord is concerned, then, in maintaining connection between the brain and higher parts of the nervous system and the periphery, through the intermediation of the cells of the grey matter of the cord. Corresponding to this function we find a gradual increase in the number of fibres in the white matter as we ascend from the sacral part of the cord to the medulla, the white matter being continually reinforced

* Until recently it was maintained, on the authority of experiments by Brown-Séquard and Ferrier, that hemisection of the spinal cord produced paralysis of the parts below on the side of the lesion and anæsthesia of the parts below on the side opposite the lesion. Thus a section through the right half of the dorsal cord was said to produce paralysis of the right leg and anæsthesia of the left leg. The right leg was said to be hyperæsthetic. More recent and careful experiments by Mott have shown conclusively that such is not the case, but that sensory impulses travel up on the same side of the cord as they enter. This conclusion is borne out by the anatomical facts of the course of the fibres from the posterior roots in the cord, and also by the work of Gotch and Horsley on the propagation of impulses in the cord.

as it ascends the cord by fibres establishing connection with the ganglion-cells forming the nuclei of the nerve-roots.

Vaso-motor impulses to the limbs travel down the lateral columns of the cord on the same side.

The Cord as Reflex Centre

In the lower animals, such as the frog, the spinal cord of itself is able to carry out many complex reflex actions. If the skin round the anus of a decapitated frog is stimulated, a sudden extension of both legs is produced, so that the animal leaps away from the stimulus. If a small piece of filter-paper moistened with acetic acid be placed on the inner side of the right thigh, the right foot will be raised and used to wipe away the offending object. If the right leg be held or be cut off, after various fruitless endeavours to remove the irritant with this limb, the left leg may be raised and used for this purpose. These and many other similar experiments show that the spinal cord separate from the upper part of the nervous system is capable in the frog of bringing about many highly complex co-ordinated movements, which are apparently purposive, *i. e.* they seem to have a definite object in view; and arguing from experiments, such as the second one we have mentioned, it has been thought that psychical phenomena may accompany these reflex actions. But it must be remembered that *summation* of afferent impulses occurs just as summation of stimuli applied to a frog's ventricle. A single stimulus, too weak to evoke a reflex contraction, may do so if repeated several times. In our experiment, the right leg being unable to remove the offending object, stimulation goes on, and the effect is summated until it is strong enough to spread to the other side of the cord and so set the left leg in motion.

The time taken up in the transmutation of afferent

into efferent impulses in the spinal cord may be estimated by measuring the interval that elapses between stimulation of a sensory nerve with a single induction shock and the resulting muscular contraction, and subtracting from the amount so determined the time taken in the passage of the impulse up and down the nerve-fibres and the latent period of the muscle, the contraction of which is recorded. The reflex time measured in this way is found to be about ·01 sec.

A slight stimulus causes reflex contraction only of the limb stimulated. A stronger stimulus causes contraction of the corresponding limb of the other side also, and the effect of a still stronger stimulus may extend to the other two limbs. With this resistance to passage of impulses in the cord across the middle line and longitudinally from one segment to another, we find a corresponding increase in the reflex time.

Effect of strychnine.—If strychnine be injected into the dorsal lymph-sac of a frog, the spinal cord is so affected that the normal resistance to passage of impulses is abolished. The slightest stimulus of the skin now evokes a maximal reflex action, there being no longer any proportionality between the magnitude of the stimulus and that of the reflex effect produced. The reflex time is not diminished, but the smallest stimulus can travel equally well in all directions in the cord. Hence the slightest touch of the skin sends all the muscles into prolonged tetanic contraction, and the frog becomes stretched out with its limbs stiff and rigid.

Inhibition.—The reflex action normally following a slight stimulus of any part of the body may be completely prevented or inhibited by strong sensory stimulation of some other part. If the optic lobes of a frog be stimulated by putting a crystal of salt on them, or the central end of the right sciatic nerve by means of a faradic current, stimulation of the skin of the left leg with acid produces no effects whatever. A striking parallel instance of this

occurs in our daily mental life. Concentration of the attention in any one direction, either by severe pain or through psychical excitement, causes smaller stimuli to be quite unheeded, so that in battle a man may be unaware that he is severely wounded until he feels faint or sees blood flowing. We may say, putting the phenomena of the spinal cord into terms of consciousness, that its ganglion-cells are so much occupied with the stronger stimulus that they do not notice a weaker stimulus applied to some other part.

When we come to the higher animals—mammals and man—there seems to be a striking difference between their spinal cord and that of the frog, in that the reflex actions which can be carried out by the cord severed from the medulla and brain are limited to those of the simplest nature. If a man has had his cord crushed in the dorsal region, tickling the soles of his feet will cause him to draw up his legs, although he is perfectly unconscious that his feet are being touched. But beyond one or two simple reflexes of this description, the spinal cord seems to have no power of carrying out co-ordinated acts. It is, however, difficult in these cases, and in experiments on the spinal cord in mammals, to eliminate the effects of *shock*. After total transverse section of the spinal cord high up, the animal is in a condition of shock, which lasts a considerable time; his vital activities are profoundly depressed, and it may be impossible to evoke even the simplest reflex action by stimulation of any sensory surface below the lesion. But if the experiment be carefully conducted, and the animal be kept alive for a considerable time, the cord little by little recovers its powers, and we then find that the spinal cord of the dog can carry out the most complicated reflex movements without any connection with the higher centres. In a dog whose cord has been divided in the dorsal region, the reflex movements required for micturition, defæcation, impregnation, and parturition may be normally carried out. If the dog, which usually squats on

the ground from the paralysis of its hinder extremities, be raised on its hind legs by the hands being placed under the fore-legs, and given a little push forwards, the animal may run along for a few steps before it collapses again into a sitting posture. In this case the reflex running movements of the hind legs, carried out by the separated spinal cord, are started by the sudden stretching of the anterior thigh muscles.

The vascular tone in the lower part of the body, which is lost for some time after the operation, is also regained.

Muscular tone.—Every muscle in the body is normally in a condition of slight continued contraction, which is known as muscular tone. If a frog with intact spinal cord be suspended by the jaw, and the nerves going to the lower limb be cut, this limb will hang down straighter than the other in consequence of the abolition of its muscular tone. The same result may be produced if, instead of dividing all the nerves of the limb, only the sensory or only the anterior roots of those nerves be divided. This shows that muscular tone is reflex, and depends for its maintenance on the intact condition of afferent paths, centre, and efferent paths. On the presence of this tone depends the phenomenon known as 'tendon-reflex' or knee-jerk. If the leg be allowed to hang loosely and the patellar tendon be struck, the extensor muscles of the thigh contract and raise the leg. This contraction is probably due to the direct stimulation of the muscle by the sudden stretching produced on striking its tendon. If the muscle has lost its tone by disease, or through section of the afferent or efferent fibres of the spinal cord, striking the tendon will no longer stretch the flabby muscle, and the tendon-reflex will be abolished. This phenomenon is of great importance in clinical medicine.

We may conclude that the cord, besides being the carrier of motor impulses from, and sensory impulses to the brain, is also able to carry out numerous complicated reflex movements; most of these movements, however, being also

under the control of the cerebral centres. Of these reflex functions of the cord the chief are—

Walking.
Micturition.
Defæcation.
Impregnation and parturition.
Muscular tone.
Vascular tone.

CHAPTER XIII

THE BRAIN

THE physiology of the brain falls naturally into two main divisions, the cerebral hemispheres, and the rest of the brain, including medulla, pons, iter and corpora quadrigemina, and third ventricle.

This second part may be considered as a prolongation of the spinal cord forwards, consisting like this of a central tube of grey matter, surrounded by a tube of white matter. Owing to the importance and complex connections of the nerve-roots which arise from this part of the neural axis (cranial nerves), the typical division of grey matter into cornua becomes lost, and we find that while some nerves take their origin from the central tube of grey matter, in other cases the collection of cells forming the nucleus has become more or less separated from the central axis.

Moreover masses of grey matter make their appearance in the white matter, which have no representative in the cord.

The roof of the neural canal, which over the third ventricle and the posterior part of the fourth is greatly thinned, consisting merely of a layer of epithelial cells, is thickened over the iter (third cerebral vesicle) to form the corpora quadrigemina, and over the pons and anterior part of the fourth ventricle it grows out into a large excrescence with complicated structure—the cerebellum. Covering the corpora quadrigemina and cerebellum is a layer of grey matter outside a central mass of white fibres. The lateral walls of the third ventricle (first cerebral vesicle) are

thickened to form the optic thalami, which contain masses of grey matter. The cerebral hemispheres are formed by hollow outgrowths from the first cerebral vesicle. These in course of development become as large as the whole of the rest of the brain put together, and grow backwards over the rest of the brain as far as the middle of the cerebellum. Their upper walls become very much thickened, and consist of white matter internally and grey matter externally. Their lower walls remain as a thin layer of undifferentiated epithelial cells; this becomes closely applied to the epithelial layer forming the roof of the third ventricle, from which it is only separated by a process of the pia mater carrying numerous blood-vessels (the velum interpositum). The lower and outer wall of the cerebral hemispheres becomes very much thickened, and forms the corpus striatum, which becomes closely applied to the front and outer part of the optic thalamus. In it two masses of grey matter are developed, the nucleus caudatus and nucleus lenticularis, separated from one another by a layer of white fibres, which is continuous with a similar layer separating the corpus striatum from the optic thalamus, and is called the internal capsule.

In the brain we may distinguish three varieties of fibres, according to their function.

1. Commissural fibres connecting one half of the brain with the other.

2. Connecting or association fibres between different parts of the brain on the same side.

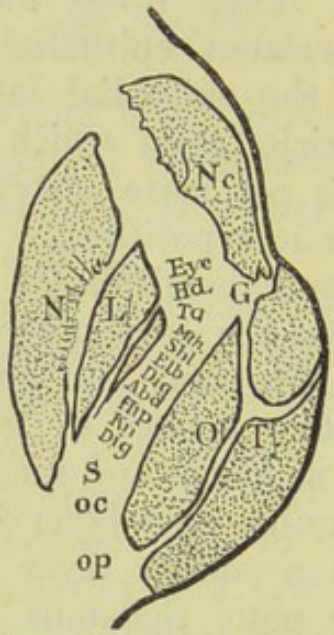
3. Tracts which act as afferent or efferent channels between the cortex and lower parts of the brain and spinal cord ('projection fibres').

The chief mass of commissural fibres is found in the corpus callosum, and serves to connect the two hemispheres.

The white matter in the interior of the hemispheres consists of radiating fibres, called the corona radiata. It carries afferent impulses to the cerebral cortex, and effe-

rent impulses from the cortex through the internal capsule to other parts of the cerebro-spinal axis. The chief mass of fibres between the cerebral cortex and spinal cord goes through the crura cerebri, which form the floor of the Sylvian iter. The crura consist of two layers of white fibres, the tegmentum above and the crusta below, separated by a layer of grey matter, the substantia nigra.

FIG. 118.



Horizontal section through basal ganglion to show arrangement of fibres in internal capsule. From before backwards the fibres go to the motor centres for the eye, head, tongue, mouth, shoulder, elbow, fingers, abdomen, hip, knee, and foot. S. Fibres going to temporo-occipital region. oc. Fibres to occipital lobe. op. Optic radiations. Nc. Nucleus caudatus. O T. Optic thalamus. N L. Nucleus lenticularis. (After Sherrington.)

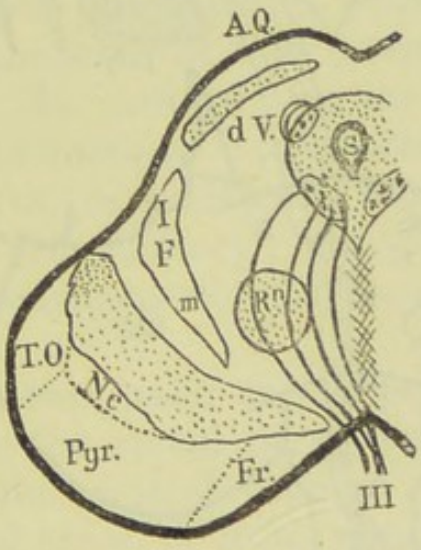
Course of the Chief Tracts of the Spinal Cord in the Brain

The fibres which are destined to form the pyramidal tracts of the cord leave the central parts of the cortex, which we shall afterwards know as the motor area, and pass through the corona radiata into the internal capsule, where they occupy the bend and the anterior two thirds

of its posterior limb. Thence they pass through the crura cerebri, taking up the middle two thirds of the crusta, and then through the pons. Emerging from the lower border of the pons, they form two thick masses, the anterior pyramids of the medulla. At the lower part of the medulla the major portion of the fibres passes across to the posterior part of the lateral column of the other side, and is continued down this side as the crossed pyramidal tract. A small number of fibres of each tract do not cross at once, but pass down in the cord in the same situation as they occupied in the medulla, forming the direct or anterior pyramidal tracts. These, however, also cross gradually in the cord before reaching their final destination—the anterior cornu of the opposite side.

The fibres of the postero-median column of the cord

FIG. 119.

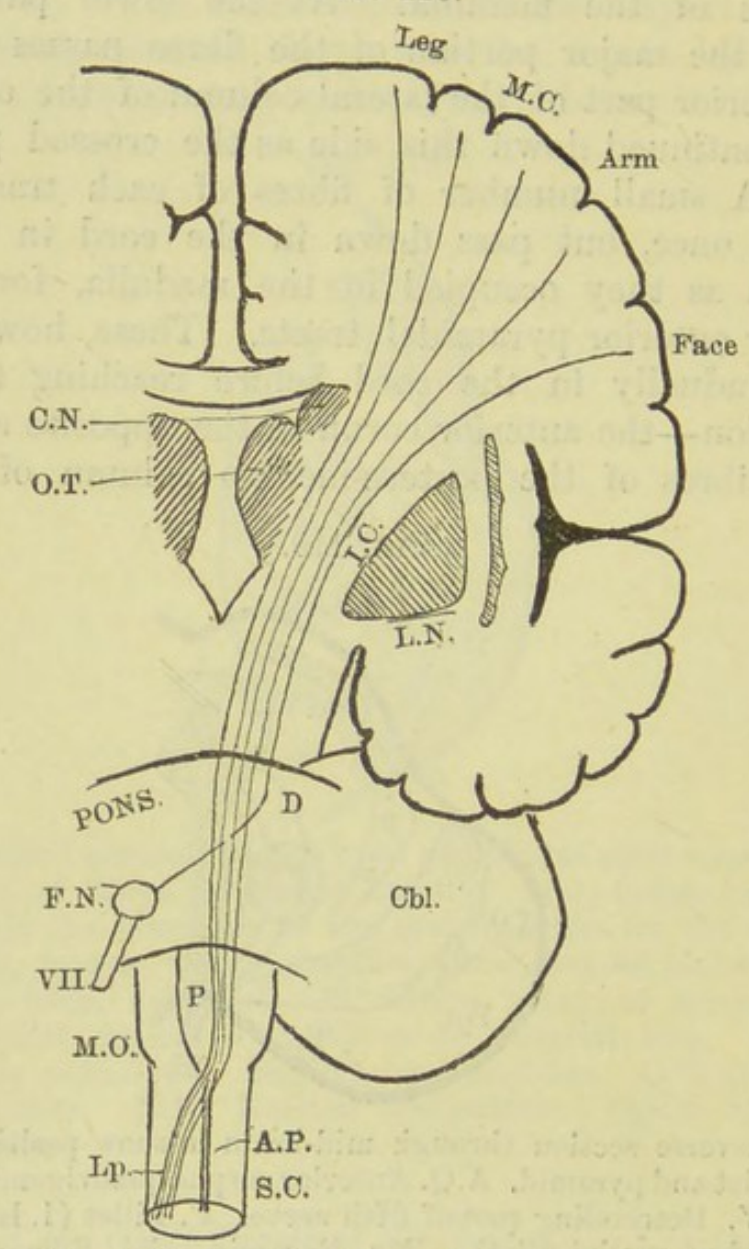


Transverse section through mid-brain to show position of fillet and pyramid. A.Q. Anterior corpus quadrigeminum. dV. Descending root of fifth nerve. F. Fillet (I, lateral, and m, mesial fillet). Pyr. Pyramid. Fr. Fibres from frontal lobe to pons. T.O. Fibres from occipital lobe to pons. Ne. Fibres from nudius caudatus to pons. III. Root of third nerve. S. Sylvian iter. Rn. Red nucleus.

end in the medulla in a little mass of grey matter, the nucleus gracilis. Those of the postero-external column

end in the nucleus cuneatus, which is just outside the nucleus gracilis. From these masses of grey matter fibres arise (arcuate fibres) which cross round the front of the

FIG. 120.



Diagrammatic vertical section through brain showing course of pyramidal fibres. M.C. Cortex on which are situated the motor centres. I.C. Internal capsule. C.N. Caudate nucleus. O.T. Optic thalamus. L.N. Lenticular nucleus. D. Point of decussation of facial fibres to F.N., facial nucleus. VII. Seventh nerve. P. Pyramids of medulla. A.P. Anterior pyramidal tract. Lp. Lateral pyramidal tract. M.O. Medulla oblongata. S.C. Spinal cord. Cbl. Cerebellum.

medulla to the opposite side in the superior pyramidal decussation. They then pass up in the tegmentum, forming the greater part of the tract known as the fillet. Some of the fibres end in the grey matter of the corpora quadrigemina, while others are continued as far as the optic thalamus. Here they end in the grey matter, and a fresh relay of fibres arises from the cells in this situation and passes through the posterior third of the hind limb of the internal capsule, and so reach the cerebral cortex. It is probable that some of the fibres of the fillet run directly to the cortex without making any connection with the thalamus. The direct cerebellar tract runs up in the restiform bodies to the cerebellum on the same side. The antero-lateral ascending tract goes up through the front part of the pons, and turning dorsally about the level of exit of the fifth nerve, curls back again, and enters the cerebellum along with the superior peduncle, ending in the grey matter of the superior lobe (vermis).

Cranial nerves.—The cranial nerves are generally reckoned as twelve in number: 1st, olfactory; 2nd, optic; 3rd, oculo-motor; 4th, or trochlear; 5th, or trigeminus; 6th; 7th, or facial; 8th, auditory; 9th, glosso-pharyngeal; 10th, vagus or pneumogastric; 11th, spinal accessory; 12th, hypoglossal.

Of these the first two stand on a different footing from the rest, which, like the spinal nerves, are outgrowths of nerve-fibres from the central tube of grey matter surrounding the neural canal, or from ganglia corresponding to the spinal posterior root-ganglion. The olfactory and optic nerves, however, are not peripheral nerves at all, but are actual outgrowths from the brain. The olfactory bulb and the retina are morphologically distinct lobes of the brain.

The *first* or *olfactory nerve* (or, more properly, olfactory lobe) has ten or twelve filaments, which pierce the cribriform plate, and are distributed to the olfactory mucous membrane. It is the central organ of smell. It is sup-

posed that impulses do not cross from one side of the body to the cerebral hemisphere of the opposite side, as is the case with all the other nerves of the body.

The *second* or *optic nerve* subserves the function of vision, and that alone. The two nerves join at the *optic chiasma*. Here there is a partial exchange of fibres, and each of the

FIG. 121.

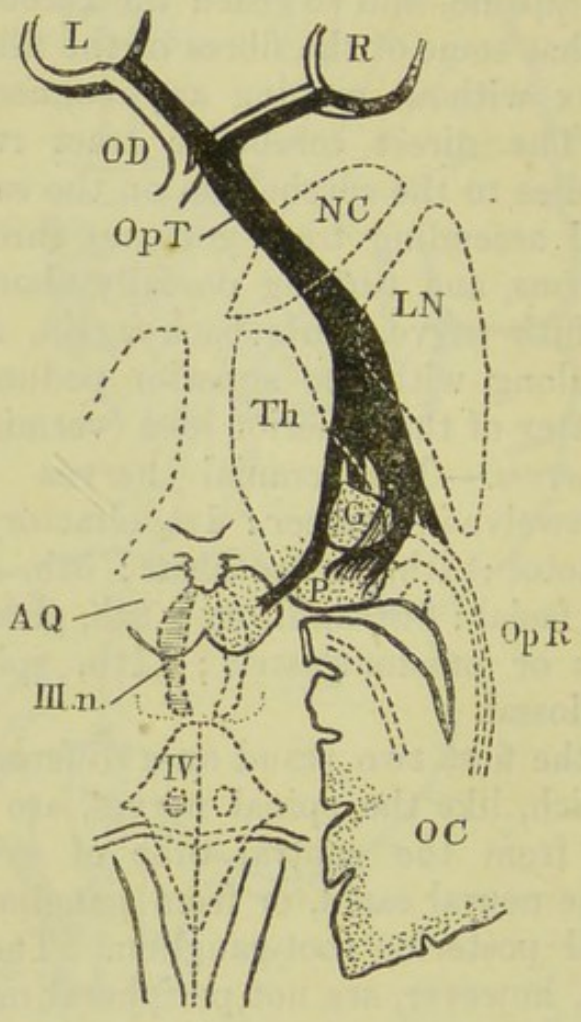


Diagram to show connections of optic tracts (after Sherrington) L, left, and R, right retina. O D. Optic decussation (chiasma). Op T. Optic tract. N C. Nucleus caudatus. L N. Lenticular nucleus. Th. Optic thalamus. G. External geniculate body. A Q. Anterior corpus quadrigeminum. P. Pulvinar. Op R. Optic radiations running to O C., the occipital cortex. III.n. Nucleus of 3rd nerve in floor of Sylvian aqueduct. IV. Fourth ventricle.

optic tracts, which are the continuations behind the chiasma of the optic nerves, contains fibres from both optic nerves.

Thus the right optic tract contains the fibres from the external half of the right retina and the internal half of the left retina. Since these are corresponding parts of the two retinæ, and are excited by light coming from the left of the person, section of one optic tract causes blindness on the opposite side (*hemianopia*). Each optic tract is connected behind with the back part of the optic thalamus (pulvinar), the external corpus geniculatum, and the anterior corpus quadrigeminum of the same side (Fig. 121). From these points fibres pass through the posterior part of the internal capsule and corona radiata ('*optic radiations*') to the cortex of the occipital lobe.

The *third* or *oculo-motor nerve* arises from a column of nerve-cells situated at the extreme hind part of the floor of the third ventricle, and from the front part of the floor of the aqueduct of Sylvius, below the anterior corpus quadrigeminum. It emerges from the inner side of the crus cerebri. It is the motor nerve for the levator palpebrarum, superior, inferior, and internal recti, and inferior oblique muscles. It also supplies the constrictor iridis and the ciliary muscle. Stimulation of it therefore causes the eye to look upwards and inwards, with contraction of the pupil, and spasm of accommodation. By careful stimulation of various parts of its nucleus the different movements of these muscles may be produced separately.

The nucleus of the *fourth nerve* is situated just behind that for the third in the floor of the Sylvian aqueduct. The fibres run from here round the aqueduct, and take their superficial origin from the valve of Vieussens, a thin plate of grey matter forming the roof of the fourth ventricle just in front of the cerebellum.

This nerve supplies only the superior oblique muscle of the eyeball.

The *fifth* or *trigeminus* resembles a spinal nerve in that

it has a motor as well as a sensory root, the latter being provided with a ganglion (Gasserian ganglion). It has a very extensive origin, owing to the fact that its sensory part represents the sensory roots of all the motor cranial nerves from the third to the hypoglossal. The middle or motor root arises from a collection of nerve-cells in the floor of the fourth ventricle. It also receives fibres from the descending root, which can be traced forwards from the nucleus as far as the level of the anterior corpora quadrigemina.

The sensory root may also be traced into a nucleus lying lateral to the motor nucleus, though in this case the fibres of the nerve probably end in the nucleus, having their trophic centre in the cells of the Gasserian ganglion. Connected with the sensory nucleus is the ascending root

FIG. 122.

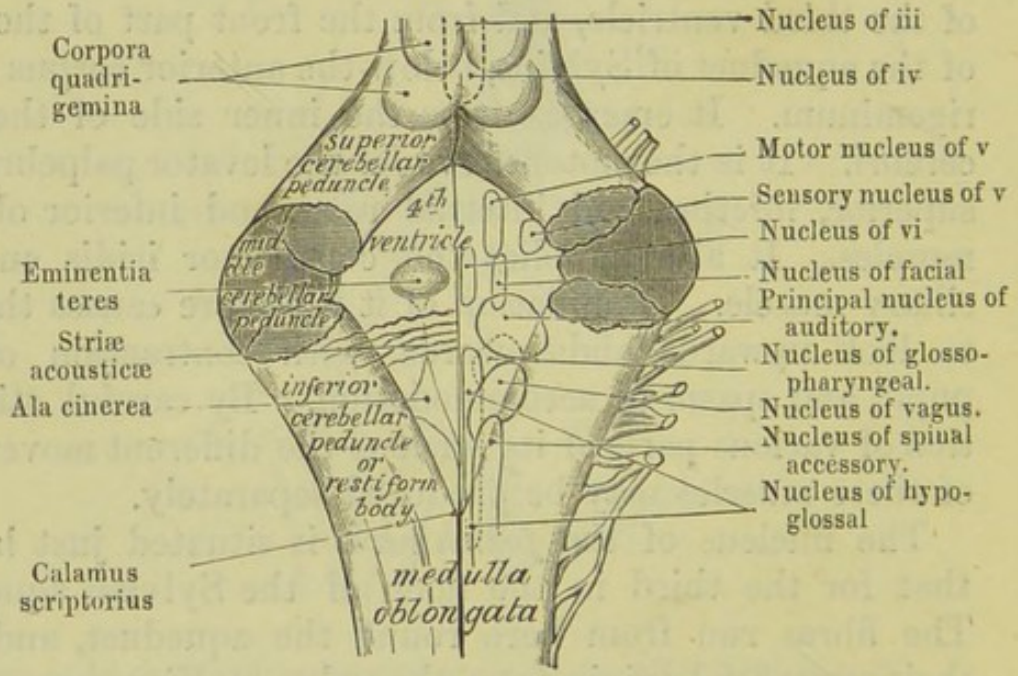


Diagram of fourth ventricle and adjacent parts, as seen from dorsal aspect, to show positions of nerve nuclei. These are marked on the right-hand half. (After Erb.)

of the fifth nerve, which can be traced downwards through the medulla as far as the level of the second cervical nerve,

where it forms a little cap of white fibres on the mass of gelatinous substance forming the head of the posterior horn, and known in the medulla as the tubercle of Rolando.

This nerve is the motor nerve for the muscles of mastication, and for the tensor tympani and tensor palati. It is the sensory nerve for the whole of the face (including eyeball, mouth, and nose). It also contains fibres to blood-vessels (chiefly dilator) derived from the cervical sympathetic, and is said to have *trophic* functions. The latter conclusion is from the fact that section of the fifth nerve in the skull is followed by ulceration and sloughing of the cornea, and finally destructive changes involving the whole eyeball. Since, however, these results may be prevented by carefully shielding the eye from all dust and

FIG. 123.

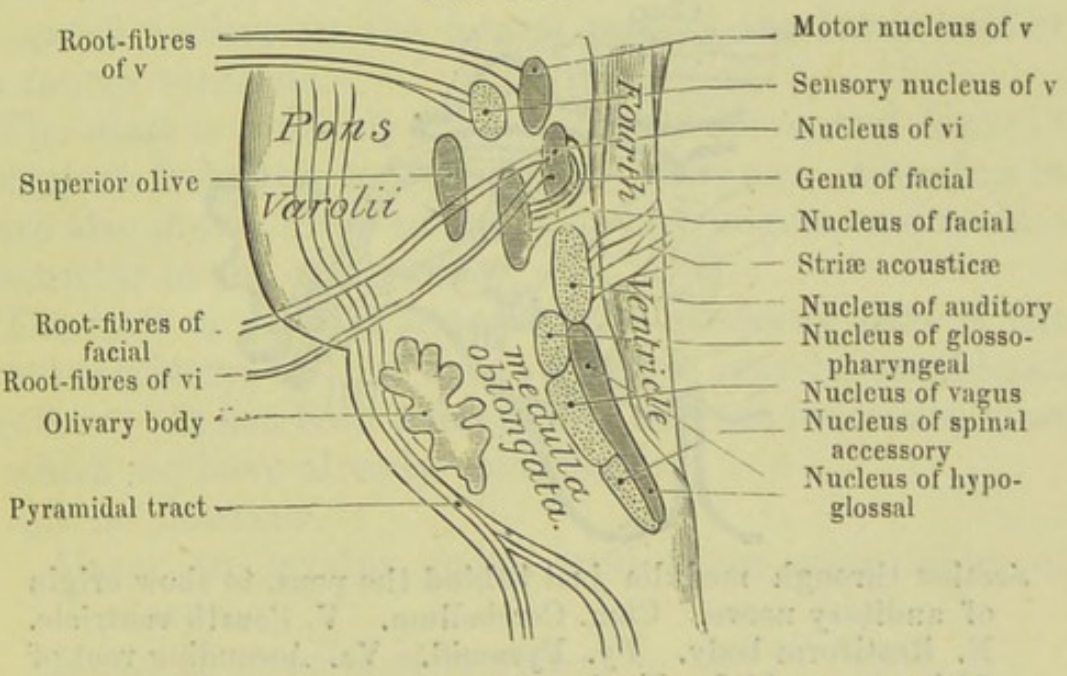


Diagram to show positions of principal nerve-nuclei in pons and medulla, side view. The organ is supposed to be split down the middle line, and the right half viewed from the mesial side. The most mesially situated nuclei are shaded, the others stippled. (After Erb.)

deleterious influences, it is probable that the ulceration is merely a secondary consequence of the anæsthesia. The

cornea being anæsthetic, foreign objects that fall on its surface are allowed to remain there, and so give rise to injurious changes and ulceration.

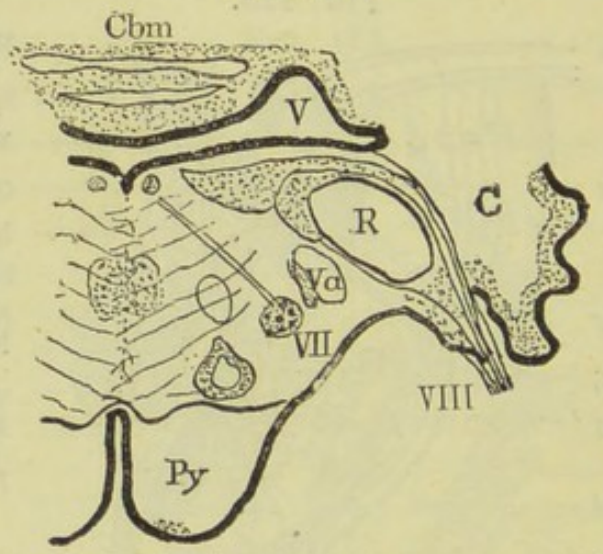
The fifth is also said to be the nerve of taste for the anterior third of the tongue, but it is very probable that the taste-fibres which run in the fifth are derived from the glosso-pharyngeal.

The *sixth* nerve, the motor nerve for the external rectus, rises from a small group of cells in the floor of the fourth ventricle near the middle line.

The nucleus for the *facial* or *seventh* nerve is situated more deeply and laterally than the preceding. It supplies all the muscles of the face, and is therefore the nerve of expression.

The chorda tympani, which is a branch of this nerve,

FIG. 124.



Section through medulla just behind the pons, to show origin of auditory nerve. Cbm. Cerebellum. V. Fourth ventricle. R. Restiform body. Py. Pyramid. Va. Ascending root of fifth nerve. VII. Nucleus of seventh nerve. VIII. Auditory nerve.

contains secretory and vaso-dilator fibres for the sub-maxillary gland. The fibres of taste which are said to run in this nerve are probably derived from the glosso-pharyngeal.

The *eighth* or *auditory* rises on a level with the hind

margin of the pons by two roots, one of which, the dorsal root, winds round the restiform body, while the other, the ventral or median root, sinks into the substance of the bulb to the inner side of the restiform body. The fibres composing the dorsal roots come from the cochlea and convey sensations of sound. The fibres pass round, dorsal to the restiform body, and end to a large extent in the so-called median nucleus, some fibres having previously made connection with a mass of cells in the angle between the two roots, known as the accessory nucleus. The ventral root consists of fibres derived from the vestibule and semicircular canals, and carries impulses connected with the reflex maintenance of equilibrium. It ends in the lateral auditory nucleus, where a number of fibres pass up with the restiform body into the cerebellum.

The ninth, tenth, and eleventh nerves arise from an elongated nucleus in the lateral part of the lower half of the fourth ventricle.

The *ninth* is probably a pure sensory nerve, and conveys sensations from tongue (taste) and pharynx. Running in it are also motor fibres to the stylo-pharyngeus and middle constrictor of the pharynx.

The *tenth* or *vagus* is joined by the accessory part of the spinal accessory, so that the two nerves may be considered together. It has both afferent and efferent functions, most of which we have already considered.

Efferent functions:

Motor to levator palati and three constrictors of pharynx.
Motor to muscles of larynx.
Inhibitory to heart.
Vaso-dilator (?) of abdominal vessels.
Motor to muscular walls of œsophagus, stomach, and intestine.
Motor to unstriated muscle in walls of bronchi and bronchioles.
Secretory to glands of stomach and pancreas.

Afferent functions :

Regulate respiration. Stimulation of central end quickens respiration and promotes especially inspiration. Stimulation of central end of superior laryngeal causes stoppage of inspiration, expiration, cough.

Depressor (from heart to vaso-motor centre).

Reflex inhibition of heart.

The external branch of the *spinal accessory* is the motor nerve of the sterno-mastoid and trapezius muscles.

The *hypoglossal* (*twelfth* nerve) arises from a nucleus in the floor of the fourth ventricle at its lower end close to the middle line.

It is a pure motor nerve, and supplies the intrinsic and extrinsic muscles of the tongue.

Since the integrity of the nuclei of the cranial nerves is a necessary condition for the carrying out of various reflex acts in which these nerves are involved, the grey matter of the fourth ventricle and aqueduct is often spoken of as if it were cut up into a series of centres distinct for every act. It must be remembered, however, that when a dozen or more centres are enumerated as being situated in the fourth ventricle, it is not meant that we can anatomically distinguish a group of cells for each act or group of actions named. When we say that a part of the nervous system is a centre for any action, we merely mean that this part forms a necessary link, or meeting of the ways, in the complicated directing of nerve impulses that takes place in every co-ordinated act.

The chief centres are the respiratory and the vaso-motor. These we have already considered. Other centres that may be enumerated are—

Centres for movements of intrinsic and extrinsic ocular muscles.

Cardiac inhibition.

Mastication, deglutition.

Sucking.

Convulsive (connected with respiratory).
Vomiting.
Diabetic (connected with vaso-motor, *v.* p. 325).
Salivary.
Centres of phonation and articulation.

Functions of the Cerebral Axis

We have already studied the phenomena exhibited by an animal (frog) possessing spinal cord alone. We can now by a study of the same or a higher animal, deprived only of its cerebral hemispheres, come to some conclusion concerning the functions of the lower parts of the brain, and, by comparison of these phenomena with those exhibited by an intact animal, of the cerebral hemispheres themselves.

When a frog's cerebral hemispheres have been excised, a casual observer would not at first notice anything abnormal about the animal. He sits up in his usual position, and on stimulation may be made to jump away, guiding himself by sight, so that he avoids any obstacles in his path. Movements of swallowing and breathing are normally carried out. The animal, thrown on to his back, immediately turns over again. If put into water, he swims about until he comes to a floating piece of wood, or any support, when he crawls out of the water and sits still. If placed on a board and the board be inclined, he begins to crawl slowly up it, and by increasing slowly its inclination he may be made to crawl up one side and down the other. But a striking difference between him and a normal frog is the almost entire absence of spontaneous motion, that is to say, motion not reflexly provoked by changes immediately taking place in his environment. All psychical phenomena seem to be absent. He feels no hunger and shows no fear, and will suffer a fly to crawl over his nose without snapping at it. "In a word, he is

an extremely complex machine, whose actions, so far as they go, tend to self-preservation ; but still a *machine* in this sense, that it seems to contain no incalculable element. By applying the right sensory stimulus to him, we are almost as certain of getting a fixed response as an organist is when he pulls out a certain stop."*

The effects of ablation of the cerebral hemispheres of the pigeon are very similar. If left to itself, the bird remains perfectly still and seems fast asleep ; if stimulated, it may be made to fly normally, and is then observed to avoid obstacles, guided by the sense of sight. Like the frog, it shows no signs of fear or hunger, and will starve to death on a heap of corn, although it will begin to eat the corn if its beak be plunged into it. In the higher mammals ablation of the cerebral hemispheres produces such severe shock that nothing can be said with regard to the working of the lower part of the brain. The rabbit, however, will survive the operation for a few hours, and during this time it can be made to run, and no symptoms of paralysis are observed. When a sensory surface or nerve is stimulated, the animal gives forth a prolonged and plaintive cry. We thus see that the axial parts of the brain, together with the corpora quadrigemina and cerebellum, contain all the necessary nervous mechanisms for the carrying out of the co-ordinated muscular actions involved in standing, running, flying, mastication, deglutition, and expression of the emotions.

Co-ordination of Muscular Actions

The first two of these functions must be considered here a little more fully. The maintenance of equilibrium depends on a series of complex reflex acts, which are dependent on incoming or afferent impulses, various centres or interlacements of nerve-paths in the grey matter, and on efferent impulses to the muscles.

* James, ' Psychology.'

The chief afferent impulses which guide the maintenance of equilibrium are those from the skin, eyes, semicircular canals, and muscles themselves. The importance of impulses from the skin is shown by those cases in which, from disease of the sensory tracts, there is anæsthesia of the soles of the feet. In these cases the patient is unable to stand with his eyes shut, and indeed may first discover that anything is wrong with him from the fact that he is apt to fall down whenever he is washing his face. The same effect may be experimentally produced by freezing the soles of the feet, so as to make them anæsthetic.

If in a brainless frog the skin be stripped from the hind limbs, it no longer sits up in a normal posture, and is unable to climb up an inclined board.

The use of visual impulses in guiding the nervous centres in the maintenance of equilibrium is shown by the preceding experiment, in which no loss of equilibrium occurred till the patient closed his eyes.

Sudden destruction of the eye in pigeons or rabbits causes these animals to spin round and round in a circle, or may cause them to fall over. The giddiness, too, that is often produced by looking at rapidly moving objects, such as a train or waterfall, shows the connection of this sense with equilibration. But by far the most important afferent impulses are those coming from the semicircular canals.

These structures form three bony tubes, which open into the vestibule by five apertures, two of the tubes uniting into one. Within these bony tubes, and separated from them by the perilymph, are three membranous canals, each of which has a dilatation or ampulla at one end, and all communicate with the utricle ; all these parts being developed from the primitive auditory vesicle. In the ampullæ are situated the ultimate terminations of the vestibular division of the auditory nerve.

When these canals are injured definite disturbances of equilibrium are produced. Thus if the horizontal canal be

divided in pigeons, the head is thrown into a series of oscillations in a horizontal plane, which are intensified by section of the corresponding canal on the opposite side, so that the animal may fall down.

After section of the posterior vertical canals, the forced movements are in a vertical plane, and the animal tends to turn somersaults head over heels. After section of the superior vertical canals the movements are still in a vertical plane, and the animal tends to turn somersaults heels over head. After destruction of all the canals on both sides the disturbances of equilibrium are most pronounced and complicated. The animal can neither stand nor fly, nor maintain any fixed attitude, but is constantly executing somersaults, and moving about so violently and incoherently that it is necessary to pad its cage to prevent it killing itself.

After some months these disorders gradually disappear, and the animal learns to guide his movements by sensa-

FIG. 125.

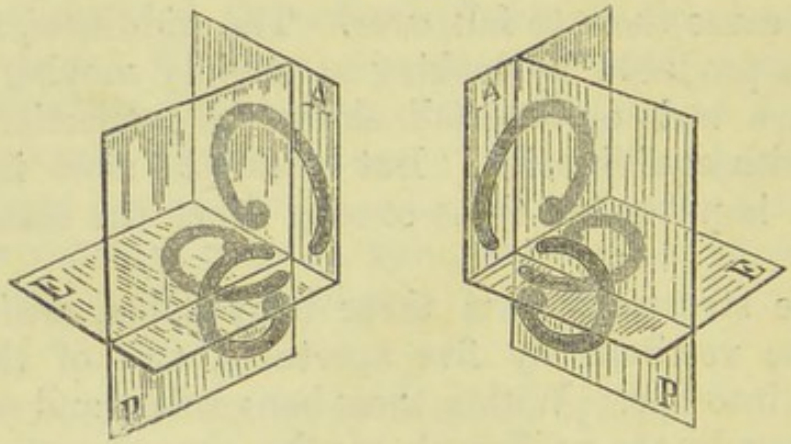


Diagram of semicircular canals to show their position in three planes at right angles to one another. It will be seen that the two horizontal canals lie in the same plane (E), and that the superior vertical of one side (A) is in the same plane as the posterior vertical (P) of the other side (from Ewald).

tions of touch and sight alone. But they are instantly brought back in all their severity if the eyes be bandaged

so as to deprive the co-ordinating centres of the guiding visual sensations.

It will be noticed that the semicircular canals on each side are in three planes at right angles to one another, and it is probable that we learn the positive movements of our body with regard to the three dimensions of space by means of impressions from the ampullary endings of the vestibular nerve. These impressions are caused by the varying pressure of the endolymph on the ampullary dilatations of the semicircular canals.

Thus a sudden turning of the head from left to right will cause movement of endolymph towards, and therefore increased pressure on, the ampullary nerve-endings of the left horizontal canal, and movement of endolymph away from, and therefore diminished pressure on, the corresponding ampulla of the right side. In this way, for movement in any given plane, the two corresponding semicircular canals of the two sides are synergic, and unite in sending impulses which guide the equilibrating centres, and inform us of the position of our head in space. "One canal can be affected by and transmit the sensation of rotation *about one axis in one direction only;* and for complete perception of rotation in any direction about any axis *six* semicircular canals are required in three pairs, each pair having its two canals parallel (in the same plane), and with their ampullæ turned opposite ways. Each pair would thus be sensitive to any rotation about a line at right angles to its plane or planes, the one canal being influenced by rotation in the one direction, the other by rotation in the opposite direction."* The two horizontal canals are in the same plane, and the posterior vertical canal of one side is in the same plane as the superior vertical of the other.

Finally, all the muscular actions required for the maintenance of equilibrium are guided and regulated by afferent

* Crum-Brown.

impulses from the muscles themselves. The muscular sense, however, is still more important in the co-ordination of muscular contractions by which locomotion is carried out. This is well exemplified in certain cases where, owing to disease of the intra-muscular sensory nerves, or of the sensory channels of the cord, there is a loss of muscular sense accompanied by loss of muscular tone and tendon-reflexes. Such cases are said to suffer from ataxy. There is no proportionality between the contractions of the various muscles used, so that some muscles act too strongly and others too feebly. In this way a vast amount of energy is expended with very little practical effect in moving the patient along.

It is difficult to say that the function of co-ordinating movements or maintaining equilibrium is limited to any distinct part of the cerebro-spinal axis. We have already seen that all the machinery necessary for carrying out some of the most complicated movements of locomotion is present in the spinal cord; and it is probable that under normal circumstances all that the higher centres do is to set this machinery going. We may say that these functions are served by the whole cerebro-spinal axis from the third ventricle to the lower end of the spinal cord, together with the outgrowths forming the corpora quadrigemina and the cerebellum. There is a good deal of evidence connecting the latter organ more closely with the co-ordination of movements than with any other function. The cerebellum can receive impressions from the eyes through the superior peduncle, from the semicircular canals through the middle peduncle, and it receives fibres which are probably sensory in function from the lower part of the body through the inferior peduncle or restiform body. Section of the middle peduncle causes marked inco-ordination of movement, the animal running round and round in a circle or rolling over and over. Stimulation of the side of the cerebellum produces movements of the same side. Stimulation of the anterior part of the

vermis (superior middle lobe) causes nodding movements of the head, with a tendency to turn head over heels. Irritation to the back part leads the animal to turn somersaults heels over head. We may say as the result of experiments that the function of the right half of the cerebellum is to prevent the body falling over to the left side, by bringing about contractions of the muscles on the right side. A cerebellar hemisphere, therefore, is connected with the body of the same side, and with the cerebral hemisphere of the opposite side. Disease of the cerebellum gives rise to a staggering gait very similar to that of a drunken man (cerebellar ataxy).

Emotional expression.—By appropriate stimuli it is possible to elicit in animals deprived of their cerebral hemispheres the outward bodily manifestations which we usually regard as the expressions of certain emotions. Now an emotion is a psychical state, or state of consciousness; but it is dependent for its production on the existence of certain bodily changes—affections of the heart, vascular system, voluntary muscles—which are involuntary and reflexly produced. The mechanism for this reflex-production is present in the lower cerebral centres, so that severe stimulation of a sensory nerve in a hemisphereless rabbit causes it to utter a long, plaintive scream. The brainless frog responds with a croak, almost indicative of pleasure, each time its back is gently stroked. In neither of these, nor in any similar cases, however, are we justified in speaking as if an emotional state of consciousness were produced. We have no reason to think that the rabbit suffers pain, or that the frog is pleased, in the two above-mentioned experiments, but merely that certain changes in the bodily condition are reflexly produced, which, if the cerebral hemispheres were present, would be represented in consciousness as an emotion of pain or pleasure.

When a patient is slightly under the influence of chloroform, it frequently happens that all the emotional expressions are preserved, although consciousness is totally

abolished; he may cry out or struggle when cut with the knife, and yet when he recovers from the anæsthetic he will state that he felt nothing whatever of the operation.

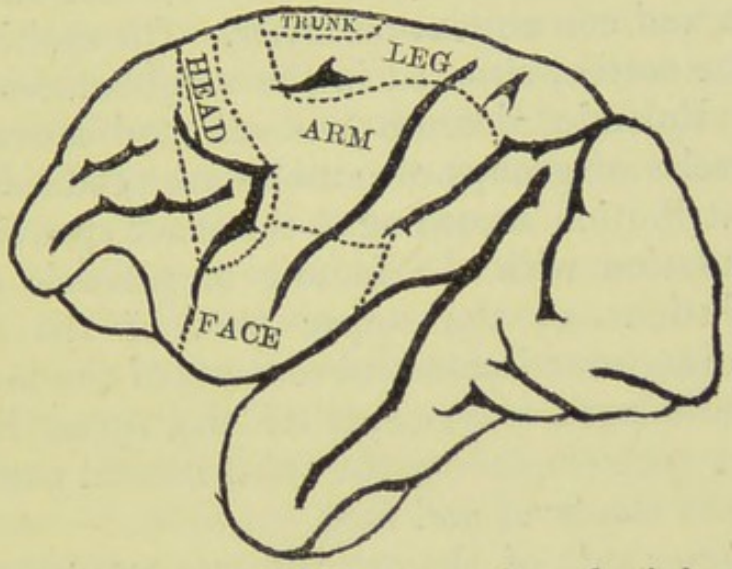
Cerebral Hemispheres

We may come to some conclusions as to the general functions of the cerebral hemispheres if we compare the behaviour of a normal animal with one that has been deprived of its cerebral hemispheres. In the former case it is quite impossible to foretell what particular reaction may be evoked by any stimulus. It may produce the same effect as when applied to a brainless animal, but in most cases the reaction is modified in various ways. The animal is no longer a mere machine that can be played on at will, but is an individual whose actions are ruled by a guiding intelligence, who is actuated by motives and by feelings of fear, hunger, pain, and the like. In short, an animal, whose cerebral hemispheres are intact, presents phenomena analogous to those which in ourselves are associated with changes in the state of consciousness, and which we call volition or feeling.

It was formerly thought that in all their functions the cerebral hemispheres acted as an entity, and that any voluntary movement or any change in the state of consciousness might be considered as carried out by all parts of the hemispheres acting together. It has long been known, however, that each cerebral hemisphere innervated the opposite side of the body. Thus if the cortex of one hemisphere be destroyed or be functionally separated from the lower parts of the brain by destruction of the internal capsule, paralysis (hemiplegia) and loss of sensation on the opposite side of the body are produced. The paralysis is limited to voluntary, and may not affect reflex or emotional movements. It is interesting to note that those movements which are usually carried out by the muscles on both sides of the body at the same time are not so affected,

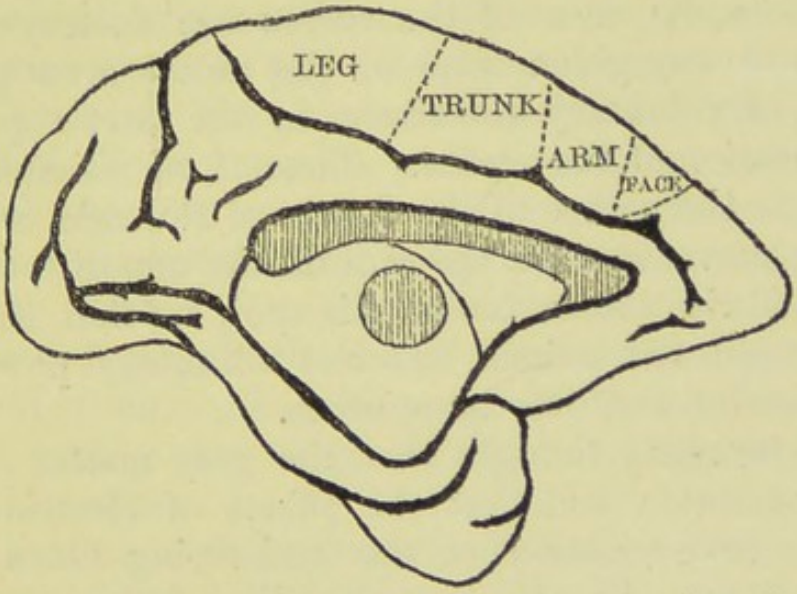
probably in consequence of the close interdependence of the bulbar and spinal centres for these movements, and

FIG. 126.



Motor centres on outer surface of monkey's brain.
(After Horsley and Schäfer.)

FIG. 127.



Motor centres on mesial surface of monkey's brain.
(After Horsley and Schäfer.)

partly because these movements are equally represented in both hemispheres.

Moreover, during the last twenty years, conclusive

evidence has been brought forward of the localisation of function in the cerebral cortex of each side of the brain. This evidence is physiological and pathological, but in both cases it falls under the head of excitation, or of destruction and consequent paralysis. On exciting certain parts of the cortex, situated in the neighbourhood of the fissure of Rolando, definite co-ordinated movements of certain muscles or groups of muscles are produced, varying in their distribution according to the exact spot stimulated. Thus stimulation with the faradic or galvanic current of the convolutions at the upper part of the fissure of Rolando causes co-ordinated movements of the lower limb; of the middle part, movements of the upper limb; and of the lower part (including the third frontal convolution), movements of the head and face.

On the inner side of the hemispheres movements of the face, arm, trunk, and leg are represented from before backwards on the marginal convolution. These experiments are corroborated by others in which definite parts of the Rolandic area of the cortex are destroyed. Destruction of any given zone of the motor area produces paralysis of voluntary movement in the part represented by this portion of the cortex. Thus if, on stimulation of a spot near the centre of the fissure of Rolando, we obtain a definite movement of the arm of the opposite side, and we then excise the cortex at this spot, we find that after the operation the animal has lost voluntary power over this movement and over none other.

It was formerly thought that the grey matter was not directly excitable, and that the effects of electric stimuli were due to excitation of the underlying fibres of the corona radiata. The direct excitability of the grey matter is, however, proved by the following considerations.

1. There is greater lost time in the grey matter than in the underlying white matter; that is, if we first stimulate the grey matter, and then shave this off and stimulate the white matter below, it is found that the latent period, which

elapses between the time when the stimulus is sent in and the time at which the contraction takes place, is far greater in the former than in the latter case.

2. It is very common, as the result of excessive stimulation of the cortex, to get, not a single contraction of the group of muscles represented in the area stimulated, but an epileptic convulsion, which starts in this group of muscles and spreads thence to all the other muscles of the body. The convulsion consists of two stages :

(*a*) The tonic stage, in which all the muscles of the body may be in a state of continued contraction.

(*b*) The clonic stage, which lasts a good deal longer than the first stage, and consists of rapid rhythmical jerking movements of the muscles. This is followed by—

(*c*) A stage of exhaustion, in which the cortex is relatively inexcitable.

If the grey matter on both sides be removed, stimulation of the white fibres of the corona radiata does not produce a typical epileptic fit.

Pathological evidence bears out the results on localisation deduced from the physiological experiments just mentioned. Thus we have cases in which a tumour pressing on a part of the motor area causes twitching movements of the limb, or more or less complete epileptic convulsions, starting in the particular limb represented in the affected area of the cortex. On the other hand, cases frequently occur in which parts of the cortex are destroyed by pressure of a growing tumour, or by stoppage of the vessels supplying that area, giving rise to paralysis of definite muscles or groups of muscles.

After a movement has been abolished by extirpation of a definite area of the cortex, a considerable amount of recovery of movement may take place. The degree to which this may occur varies in different classes of animals, being more complete in the lower animals, such as the dog and rabbit, than in the monkey and man. It probably depends on the taking up of the functions of the extirpated

area, partly by the adjoining regions of the cortex, and partly by the corresponding centre of the opposite hemisphere, all the centres of the two sides of the brain being functionally connected by means of the corpus callosum.

A point of considerable importance is the fact that movements rather than muscles are cortically represented. Thus stimulation of the right frontal lobes causes a movement (conjugate deviation) of both eyes to the left. In this movement the external rectus of the left side and the internal rectus of the right side are both set in action by stimulation of the right cortex. Similarly, we may produce movement of the head to the left by stimulation of the proper spot of the right cortex. In this movement the right sterno-mastoid and the left external oblique muscles are involved.

When we speak of motor centres it must not be supposed that motor impulses start *de novo* in the pyramidal cells of these centres. Here, as in all other parts of the central nervous system, the activity of the cells is excited exclusively by impulses arriving at them from other parts, and ultimately from the periphery of the body. These impulses, since they are afferent, so far as the pyramidal cell is concerned, may be spoken of as sensory, and the collection of exalted reflex centres which make up the Rolandic area may therefore be justly termed *sensori-motor*. In fact, there is evidence that it is in the motor area that the sensation of touch and pressure on the corresponding limbs is perceived, and that the motor effect of existing area is normally produced as a reaction to such touch or pressure sensations. Hence in extensive lesions of the motor area sensation as well as movement may be affected, and a certain amount of anæsthesia accompanying the paralysis produced.

Sensory areas.—If in the monkey the right occipital lobe is stimulated, there is movement of both eyes to the left. This experiment by itself is capable of two interpretations :

either the occipital lobe is to be regarded as a motor centre to the ocular muscles, or it is a sensory centre of sight, and the animal looks towards the left because visual sensations are aroused and referred to the left side of the field of vision. The latter explanation is shown to be true by the effects of extirpation. If the occipital cortex be destroyed, the animal is rendered blind on the side opposite the lesion. It is said to suffer from hemianopia (half-blindness). Excision of both the occipital lobes causes total blindness. Since the rays of the left half of the field of vision fall on the right-hand side of the two retinæ, and left hemianopia is produced by destruction of the right occipital lobe, it is evident that the temporal half of the right retina and the nasal half of the left retina are innervated from the right occipital cortex. The connection, however, of the occipital lobe with the retina of the other side is more complete than with the retina of the same side, so that after destruction of the right lobe loss of vision is more extensive in the left than in the right eye.

FIG. 128.

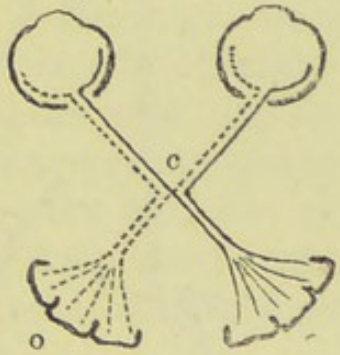


Diagram showing functional connection of occipital lobes with the two retinæ. c. Optic chiasma. o. Occipital lobes.

Our evidence as to the localisation of the other senses in the cortex is less complete. The sense of hearing is located by Ferrier in the superior temporo-sphenoidal lobe. Stimulation of this part causes pricking of the ears ; destruction of it produces different effects according to the experi-

menter ; it may give rise to deafness on the opposite side (Ferrier), or to no appreciable results (Schäfer).

Smell and taste have been localised in the caput cornu Ammonis and the uncinate gyrus.

Fig. 129.

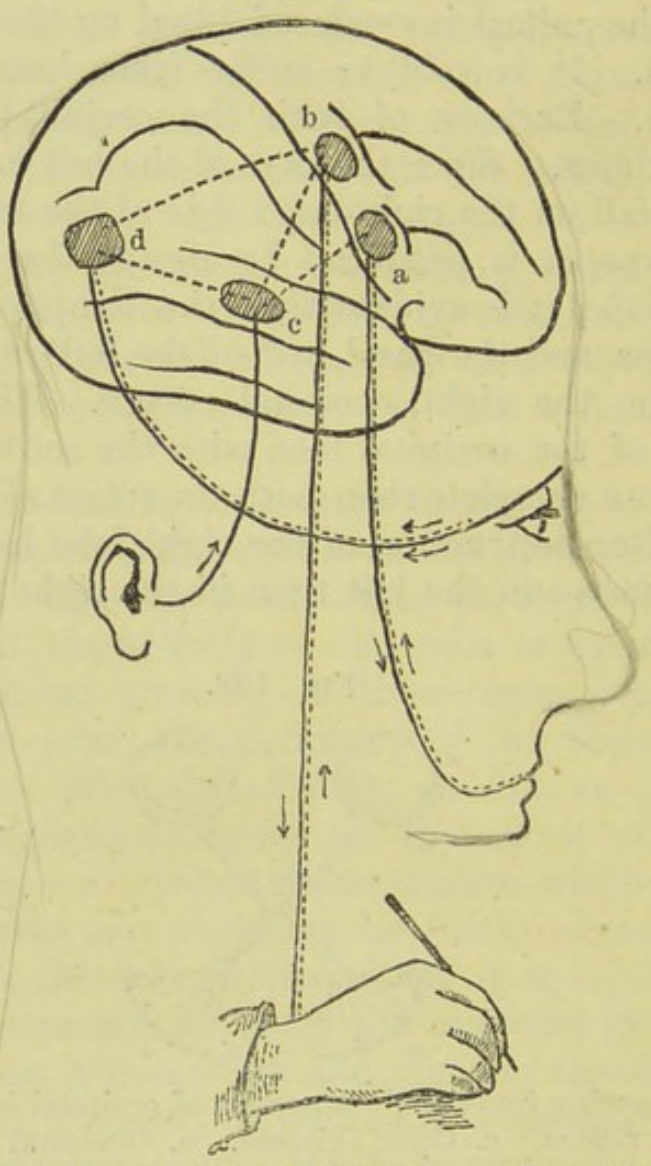


Diagram of cortical areas engaged in speech and writing (Ross). a. Broca's convolution (motor lip and tongue area). b. Arm area. c. Word auditory centre. d. Visual word centre.

Tactile sensibility is probably represented in the gyrus fornicatus, destruction of this convolution on one side causing hemianæsthesia on the opposite side of the body.

It is now generally believed that muscular sensibility is cortically represented in the same region as muscular movements, *i. e.* in the Rolandic area.

Aphasia.—If the cortex on the left side is destroyed, power of speech is totally lost. The same effect is produced if the lesion be limited to a small area in the third left frontal convolution (Broca's convolution). Our normal right-handedness is necessarily associated with and caused by the activities of the left hemisphere predominating over and guiding those of the right. In the movements that stand highest in the evolution of the cerebral functions, those of speech, the predominance of the left side is so marked that destruction of the centre for lips and tongue on this side causes complete loss of the delicately co-ordinated movements by which speech is produced.

Besides this motor aphasia, which is brought about by a lesion of Broca's convolution, speech may be destroyed by injury of the sensory centres (sensory aphasia). Thus, in some cases in which the left superior temporo-sphenoidal lobe was involved, there has been a condition of word-deafness. The patient could not understand anything that was said to him. He might be able to take volubly, but the words were mere gibberish ; his auditory word centre being absent, he was unable to appreciate the meaning of what he was saying, and so the motor processes went on unchecked by the criticism of sensory impressions. The talking of a man with word-deafness may be compared to the walking of a man with complete loss of muscular sense.

In the same way a lesion in the left occipital lobe may cause loss of power to read (alexia) from blotting out of all the higher visual memories, and more especially those connected with written and printed words.

Any of these lesions may be attended with inability to write, which in most people is intimately dependent on the auditory and motor speech memories. Most people in writing may be seen to move their lips slightly as they

articulate the words to themselves, thus showing that in writing the arm centre is acting in subordination to the mouth-speech centre in the third left frontal convolution.

Fig. 129 represents simply the relationships of the various centres on the left side to one another in speaking and writing.

CHAPTER XIV

REPRODUCTION

THROUGHOUT the animal kingdom we find the welfare of the individual subordinated to that of the species. . The crowning act of an animal's life is the production of a new individual, fitted in all respects to take the place of the parent organism, and so to maintain the race on the earth. In the case of the lowliest unicellular organisms, which reproduce themselves only by fission, we cannot rightly speak of death from natural causes. One amœba divides into two new individuals similar to it in every way, and these in their turn divide again. Hence the amœbæ have with some right been spoken of as immortal. It is evident that any accommodation of the organism to its environment must, since it affects the whole cell, be transmitted in equal degree to the cells that are the offspring of the division of the parent. And so we may, in course of time, get a gradual change of type in the organism.

As we go higher in the scale we meet with more highly differentiated organisms, consisting of cell colonies, each member of which has its own appointed task to fulfil; and here we find that the office of reproduction also is confined to one cell or group of cells. The immortality of the amœba has been transmitted to this group of cells. From this point onwards, in the scale of animal life, we may regard the reproductive cells or germ-plasma as being continuous through successive generations. With the production of each new generation the germ-plasma divides into two parts: one part, the somatic half, forming what

is generally understood as the individual, and being differentiated into various forms of cells, to perform the multifarious functions of reaction associated with life; and the other half, persistent in its primitive form as the reproductive part of the individual, ready when the time comes to divide again and give birth to a new generation.

There are, however, many unicellular organisms in which the processes of reproduction are not quite so simple. These are able to multiply for a few generations by simple fission. At the end of this time, for the production of a new generation or series of generations the conjoint action of two cells is required. In this process of *conjugation* two unicellular organisms come together and unite, their nuclei fusing to form one nucleus; the single cell thus made is capable of producing by fission several more generations. Here the cells that fuse are exactly alike in all respects. A little higher in the scale, however, among the multicellular organisms, we find the cells, which conjugate to form a new cell capable of developing into an individual, present somewhat different characters. The one cell, which has generally a certain amount of stored-up reserve-material in its protoplasm, is the female element, and is called the ovum. The other cell, which is chiefly limited to the nuclear substance, is called the spermatozoon, and is the male element. This is the sexual mode of reproduction, which obtains in all the higher animals.

The conjugation of these two cells is not the union of the whole of two ordinary cells of two individuals. We find that both ovum and spermatozoon, before their union, undergo certain important changes, which have been more fully studied in the case of the former. The nucleus of the ovum just before fertilisation divides into two parts; one half is extruded with a small amount of the protoplasm, and the other remains in the main body of the ovum. The nucleus then undergoes division a second time, and again one half is extruded with a little proto-

plasm. The two extruded cells are spoken of as polar bodies, and do not undergo any further modification. The part of the nucleus left in the ovum is the female *pronucleus*. A similar change takes place in the male element, and the nuclei of the spermatozoa are equivalent to female pronuclei. These male and female pronuclei have the power of uniting together to form a whole nucleus, which is then capable of undergoing a long series of divisions to form a new individual. The union is effected by the penetration of the spermatozoon, which is in the higher animals mobile, into the ovum. Here for a while two nuclei are seen, the male and female pronuclei. They then fuse together, and the fertilised ovum is now potentially a new individual, partaking of the characteristics of both its parents.

Sexual life of man.—The period of active sexual life, during which the individual is capable of begetting or bearing children, begins in both sexes at the age of fourteen to sixteen, known as the age of puberty. In women, the beginning of this period is marked by the onset of menstruation. This is the occurrence of a flow of mucus and blood, which arises in the uterus, from the genital organs ; it lasts from three to five days, and recurs regularly every four weeks. Menstruation is associated with ovulation, which consists in the discharge of an ovum from the ovary. This latter contains follicles enclosing an ovum, which are known as the *Graafian follicles*. They are lined with a layer of cells—the *membrana granulosa*—which surround the ovum. In the course of development these cells proliferate and divide into two layers, each several cells thick, one of which lines the follicle, and the other—*discus proligerus*—encloses the ovum. The space between them is filled with colourless fluid which contains proteids. This fluid gradually increases in amount until it forms a large projection on the surface of the ovary. At or just before each menstrual period a ripe Graafian follicle ruptures, and the ovum is discharged into the fimbriated

extremity of the Fallopian tube, down which it is conducted to the uterus. This is accompanied with congestion of the genital organs, especially of the uterus, in consequence of which some of the smaller vessels of the uterine mucous membrane rupture, and give rise to the discharge of bloody fluid. The discharge of blood is accompanied with the fatty degeneration and disappearance of the most superficial parts of the mucous membrane itself.

When the Graafian follicle ruptures, hæmorrhage takes place into its interior. This is followed by a rapid proliferation of the cells of the membrana granulosa, which grows in folds into the cavity, absorbing the blood-clot, and transforming the hæmoglobin into a yellow pigment. Hence for some weeks after discharge of an ovum its Graafian follicle may be recognised as a yellow spot, which is known as the *corpus luteum*. This is often spoken of as the *spurious* corpus luteum, to distinguish it from the corpus luteum of pregnancy. If pregnancy does not follow the discharge of the ovum, the corpus luteum disappears in from one to two months. If, however, pregnancy occurs, the corpus luteum becomes very large, forming a prominent projection on the surface of the ovary, and is to be seen almost to the end of pregnancy. Menstruation ceases during pregnancy, and is also generally absent during lactation. It ceases altogether between the ages of forty-five and fifty. After this time, which is known as the climacteric, the woman is no longer capable of bearing children.

Impregnation.—In animals which have a rutting season, ovulation is also accompanied by a flow of blood from the genital organs, and it is during this period, which corresponds to the menstrual period, that impregnation is effected. In the human species impregnation may be effected at any time, and the union of spermatozoa with the ova may occur in the uterus, Fallopian tubes, or even in abnormal cases on the surface of the ovary.

If the ovum be not fertilised, it is cast out with the blood and products of disintegration of the uterine mucous membrane at each menstrual period. If, however, it be fertilised while in the Fallopian tube, a considerable thickening of the uterine mucous membrane takes place from proliferation of its cells, and it at the same time becomes very vascular. When the ovum reaches the uterus it becomes embedded in the mucous membrane covering the fundus of the uterus, which grows round and completely encloses it. This thickened mucous membrane, which is called the *decidua*, becomes fused with the outer layer of the ovum, and the latter, by means of its blood-vessels, derives its nourishment from the uterine mucous membrane.

At about the eighth week after impregnation the formation of the *placenta* takes place in the following manner :—A

FIG. 130.

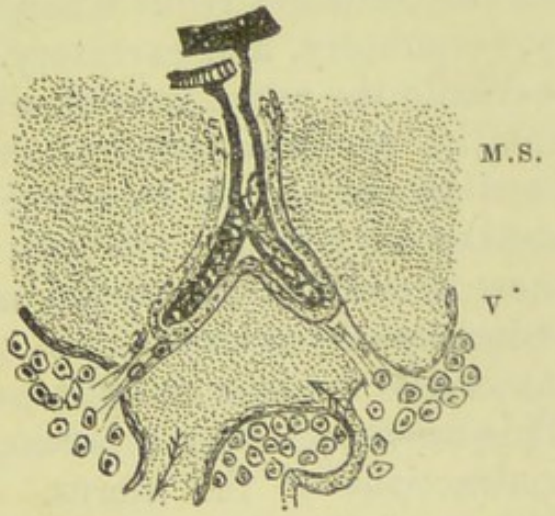


Diagram to show structure of human placenta. M.S. Maternal venous sinus. V. Villus (outgrowth from chorion), containing artery and vein with capillaries derived from the umbilical vessels of the fœtus, and covered with a single layer of epithelial cells.

process of the internal hypoblastic layer of the embryo grows out, carrying with it fœtal blood-vessels, and these blood-vessels with their containing mesoblastic tissue extend

so as to completely surround the embryo. This outgrowth is intimately applied to the decidua. At one spot it becomes hypertrophied, and here sends in villi, covered with a single layer of cells and supplied with blood-vessels; these project into maternal venous sinuses which have developed in the thickened mucous membrane of the uterus.

Through the medium of this placenta the developing animal obtains all the nutrient material it requires, both oxygen and combustible foodstuffs. The vessels of the fœtus are not in direct communication with those of the mother. The interchange of material between the two must be effected by the cells covering the placental villi, and takes place in fact through two layers of cells, the endothelium of the fœtal vessels and the epithelium of the villi. The placenta at the same time serves as an excretory organ for the fœtus, the effete material of the latter passing from the capillaries to the blood in the venous sinuses which bathe and surround the villi. The placenta is therefore alimentary, respiratory, and excretory.

Parturition.—While the ovum is undergoing its wonderful development, in which a complete human being is formed out of a single cell by division and differentiation, the uterus becomes very much enlarged, and its walls thickened by new growth of unstriated muscular tissue. At the end of nine months from the date of impregnation the development of the fœtus is complete, and parturition takes place. This consists in the expulsion of the fœtus by muscular contractions of the uterus. Parturition or labour is divided into three stages. In the first stages the contractions of the uterus, which are painful, and are hence spoken of as 'pains,' are devoted to dilating the os uteri. This is effected by contractions of the longitudinal muscles of the uterine wall, at the same time that the fœtus, contained in its bag of membranes, is forced against and expands the os.

When the os is fully dilated the uterine contractions

change in character, becoming more prolonged, and are accompanied by strong contractions of the abdominal muscles, which force the child out through the vagina.

A short time after the birth of the child the pains recommence, and expel the placenta with the decidua and the fœtal membranes.

In this third stage the connection of the uterine vessels with the placental sinuses is necessarily torn through. Bleeding, however, is prevented by the fact that the muscular fibres of the uterus remain firmly contracted after birth, compressing and obliterating the lumen of the torn vessels.

Directly the child is born, the uterus, contracting on the placenta, compresses its vessels, and prevents a further supply of oxygen to the fœtal vessels. The child therefore becomes asphyxiated, and the venous blood, acting on the medullary centres, calls forth the first act of respiration, and the process is started which is to supply the needs of the new individual with oxygen for the rest of its life.

Parturition is obviously a complex reflex act, and depends for its normal carrying out on the integrity of the nervous connections of the uterus with the spinal cord. The centre for the act of parturition lies in the lumbar spinal cord, and it has been shown that parturition may go on normally in a bitch whose cord has been completely divided in the dorsal region. This act is, then, not necessarily dependent on the co-activity of the voluntary centres.

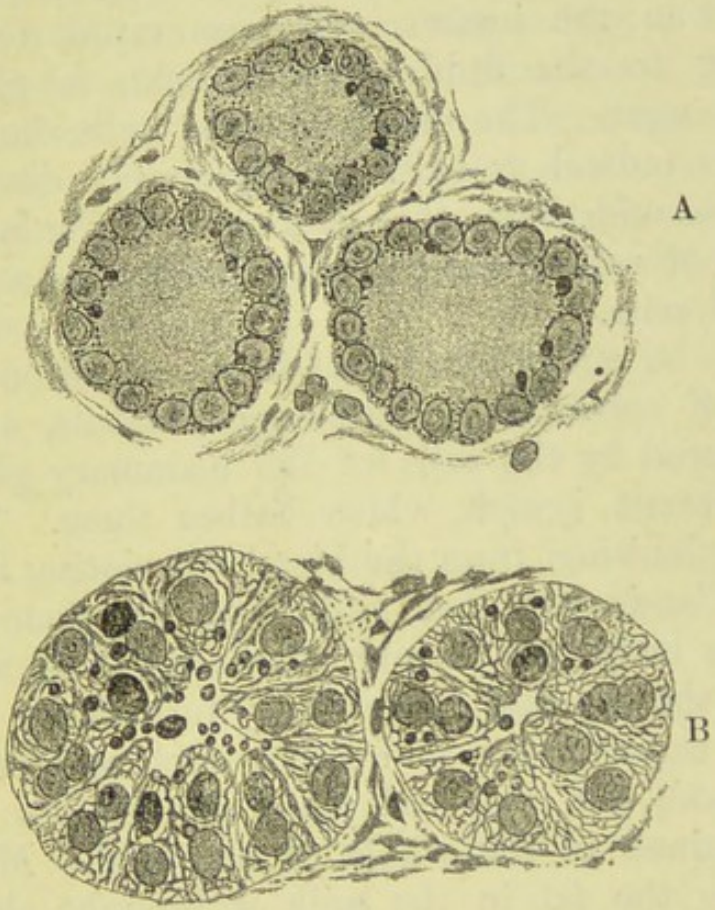
After birth the enlarged uterus rapidly diminishes in size, in consequence of the atrophy and disintegration of the newly formed muscular tissues, and this *involution* is complete at the end of three months.

Lactation.—The young child at birth is not independent, but relies for many years for nourishment and protection on the parents. For the first twelve months of the child's existence, under normal circumstances, it is nourished

entirely on the secretion of the mammary glands of the mother. The mammary glands vary largely in appearance according to the condition of the woman from which they are taken. Before impregnation they are small, and on microscopical examination are seen to consist of a number of branching sinuous tubules, which are cut in various directions, and so give the appearance of a number of alveoli. These tubules are filled with a solid mass of epithelial cells. If impregnation occurs, a marked hypertrophy of the gland takes place, caused by the outgrowth of new columns of cells and the formation of new tubules from the pre-existing ones. At the same time the whole gland becomes more vascular from the enlargement of the blood-vessels in the interstitial connective tissue between the tubules. At the end of pregnancy the cells in the interior of the tubules undergo disintegration, leaving them lined with only a single layer of cells. The active secretion of milk begins shortly before or immediately after birth. The first milk that is secreted, which is called the *colostrum*, differs markedly from normal milk as already described (p. 337). It contains less casein and fat, but more albumen than ordinary milk, and has in addition a certain amount of globulin. Owing to the large amount of these last two bodies, colostrum coagulates on boiling. Under the microscope, colostrum shows the presence of a number of cells with nuclei, or masses of protoplasm without nuclei (colostrum corpuscles). Some of these examined in fresh warm milk show amœboid movements. They probably have a twofold origin, from leucocytes which have wandered into the lumen of the gland, and from central cells of the tubules which have undergone disintegration. The active secretion of ordinary milk sets in on the second or third day after delivery. In the gland-cells we may distinguish a resting and an active condition, just as in the case of other glands. In the acini of a resting gland the lumen is wide and filled with milk, and the cells form a single flat nucleated layer at the periphery. The

inner margins of some of the cells show jagged edges, and the protoplasm of all the cells contains a few small granules. In an active gland, on the other hand, the cells,

FIG. 131.



Sections of mammary gland of guinea-pig (fat-granules stained black with osmic acid).

A. During rest.
B. During active secretion. It will be noticed that in this case the active formation of products of cell-metabolism (granules, &c.) begins with the commencement of secretion, and does not occur almost exclusively during rest, as in the salivary glands. In the mammary gland, the active growth of protoplasm, formation of granules from the protoplasm, and discharge of these granules in the secretion, appear to go on at one and the same time.

which are long and columnar, project far into the lumen. Many have two nuclei, and the central parts of all the

cells are filled with fat-granules and finer granules, which are probably proteid in character (cf. Fig. 131).

The process which goes on in the transition from the resting to the discharged condition is as follows. In some of the cells, the central part, with its contained degenerated daughter nucleus, breaks away entirely from the basal part, and in the lumen undergoes rapid disintegration, furnishing to the fluid there proteid, fat-globules, and probably sugar. The change in the cells, however, need not be so radical as this. Many simply discharge their fat-globules and their other contents into the lumen. This discharge of cell-contents is accompanied by a secretion of water and salts.

It must be remembered that in the secretion of milk its three chief constituents, caseinogen, lactose, and fat, are manufactured by the cells of the mammary glands out of the indifferent lymph which bathes them. This in its turn is replenished from the blood circulating through the gland. Caseinogen and milk-sugar are found nowhere else in the body, nor in any other animal secretion. The fact that the fat also is especially formed by the cells is shown by experiments, in which a bitch was fed on pure proteid food, and excreted more fats in her milk than were contained in the whole of her food. Moreover an increase in the fat in the milk is brought about by an increased proteid diet, but not by an increased fatty diet.

We see that the mammary gland in its mode of activity holds a position midway between the submaxillary mucous gland and the sebaceous glands of the skin. In the former the cells manufacture a stuff—mucigen—out of materials brought to them by the blood, and this is discharged as mucin when occasion requires, part of the protoplasm of the cells always remaining intact, ready to build and store up mucigen in its meshes. In the sebaceous gland the secretion is furnished entirely by the disintegrated cells themselves, a continual new formation of cells going on at the periphery of the acini; the older cells, as they are

forced towards the centre, undergo fatty degeneration, die, disintegrate, and are cast out as the fatty material known as *sebum* on the surface of the skin and at the roots of the hair.

The further rearing of the child, its maintenance and education to fit it to become a useful member of society (that is, one fit to continue the race on the earth), are as much physiological necessities for the continuation of the species as the processes we have just been discussing. We are, however, here concerned with physiology in its narrower sense, and need not carry it so far as the branch of this science known as sociology, the office of which it is to treat of these questions.

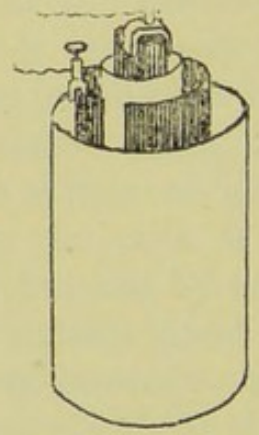
APPENDIX

A DESCRIPTION OF SOME ELECTRICAL INSTRUMENTS USED IN PHYSIOLOGY

THE first requisite of the physiologist, if he desires to use electrical currents for excitation or any other purposes, is a source of a constant current. For this purpose two forms of batteries are chiefly used, Daniell's and Grove's cells.

A Daniell's cell (Fig. 132) consists of an outer pot con-

FIG. 132.



Daniell's cell.

taining a saturated solution of copper sulphate, in which is immersed a copper cylinder. To the cylinder at the top a binding screw is attached, by which the connection of the copper with a wire terminal is effected. Within the copper cylinder is a second pot of porous clay, filled with dilute sulphuric acid, in which is immersed a rod of

amalgamated zinc. In this cell the zinc is the positive and the copper the negative *element*. Hence the current flows (in the cell) from zinc to copper, and if the binding screws of the two elements are connected by a wire, the current flows in the wire (outer circuit) from copper to zinc, thus completing the circuit. Since in the outer circuit the current flows from copper to zinc, the terminal attached to the copper is called the positive *pole*, and that to the zinc the negative pole.

When the current is required to be very constant, the zinc may be immersed in a saturated solution of zinc sulphate instead of dilute sulphuric acid.

A Daniell's cell, though very constant, gives only a small current, owing to its small electromotive force and

FIG. 133.

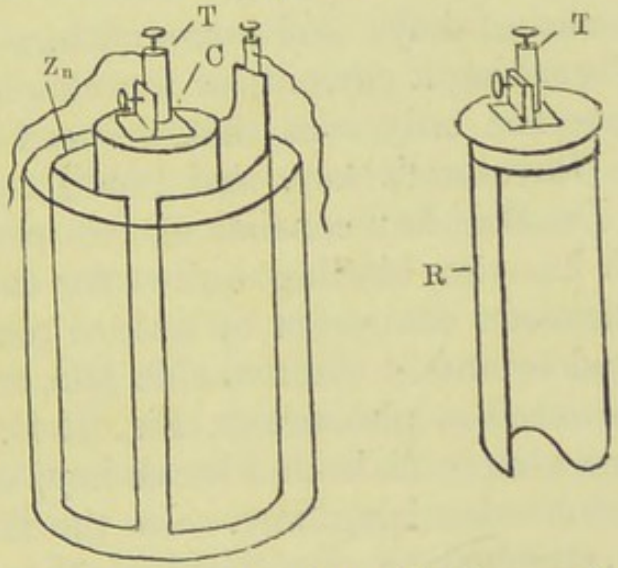


Diagram of Grove's cell. Zn. Zinc cylinder. C. Inner porous cell. T. Terminal or binding screw of platinum. R. Sheet of platinum.

high internal resistance. When a stronger current is required, a Grove's cell (Fig. 133) may be used. In this cell the zinc is in the form of a cylinder, immersed in a cell containing dilute sulphuric acid. Within the cylinder is a porous pot filled with strong nitric acid, in which is

immersed a sheet of platinum. In many cases the porous cell is made flat, and the zinc plate bent up round it, in order to decrease the distance between zinc and platinum, and so make the resistance as small as possible. In this cell the zinc is the positive and the platinum the negative plate ; and so the terminal attached to the zinc is the negative, and that attached to the platinum the positive pole.

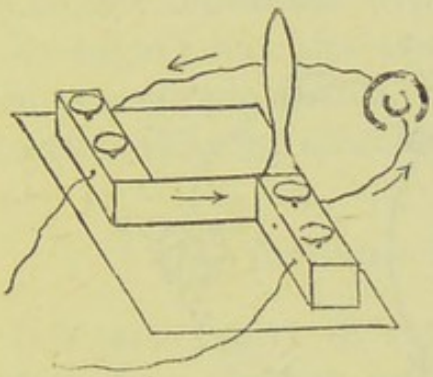
Another very convenient form of battery, though not so constant as the two forms just described, is the *bichromate* battery, with a single fluid. This consists of a plate of zinc between two plates of carbon. The whole are arranged so that they can be immersed in or drawn out of the fluid at pleasure. The fluid used is a mixture of sulphuric acid and potassium bichromate. The wire attached to the carbons is the positive pole, and the current in the outer circuit flows from carbon to zinc.

Various forms of keys and commutators are used for making and breaking a current, or for changing its direction. Of these the only ones that we need here describe are Du Bois Reymond's key, and Pohl's commutator or reverser. A Du Bois key consists of two pieces of brass, each of which has two binding screws for the attachment of wires. These are connected by a third piece, or bridge, which is jointed to one of the two side bits, so that it may be raised or lowered at pleasure (*v.* Fig. 134). It may be used either as a simple make-and-break key, or, as is more usual, as a short-circuiting key. In the first case one brass bank is attached to one terminal, the other to the other terminal. If the bridge be now lowered, the connection is made and the current passes. If the bridge be raised, the current is broken.

Figs. 134 A and B show the way in which the key is arranged for short-circuiting. It will be seen that four wires are attached to the key ; two going to the battery, and two we may suppose going to a nerve. When the bridge is down, as in Fig. 134 A, the current from the cell on coming to the key has a choice of two routes. It may

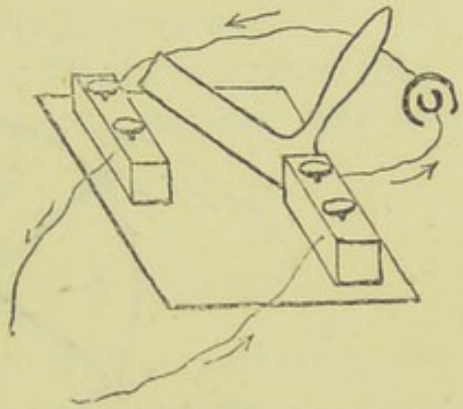
either go through the brass bridge, or through the other wires and nerve. The resistance of the nerve, however,

FIG. 134 A.



Du Bois key, closed.

FIG. 134 B.



Du Bois key, open.

is about 100,000 ohms, whereas that of the bridge is not the thousandth part of an ohm. When a current divides, the amount of current that goes along any branch is inversely proportional to the resistance. Here the resistance in the nerve circuit is practically infinite compared with that in the brass bridge, and so all the current goes through the bridge and none through the nerve. We say, then, that the current is *short-circuited*. If, however, the bridge be raised, as in Fig. 134 B, then the only way the current can go is through the nerve, and so the whole of the current takes this course. This form of key is indispensable when exciting nerves with currents of high intensity. If an ordinary make-and-break key only be interposed in the circuit, excitation may occur even when the key is raised, the current having high enough potential to complete itself through the table and stand on which the preparation lies. This is called *unipolar excitation*, and obviously cannot occur when the current is short-circuited.

Pohl's reverser is an arrangement for changing the direction of the current. It consists of a slab of ebonite or paraffin or other insulating material, in which are six small holes filled with mercury. A binding screw is in connec-

tion with the mercury in each of these holes. Two cross-wires (not in contact with one another) join two sets of pools together, as shown in Fig. 135.

FIG. 135.

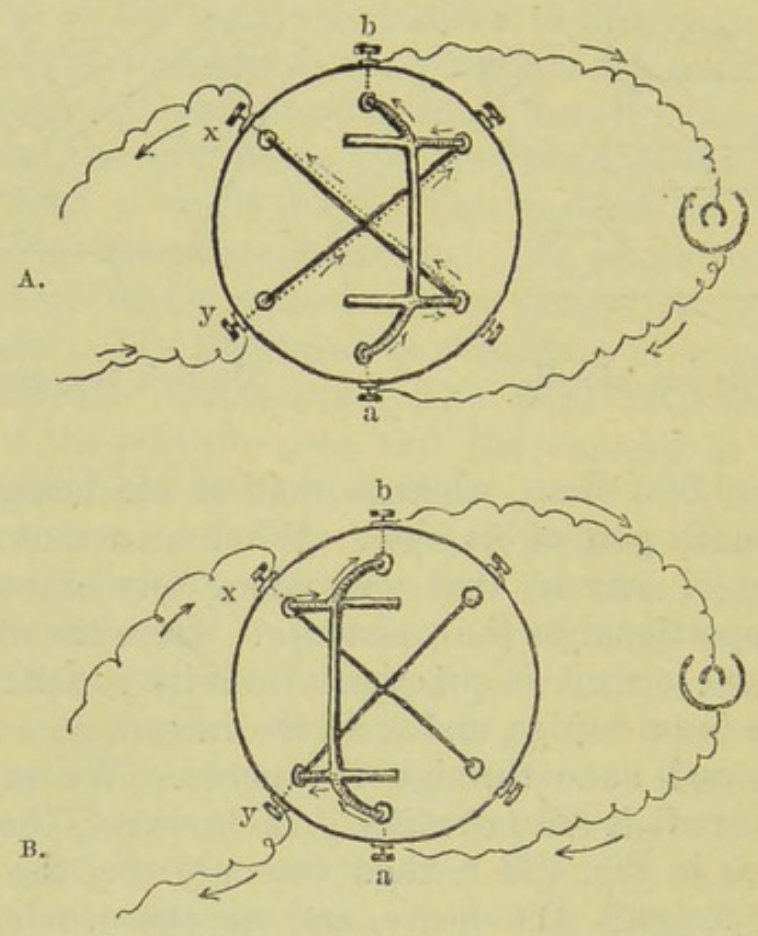


Diagram of Pohl's reverser.

A cradle consisting of two wires joined by an insulating handle carries two arcs of wire by which the pools at a and b may be put into connection with either x and y, or the corresponding pools on the opposite side. It will be seen that with the cradle tipped to one side, as in Fig. 135 A, the current from the battery enters the reverser at a ; this proceeds up the wire of the cradle, down towards the right, then along the cross-wire to the pool at x. x is therefore the anode, and y the kathode.

In Fig. 135 B the cradle has been swung over to the

other side. Here the cross-wires are not used at all by the current, which passes from a up the sides and down the curved wire to y. In this case y is now the anode and x the kathode, and the direction of the current through the circuit connected with x and y is reversed.

By taking out the cross-wires, Pohl's reverser may be used as a simple switch, by which the current may be led into two different circuits in turn.

The Induction Coil (Du Bois Reymond)

If a coil of wire in connection with a galvanometer be placed close to (but insulated from) another coil through which a current may be led from a battery, it is found that on make-and-break of the current of the second coil a momentary current is induced in the first. The induced current on make is in the reverse, that on break in the same direction as the primary current. The electromotive force of the induced current is proportional to the number of turns of wire in the coils. This principle is made use of in the construction of the induction apparatus. This consists of two coils, each containing many turns of wire. The smaller coil, R_1, consisting of a few turns of comparatively thick wire, is the primary coil, and is put into connection with a battery. It has within it a core of soft iron wires, which has the effect of attracting the lines of force, concentrating them, and so increasing its power of inducing secondary currents. The secondary coil, R_2, of a large number of turns of very thin wire, is arranged so as to slide over the primary coil. It is provided with two terminals, which may be connected with the nerve or other tissue that we wish to stimulate. Since the electromotive force of the induced current is proportional to the number of turns of wire, it is evident that the electromotive force of the current delivered by the induction coil may be many thousand times that of the battery current flowing through the primary coil. The induced currents increase rapidly

in strength as the coils are approached to one another; the strength of these, therefore, may be regulated by shoving the secondary up to or away from the primary coil.

FIG. 136.

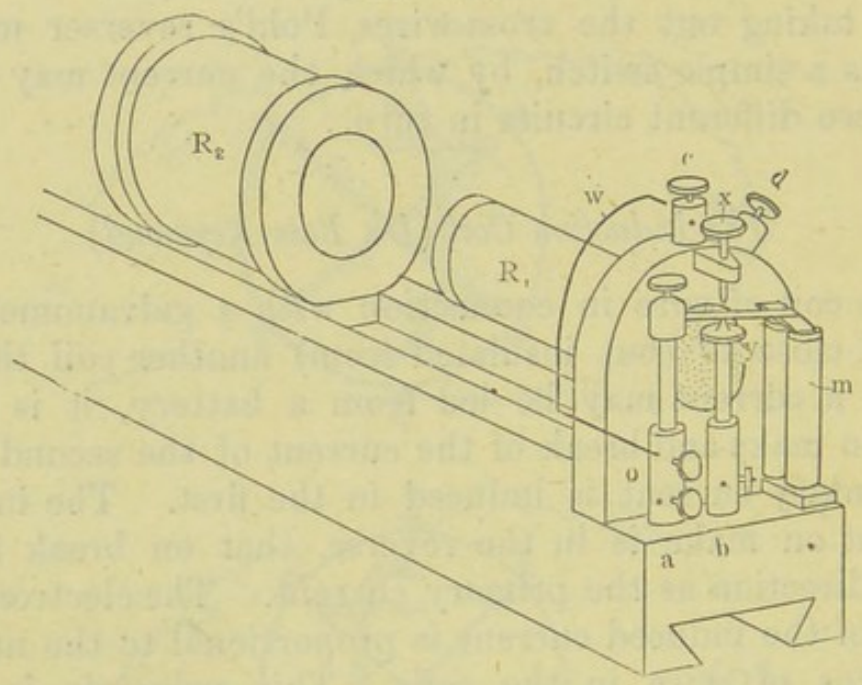


Diagram of inductorium. R_1, Primary; R_2, secondary coil. m. Electro-magnet of Wagner's hammer. w. Helmholtz's side wire.

A short-circuiting key is always placed between the secondary coil and the nerve to be stimulated.

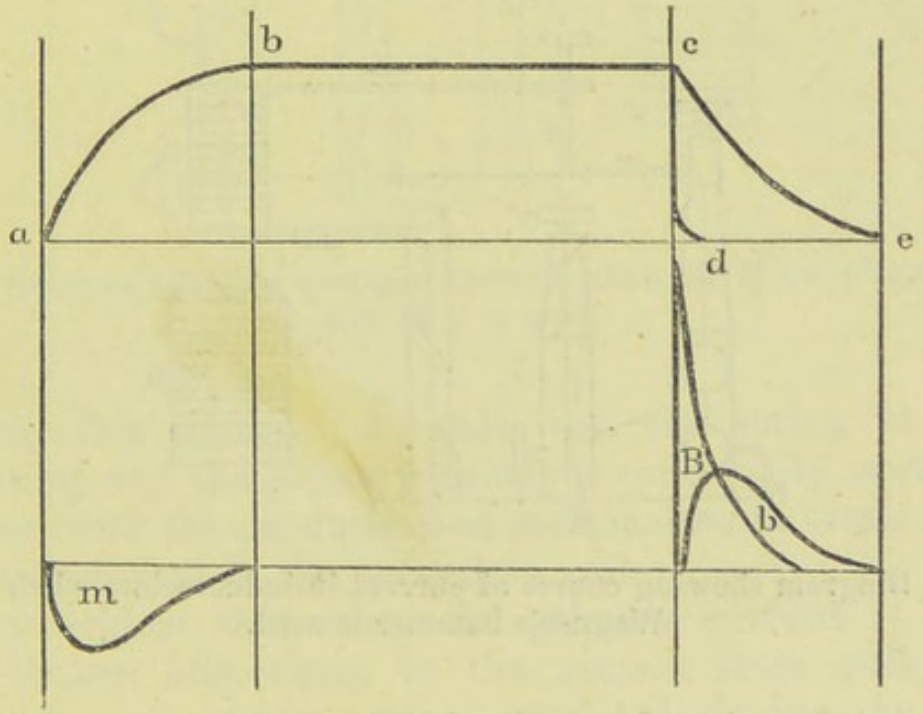
If only single induction shocks are to be used, a make-and-break key is put in the primary battery circuit, and the two wires from the battery and key are attached to the two top screws of the primary coil (c and d, Fig. 136). It is then found that the shock given by the induced current on break of the primary current is much stronger than that on make.

In endeavouring to explain this difference in the intensity of the make-and-break induction shocks, it must be remembered that the intensity of the momentary current induced in the secondary coil at make or break of the primary current is proportional (1) to the number of turns

of wire in each coil ; (2) inversely to the mean distance between the coils (*i. e.* the nearer the coils, the stronger the induced current) ; (3) to the *rate of change* in strength of the primary current. Now, when a current is made through the primary coil, induction takes place not only between primary and secondary coils, but also between the individual turns of the primary coil itself. This current of self-induction, being opposed in direction to the battery current, hinders and delays the attainment by the latter of its full strength, and so slows the *rate of change* of current in the primary coil. Hence the intensity of the momentary current induced in the secondary coil is less than it would have been without the retarding effect of self-induction.

At break of the current, an extra current is also produced in the primary coil in the same direction as the

FIG. 137.



battery current, and therefore tending to reduce the rate of charge of the current from full strength to nothing. In this case, however, the primary circuit being broken, the

current of self-induction cannot pass without jumping the great resistance offered by the air, so that its retarding effect on the rate of disappearance of the primary current may be practically disregarded. In Fig. 137 the line a b c d will represent the changes occurring in the primary current at make-and-break, a b corresponding to the make and c d to the break. The lower line represents the momentary currents induced in the secondary circuit, m being the current of low intensity and long duration produced by the make, and B the shock of high intensity and short duration caused by the sharp break of the primary current.

When we desire to use faradic stimulation—that is, secondary induced shocks rapidly repeated 50 to 100 times a second—we make use of the apparatus attached to the coil, known as Wagner's hammer (Figs. 136 and 138). In

FIG. 138 A.

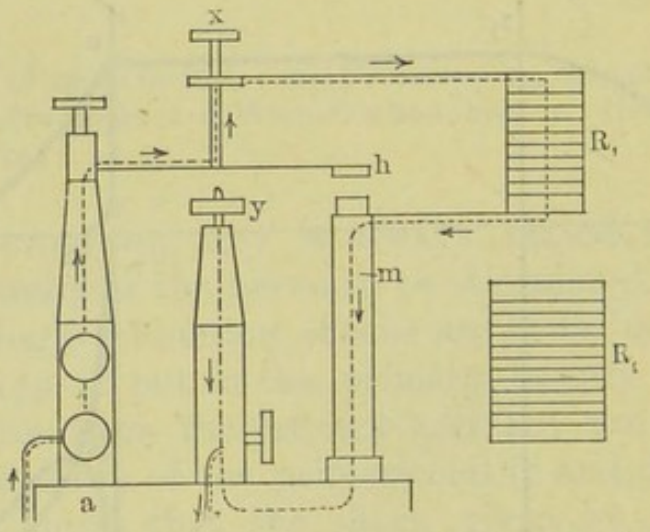


Diagram showing course of current in inductorium when Wagner's hammer is used.

this case the wires from the battery are connected to the two lower screws (a and b, Fig. 136). Fig. 138 A shows the direction of the current when Wagner's hammer is used. The current enters at a, runs up the pillar and along the

spring to the screw x. Here it passes up through the screw, and through the primary coil R_1. From the primary coil it passes up the small coil m, and from this to the terminal b and back to the battery. But in this course the coil m is converted into an electro-magnet. The hammer h attached to the spring is attracted down, and so the spring is drawn away from the screw x, and the current is therefore broken. The break of the current destroys the magnetic power of the coil, the spring jumps up again and once more makes circuit with the screw x, only to be drawn down again

FIG. 138 B.

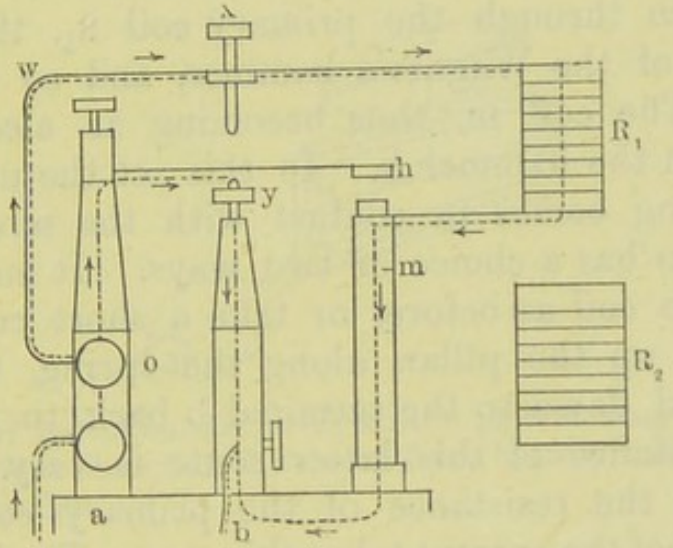


Diagram showing course of current when the Helmholtz's side wire is used.

directly this occurs. In this way the spring is kept vibrating, and the primary circuit is continually made and broken, with the production at each make-and-break of an induced current in the secondary coil.

It is evident that when the primary current is made and broken fifty times in the second, there will be a hundred momentary currents produced during the same period in the secondary coil. Every alternate one of these produced by the break of current in the primary will be much stronger than the intervening currents produced by

the make. In order to equalise make-and-break induction shocks, so that a regular series of momentary currents of nearly equal intensity may be produced, the arrangement known as Helmholtz's is used. In this arrangement the side wire, w, shown in Fig. 136, and diagrammatically in Fig. 138 B, is used to connect the binding screw o with the binding screw c at the top of the coil. The screw x is raised, so as not to touch the spring, and the lower screw y is moved up till it comes nearly in contact with the under surface of the spring. If we consider the direction of the current now, we see that it enters as before at the terminal, travels up the Helmholtz's wire w to the screw c, from thence through the primary coil R_1, then through the coil m of the Wagner's hammer, and so back to the battery. The coil m, thus becoming an electro-magnet, draws down the hammer h. In this act the under surface of the spring comes in contact with the screw y. The current then has a choice of two ways. It may either go through the coil as before, or take a short cut from the terminal a, up the pillar, along the spring, through the screw y, and down to the terminal b back to the battery. As the resistance of this latter route is very small compared with the resistance of the primary coil, &c., the greater part of the current takes this way. The infinitesimal current which now passes through the coil of Wagner's arrangement is insufficient to magnetise this, and the hammer springs up again ; thus the process is restarted, and the spring vibrates rhythmically. With this arrangement the primary current is never broken, but only short-circuited, and so diminished very largely. Hence the retarding influence of self-induction is as potent with "break" as with make of the current, and the effects on the secondary coil in the two cases are approximately equal. In Fig. 137 c e represents the change in the primary current when the current is short-circuited instead of being broken, and b represents the effect produced in the secondary coil. It will be seen that the

currents m and b are practically identical in intensity and duration.

The *galvanometer* is an instrument used to measure strength of current. Its construction depends on the fact that if a small compass be suspended within a coil of wire, and a current be passed through the wire, the compass is deflected, and tends to take up a position at right angles to its former one. In practice a pair of such magnetic needles are usually employed, arranged reversely, as in Fig. 139, where a and n represent the north-seeking ends

FIG. 139.

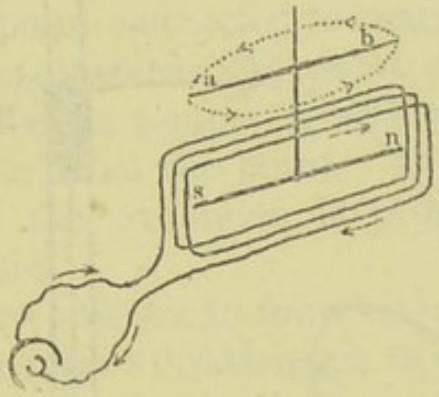


Diagram of galvanometer, with astatic pair of magnets. The arrows show direction of current from battery, and the swing of the needles.

of the magnets a b and s n. On arranging them in this way the effect of the earth's magnetism on them is weakened or annulled, and they are spoken of as *astatic*. A bar compass is suspended over the galvanometer, by the adjustment of which the force with which the suspended pair of magnets tends to 'set' in one direction may be increased or diminished. In Thomson's galvanometer, as it is used for nerve work, the coils of wire have a resistance of 5000 to 20,000 ohms. Between the two magnets is fixed a small mirror. The swing of the magnet is recorded by observing the excursion of a spot of light reflected by this mirror on to a horizontal graduated scale.

In thermo-electric experiments, when very small differ-

ences of potential have to be measured through a small resistance, the galvanometer must also have a small resistance, which here should be not more than one ohm.

The *capillary electrometer* is an instrument for recording and measuring difference of potential. That is to say, if connected with two points, it measures the force which would make a current flow between these two points if they were connected with a wire.

FIG. 140.

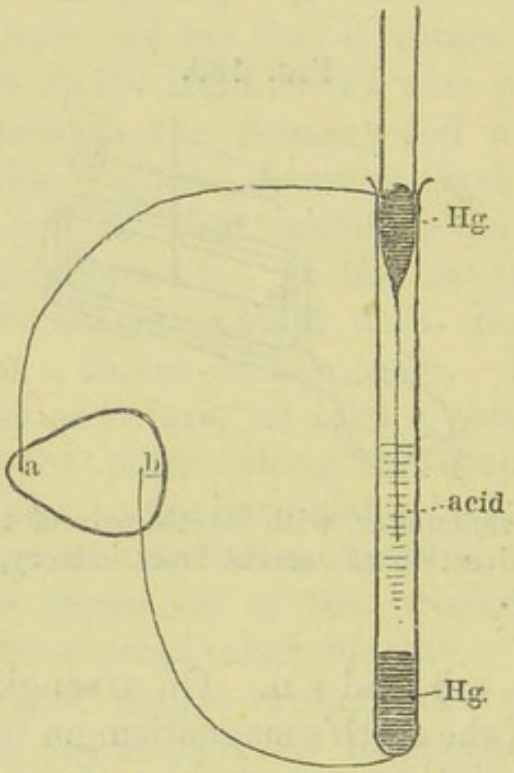


Diagram of capillary electrometer. Hg. Mercury. The two terminals are represented as leading off two points at the base and apex of a frog's heart, a b.

Its structure is very simple. It consists of a glass tube drawn out to a fine capillary point. This tube with the capillary is filled with mercury. The point dips into a wide tube containing dilute sulphuric acid, at the bottom of which is a little mercury. Two platinum wires melted into the glass and dipping into the mercury serve as terminals. In consequence of capillary attraction the acid

ascends some way into the capillary tube, and the force of this can sustain, with fine capillaries, the weight of several inches of mercury.

When the instrument is used, the meniscus of the mercury in the capillary at its junction with the acid is observed under the microscope, or a magnified image of it is thrown on a screen with the aid of the lime or electric light.

If now the capillary and acid be connected with two points, it will be observed that any difference in the potential of these two points causes a movement of the meniscus. If the point connected to acid be negative as compared with the point connected to mercury in capillary, the meniscus moves towards the point of the capillary. If the acid be positive as compared with the capillary, the meniscus moves away from the point. It is further found that the extent of the excursion is proportional to the difference of potential.

Since the capillary appears to have no latent period, and is free from instrumental vibrations, it is extremely useful in recording the quick changes in potential occurring in the diphasic electrical changes that accompany every contraction-wave in the body.

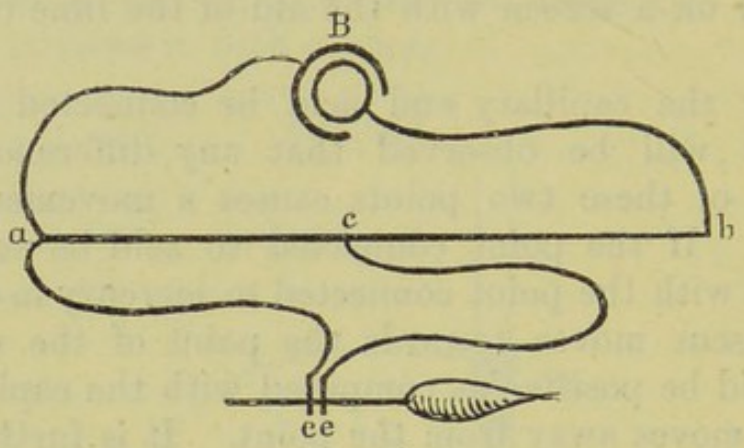
The excursions lend themselves well to photography, so that we may obtain a graphic record of every electrical variation, and thus determine its extent and its time relations.

It must be remembered that this instrument is an electrometer (measurer of difference of potential), and not a galvanometer (current measurer). When the electrometer is connected with two points at different potential no current passes through it. Hence the use of non polarisable electrodes is not so essential in experiments with this instrument as when we make use of the galvanometer.

The *rheochord* is used to modify the amount or strength of current flowing through a preparation. One form of it

is represented in Fig. 141. A constant source of current at B causes a flow of electricity from a to b through a straight way. As the resistance of this wire is the same throughout its length, the fall of potential from a to b must be constant.

FIG. 141.



The nerve, or whatever preparation that is used, is connected with the straight wire at two points, at a and at c, by means of a sliding contact or rider. Supposing that there is an electromotive difference of one volt between a and b, it is evident that if c is pushed close to b, the E.M.F. acting on the nerve will be also one volt. The E.M.F., however, may be made as small as we like by sliding *c* nearer to *a*. Thus if *a b* is one metre, and there is a difference of one volt between the two ends, then if c be one centimetre from *a*, the E.M.F. acting on the nerve will be $\frac{1}{100}$ volt. Thus we alter the current passing through the nerve by altering the E.M.F. which drives the current.

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