A TEXT-BOOK

OF

PHYSIOLOGY

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THIRD AMERICAN

FROM THE FOURTH AND REVISED ENGLISH EDITION.

WITH EXTENSIVE NOTES AND ADDITIONS,

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WITH TWO HUNDRED AND SEVENTY-ONE ILLUSTRATIONS.

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PREFACE TO THE THIRD AMERICAN EDITION.

THE continued large demand for this most excellent work of Dr. Foster, has encouraged both the author and editor to endeavor to render the present edition even more valuable to the student of physiology than its predecessors. Numerous additions, corrections, and alterations have been made, and it is believed that in its present form the usefulness of the book will be found to be much increased.

PHILADELPHIA, *July,* 1885.

A*

PREFACE TO THE FOURTH ENGLISH EDITION.

In previous Editions of this work I endeavored, by the use of small and large print, to distinguish between the more important and stable portions of Physiology, which ought to be made known to every one engaged in a serious study of the science, and the less settled, often controverted views which should be attacked by the more advanced students only. Experience, however, has taught me that the advantages of such a plan are more than counterbalanced by its disadvantages. I especially felt that the amount of space which I could fairly allow to the small print paragraphs was wholly insufficient to permit me to do justice to the conflicting views which I strove, in them, to expound.

In this Edition accordingly I have made no attempt at any such distinction, and have used small print almost exclusively for the description of methods and apparatus. This step involving, as it necessarily did, the transference, into the body of the work, of some of the statements which previously had found their place in the small print portions, has given the volume, at first sight, the appearance of having been largely altered. This, however, is not the case. For good or for bad, the book remains very much as it was; and though I have done my best to remove some of the many defects present in previous editions, I have been encouraged by the favor with which those editions have been successively received, to persevere in the views which I have always held as to which are the parts of physiology most to be insisted on,

and which may be lightly touched or wholly omitted; and though I would still most strenuously repudiate the idea, put forward by some, that there is such a thing as a physiology for medical men, different from that physiology which is a part of science, I have tried to make this volume especially useful to medical students.

My decision to do away with the small print portions of former editions has been largely determined by the fact that my former pupils, now my colleagues at Cambridge, have undertaken to join with me in treating these higher or advanced parts of physiology in a more extended and satisfactory form. And the hope that the result of their labors will soon appear has led me, in this volume, to omit all references, and to use as little as possible the personal authority of the names of investigators. The fondness of students for the use of names of persons is as marked as the pertinacity with which they use them wrongly; and if any observer may feel aggrieved at his name being absent from an ordinary text-book, he may at least have the satisfaction of reflecting that the omission of all names does something to prevent others receiving the credit of his labors.

I cannot say how much I am indebted to the continued help of those friends who assisted me in former editions; and I have also to acknowledge with gratitude the aid afforded me by Prof. C. S. Roy, to whose kindness I owe several of the new illustrations.

The appendix on chemical matters, as in former editions, has been under the care of Mr. Sheridan Lea; in this, which stands on a somewhat different footing from the rest of the work, references and names of authors have been retained.

TRINITY COLLEGE, CAMBRIDGE.
February 1883.

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A TEXT-BOOK OF PHYSIOLOGY.

INTRODUCTORY.

AMONG the simpler organisms known to biologists, perhaps the most simple as well as the most common is that which has received the name of Amœba. There are many varieties of amœba, and probably many of the forms which have been described are, in reality, merely amœbiform phases in the lives of certain animals or plants; but they all possess the same general characters. Closely resembling the white corpuscles of vertebrate blood, they are wholly or almost wholly composed of undifferentiated proto-

[FIG. 1.
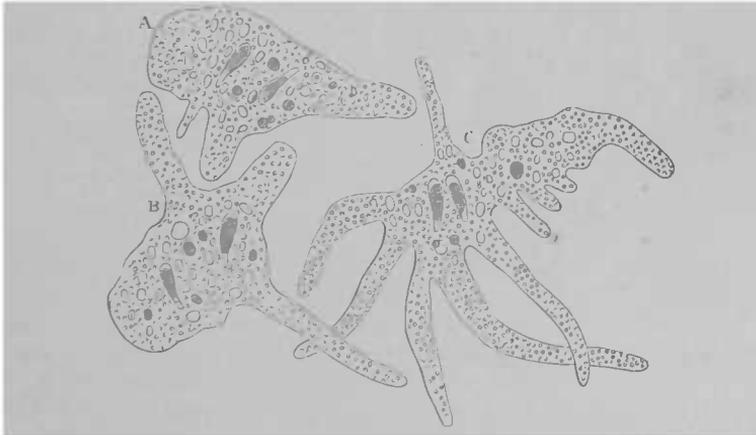
Amœba princeps, shown in different forms (A, B, C) assumed by the same animal.]

plasm, in the midst of which lies a nucleus, though this is some-times absent. In many a distinction may be observed between a more solid external layer or *ectosarc*, and a more fluid granular interior or *endosarc;* but in others even this primary differentia-

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tion is wanting. By means of a continually occurring flux of its protoplasmic substance, the amœba is enabled from moment to moment not only to change its form, but also to shift its position. By flowing round the substances which it meets, it, in a way, swallows them ; and having digested and absorbed such parts as are suitable for food, ejects or rather flows away from the useless remnants. It thus lives, moves, eats, grows, and after a time dies, having been during its whole life hardly anything more than a minute lump of protoplasm. Hence to the physiologist it is of the greatest interest, since in its life the problems of physiology are reduced to their simplest forms.

Now the study of an amœba, with the help of knowledge gained by the examination of more complex bodies, enables us to state that the undifferentiated protoplasm of which its body is so largely composed exhibits certain fundamental phenomena which we may speak of as " vital."

1. It is **contractile**. There can be little doubt that the changes in the protoplasm of an amœba which bring about its peculiar "amœboid" movements, are identical in their fundamental nature with those which occurring in a muscle cause a contraction : a muscular contraction is essentially a regular, an amœboid movement an irregular flow of protoplasm. The substance of the amœba may therefore be said to be contractile.

2. It is **irritable** and **automatic**. When any disturbance, such as contact with a foreign body, is brought to bear on the amœba at rest, movements result. These are not passive movements, the effects of the push or pull of the disturbing body, proportionate to the force employed to cause them, but active manifestations of the contractility of the protoplasm—that is to say, the disturbing cause, or "stimulus," sets free a certain amount of energy previously latent in the protoplasm, and the energy set free takes on the form of movement. Any living matter which, when acted on by a stimulus, thus suffers an explosion of energy, is said to be "irritable." The irritability may, as in the amœba, lead to movement ; but in some cases no movement follows the application of the stimulus to irritable matter, the energy set free by the explosion taking on some other form than movement— *ex. gr.*, heat. Thus a substance may be irritable and yet not contractile, though contractility is a very common manifestation of irritability.

The amœba (except in its prolonged quiescent stage) is rarely at rest. It is almost continually in motion. The movements cannot always be referred to changes in surrounding circumstances acting as stimuli ; in many cases the energy is set free in

consequence of internal changes, and the movements which result are called spontaneous or automatic movements. We may therefore speak of the protoplasm of the amœba as being irritable and automatic.

3. It is **receptive** and **assimilative**. Certain substances serving as food are received into the body of the amœba, and there in large measure dissolved. The dissolved portions are subsequently converted from dead food into new living protoplasm, and become part and parcel of the substance of the amœba.

4. It is **metabolic** and **secretory**. *Pari passu* with the reception of new material, there is going on an ejection of old material, for the increase of the amœba by the addition of food is not indefinite. In other words, the protoplasm is continually undergoing chemical change (metabolism), room being made for the new protoplasm by the breaking up of the old protoplasm into products which are cast out of the body and got rid of. These products of metabolic action have, in many cases at all events, subsidiary uses. Some of them, for instance, we have reason to think, are of value for the purpose of dissolving and effecting other preliminary changes in the raw food introduced into the body of the amœba; and hence are retained within the body for some little time. Such products are generally spoken of as "secretions." Others which pass more rapidly away are generally called "excretions." The distinction between the two is an unimportant and frequently accidental one.

The energy expended in the movements of the amœba is supplied by the chemical changes going on in the protoplasm, by the breaking up of bodies possessing much latent energy into bodies possessing less. Thus the metabolic changes which the food (as distinguished from the undigested stuff mechanically lodged for a while in the body) undergoes in passing through the protoplasm of the amœba are of three classes: those preparatory to and culminating in the conversion of the food into protoplasm, those concerned in the discharge of energy, and those tending to economize the immediate products of the second class of changes by rendering them more or less useful in carrying out the first.

5. It is **respiratory**. Taken as a whole, the metabolic changes are preëminently processes of oxidation. One article of food—*i. e.*, one substance taken into the body, viz., oxygen, stands apart from all the rest, and one product of metabolism peculiarly associated with oxidation, viz., carbonic acid, stands also somewhat apart from all the rest. Hence the assumption of oxygen and the excretion of carbonic acid, together with such of the metabolic

processes as are more especially oxidative, are frequently spoken
of together as constituting the respiratory processes.

6. It is **reproductive.** The individual amœba represents a
unit. This unit, after a longer or shorter life, having increased
in size by the addition of new protoplasm in excess of that which
it is continually using up, may, by fission (or by other means)
resolve itself into two (or more) parts, each of which is capable
of living as a fresh unit or individual.

Such are the fundamental vital qualities of the protoplasm of
an amœba; all the facts of the life of an amœba are manifesta-
tions of these protoplasmic qualities in varied sequence and sub-
ordination.

The higher animals, we learn from morphological studies, may
be regarded as groups of amœbæ peculiarly associated together.
All the physiological phenomena of the higher animals are simi-
larly the results of these fundamental qualities of protoplasm
peculiarly associated together. The dominant principle of this
association is the physiological division of labor corresponding to
the morphological differentiation of structure. Were a larger or
" higher " animal to consist simply of a colony of undifferentiated
amœbæ, one animal differing from another merely in the number
of units making up the mass of its body, without any differences
between the individual units, progress of function would be an
impossibility. The accumulation of units would be a hindrance
to welfare rather than a help. Hence, in the evolution of living
beings through past times, it has come about that in the higher
animals (and plants) certain groups of the constituent amœbiform
units or cells have, in company with a change in structure, been
set apart for the manifestation of certain only of the fundamental
properties of protoplasm, to the exclusion or at least to the
complete subordination of the other properties.

These groups of cells, thus distinguished from each other at
once by the differentiation of structure and by the more or less
marked exclusiveness of function, receive the name of " tissues."
Thus the units of one class are characterized by the exaltation of
the contractility of their protoplasm, their automatism, meta-
bolism, and reproduction being kept in marked abeyance. These
units constitute the so-called muscular tissue. Of another tissue,
viz., the nervous, the marked features are irritability and auto-
matism, with an almost complete absence of contractility and a
great restriction of the other qualities. In a third group of
units, the activity of the protoplasm is largely confined to the
chemical changes of secretion, contractility and automatism (as
manifested by movement) being either absent or existing to a
very slight degree. Such a secreting tissue, consisting of

epithelium-cells, forms the basis of the mucous membrane of the alimentary canal. In the kidney, the substances secreted by the cells, being of no further use, are at once ejected from the body. Hence the renal tissue may be spoken of as excretory. In the epithelium-cells of the lungs, the protoplasm plays an altogether subordinate part in the assumption of oxygen and the excretion of carbonic acid. Still, we may perhaps be permitted to speak of the pulmonary epithelium as a respiratory tissue.

In addition to these distinctly secretory or excretory tissues, there exist groups of cells specially reserved for the carrying on of chemical changes, the products of which are neither cast out of the body, nor collected in cavities for digestive or other uses. The work of these cells seems to be of an intermediate character; they are engaged either in elaborating the material of food that it may be the more easily assimilated, or in preparing used-up material for final excretion. They receive their materials from the blood and return their products back to the blood. They may be called the metabolic tissues *par excellence.* Such are the fat-cells of adipose tissue, the hepatic cells (as far as the work of the liver other than the secretion of bile is concerned), and probably many other cellular elements in various regions of the body.

Each of the various units retains to a greater or less degree the power of reproducing itself, and the tissues generally are capable of regeneration in kind. But neither units nor tissues can reproduce other parts of the organism than themselves, much less the entire organism. For the reproduction of the complex individual, certain units are set apart in the form of ovary and testis. In these all the properties of protoplasm are distinctly subordinated to the work of growth.

Lastly, there are certain groups of units, certain tissues, which are of use to the body of which they form a part, not by reason of their manifesting any of the fundamental qualities of proto-plasm, but on account of the physical and mechanical properties of certain substances which their protoplasm has been able by virtue of its metabolism to manufacture and to deposit. Such tissues are bone, cartilage, connective tissue in large part, and the greater portion of the skin.

We may, therefore, consider the complex body of a higher animal as a compound of so many tissues, each tissue correspond-ing to one of the fundamental qualities of protoplasm, to the development of which it is specially devoted by the division of labor. It must, however, be remembered that there is probably a distinct limit to the division of labor. In each and every tissue, in addition to its leading quality, there are more or less pronounced remnants, or at least some traces of all the other

protoplasmic qualities.   Thus, though we may call one tissue *par excellence* metabolic, all the tissues are to a greater or less extent metabolic.   The energy of each, whatever be its particular mode, has its source in the breaking-up of the protoplasm.   Chemical changes, including the assumption of oxygen and the production complete or partial of carbonic acid, and therefore also entailing a certain amount of secretion and excretion, must take place in each and every tissue.   And so with all the other fundamental properties of protoplasm ; even contractility, which for obvious mechanical reasons is soonest reduced where not wanted, is present in many other tissues besides muscle.   And it need hardly be said that each tissue retains the power of assimilation. However thoroughly the material of food be prepared by digestion and subsequent metabolic action, the last stages of its conversion into living protoplasm are effected directly and alone by the tissue of which it is about to form a part.

Bearing this qualification in mind, we may draw up a physiological classification of the body into the following fundamental tissues :

1. The eminently contractile : the muscles.

2. The eminently irritable and automatic : the nervous system.

3. The eminently secretory, or excretory : digestive, urinary, and pulmonary, etc., epithelium.

4. The eminently metabolic : fat-cells, hepatic cells, lymphatic and ductless glands, etc.

5. The eminently reproductive : ovary, testis.

6. The indifferent or mechanical : cartilage, bone, etc.

All these separate tissues, with their individual characters, are, however, but parts of one body ; and in order that they may be true members working harmoniously for the good of the whole, and not isolated masses each serving its own ends only, they need to be bound together by coördinating bonds.   Some means of communication must necessarily exist between them.   In the mobile homogeneous body of the amœba, no special means of communication are required.   Simple diffusion is sufficient to make the material gained by one part common to the whole mass, and the native protoplasm is physiologically continuous, so that an explosion set up at any one point may be immediately propagated throughout the whole irritable substance.   In the higher animals, the several tissues are separated by distances far too great for the slow process of diffusion to serve as a sufficient means of communication, and their primary physiological continuity is broken by their being embedded in masses of formed material, the product of the indifferent tissues, which being devoid of irritability, present an effectual barrier to the propagation of molecular explosions.   It thus becomes necessary that in the

increasing complexity of animal forms, the process of differentiation should be accompanied by a corresponding integration, that the isolated tissues should be made a whole by bonds uniting them together. These bonds, moreover, must be of two kinds.

In the first place, there must be a ready and rapid distribution and interchange of material. The contractile tissues must be abundantly supplied with material best adapted by previous elaboration for direct assimilation, and the waste products arising from their activity must be at once carried away to the metabolic or excretory tissues. And so with all the other tissues. There must be a free and speedy intercourse of material between each and all. This is at once and most easily effected by the regular circulation of a common fluid, the blood, into which all the elaborated food is discharged, from which each tissue seeks what it needs, and to which each returns that for which it has no longer any use. The carrying on such a circulation of fluid, being in large measure a mechanical matter, needs a machinery, and calls forth an expenditure of energy. The machinery is supplied by a special construction of the primary tissues, and the energy is arranged for by the presence among these of contractile and irritable matter. Thus to the fundamental tissues there is added, in the higher animals, a vascular bond in the shape of a mechanism of circulation.

In the second place, no less important than the interchange of material is the interchange of energy. In the amœba the irritable surface is physiologically continuous with the more internal protoplasm, while each and every part of the body has automatic powers. In the higher animal, portions only of the skin remain as eminently irritable or sensitive structures, while automatic actions are chiefly confined to a central mass of irritable nervous matter. Both forms of irritable matter are separated, by long tracts of indifferent material, from those contractile tissues through which they chiefly manifest the changes going on in themselves. Hence the necessity for long strands of eminently irritable tissue to connect the skin and contractile tissues as well with each other as with the automatic centres. Similar strands are also needed, though perhaps less urgently, to connect the other tissues with these and with each other. To the vascular bond there must be added an irritable bond, along the strands of which, impulses set up by changes in one or another part, may travel in determinate courses for the regulation of the energy of distant spots. In other words, part of the irritable tissues must be specially arranged to form a coördinating nervous system.

Still further complications have yet to be considered. In the life of a minute homogeneous amœba, possessing no special form or structure, there is little scope for purely mechanical opera-

tions.   As, however, we trace out the gradual development of the
more complex animal forms, we see coming forward into greater
and greater prominence the arrangement of the tissues in definite
ways to secure mechanical ends.   Thus the entire body acquires
particular shapes, and parts of the body are built up into mechan-
isms, the actions of which are to the advantage of the individual.
Into the composition of these mechanisms or " organs " the active
fundamental tissues, as well as the passive or indifferent tissues,
enter ; and the working of each mechanism, the function of each
organ, is dependent partly on the mechanical conditions offered
by the passive elements, partly on the activity of the active ele-
ments.   The vascular mechanism, of which we have just spoken,
is such a mechanism.   Similarly the urgent necessity for the
access of oxygen to all parts of the body, has given rise to a
complicated respiratory mechanism ; and the needs of copious
alimentation, to an alimentary or digestive mechanism.

Further, inasmuch as muscular movement is one of the chief
ends, or the most important means to the chief ends, of animal
life, we find the animal body abounding in motor mechanisms,
in which the prime mover is muscular contraction, while the
machinery is supplied by complicated arrangements of muscles
with such indifferent tissues as bone, cartilage, and tendon.   In
fact, the greater part of the animal body is a collection of mus-
cular machines, some serving for locomotion, others for special
manœuvres of particular members and parts, others as an assist-
ance to the senses, and yet others for the production of voice, and,
in man, of speech.

Lastly, the simple automatism of the amœba, with its simple
responses to external stimuli, is replaced in the higher animals
by an exceedingly complex volition affected in multitudinous
ways by influences from the world without ; and there is a cor-
respondingly complex central nervous system.   And here we
meet with a new form of differentiation unknown elsewhere.
While the contractility of the amœbal protoplasm differs but
slightly from the contractility of the vertebrate striated muscle,
there is an enormous difference between the simple irritability of
the amœba and the complex action of the vertebrate nervous
system.   Excepting the nervous or irritable tissues, the funda-
mental tissues have in all animals the same properties, being, it
is true, more acute and perfect in one than in another, but re-
maining fundamentally the same.   The elementary muscular
fibre of a mammal is a mass of differentiated protoplasm, forming
a whole physiologically continuous, and in no way constituting
a mechanism.   Each fibre is a counterpart of all others ; and the
muscle of one animal differs from that of another in such par-
ticulars only as are wholly subordinate.   In the nervous tissues

of the higher animals, on the contrary, we find properties un-
known to those of the lower ones ; and in proportion as we ascend
the scale, we observe an increasing differentiation of the nervous
system into unlike parts.   Thus we have, what does not exist in
any other tissue, a mechanism of nervous tissue itself, a central
nervous mechanism of complex structure and complex function,
the complexity of which is due not primarily to any mechanical
arrangements of its parts, but to the further differentiation of
that fundamental quality of irritability and automatism which
belongs to all irritable tissues, and to all native protoplasm.

In the following pages I propose to consider the facts of phys-
iology very much according to the views which have been just
sketched out.   The fundamental properties of most of the ele-
mentary tissues will first be reviewed, and then the various
special mechanisms.   It will be found convenient to introduce
early the account of the vascular mechanism, and of its nervous
coördinating mechanism, while the mechanisms of respiration
and alimentation will be best considered in connection with the
respiratory and secretory tissues.   The description of the purely
motor mechanisms will be brief; and, save in a few instances,
confined to a statement of general principles.   The special func-
tions of the central nervous system, including the senses, must
of necessity be considered by themselves.   The tissues and
mechanism of reproduction and the phenomena of the decay and
death of the organism will naturally form the subject of the
closing chapters.

BOOK I.

BLOOD—THE TISSUES OF MOVEMENT—THE VASCULAR MECHANISM.

CHAPTER I.

BLOOD.

BLOOD, when flowing in a normal condition through the blood-vessels, consists of an almost colorless fluid, the plasma, in which are suspended a number of more solid bodies, the red and white corpuscles. Were we anxious to give a formal completeness to the classification of the various parts of the body into tissues, we might speak of the blood as a tissue of which the corpuscles are the essential cellular elements, while the plasma is a liquid matrix. We might compare it to a cartilage, the firm matrix of which had become completely liquefied so that the cartilage-corpuscles were perfectly free to move about.

In regarding blood as tissue, however, we come upon the difficulty that it, unlike all the other tissues, possesses no one characteristic property. The protoplasm of the white corpuscles is native undifferentiated protoplasm, in no respect fitted for any special duty ; and though, as we shall see, the red corpuscles have a definite respiratory function, inasmuch as they are carriers of oxygen from the lungs to the several tissues, still this respiratory work is only one of the very many labors of the blood. It will be therefore far more profitable, indeed necessary, to treat of the blood, not as a tissue by itself, but as the great means of communication of material between the tissues properly so called. Its real usefulness lies not so much in any one property of either its corpuscles or its plasma, as in its nature fitting it to serve as the great medium of exchange between all parts of the body. The receptive tissues pour into it the material which they have re-

ceived from without, the excreting tissues withdraw from it the things which are no longer of any use, and the irritable, the contractile, and indeed all the tissues, seek in it the substances (including oxygen) which they need for the manifestation of energy or for the storing up of differentiated material, and return to it the waste products resulting from their activity. All over the body everywhere there is so long as life lasts a double current, here rapid, there slow, of material from the blood to the tissues, and from the tissues to the blood.

It, together with lymph (whether in the lymph-canals or in the interstices of the tissues), may, as Bernard has suggested, be regarded as *an internal medium* bearing the same relations to the constituent tissues that the external medium, the world, does to the whole individual. Just as the whole organism lives on the things around it, its air and its food, so the several tissues live on the complex fluid by which they are all bathed and which is to them their immediate air and food.

From this it follows, on the one hand, that the composition and characters of the blood must be for ever varying in different parts of the body and at different times; and on the other hand, that the united action of all the tissues must tend to establish and maintain an average uniform composition of the whole mass of blood. The special changes which blood is known to undergo while it passes through the several tissues will best be dealt with when the individual tissues and organs come under our consideration. At present it will be sufficient to study the main features, which are presented by blood, brought, so to speak, into a state of equilibrium by the common action of all the tissues.

Of all these main features of blood, the most striking, if not the most important, is the property it possesses of clotting or coagulating when shed.

Sec. 1.—The Coagulation of Blood.

Blood, when shed from the bloodvessels of a living body, is perfectly fluid. In a short time it becomes viscid; it flows less readily from vessel to vessel. The viscidity increases rapidly until the whole mass of blood under observation becomes a complete jelly. The vessel into which it has been shed, can at this stage be inverted without a drop of the blood being spilt. The jelly is of the same bulk as the previously fluid blood, and if forcibly removed, presents a complete mould of the interior of the vessel. (Fig. 2.) If the blood in this jelly stage be left untouched in a glass vessel, a few drops of an almost colorless fluid soon make their appearance on the surface of the jelly. Increas-

ing in number, and running together, the drops after a while form a superficial layer of pale straw-colored fluid. Later on, similar layers of the same fluid are seen at the sides, and finally at the bottom of the jelly, which, shrunk to a smaller size and of

[FIG. 2.

[Fig. 3.

Bowl of recently Coagulated Blood, showing the whole mass uniformly solidified. After DALTON.]
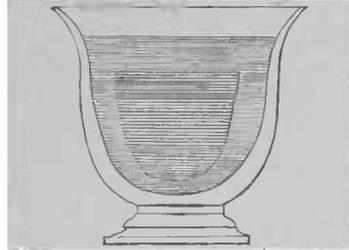
Bowl of Coagulated Blood, after twelve hours, showing the clot contracted and floating in the fluid serum. After DALTON.]

firmer consistency, now forms a clot, or *crassamentum*, floating in a perfectly fluid *serum*. (Fig. 3.) The shrinking and condensation of the clot, and the corresponding increase of the serum, continue for some time. The upper surface of the clot is gener-

[FIG. 4.
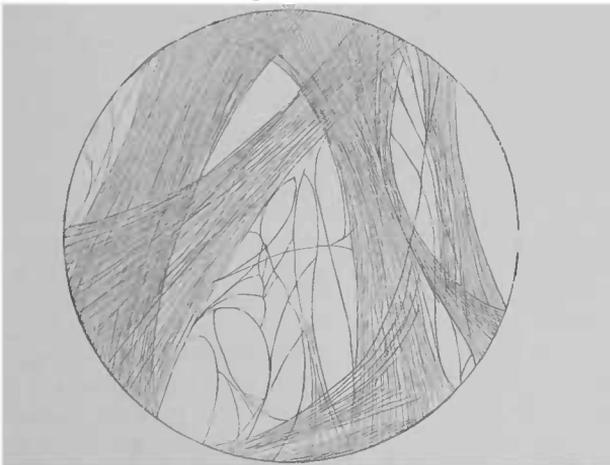
Coagulated Fibrin, showing its fibrillated condition. After DALTON.]

ally cupped. A portion of the clot examined under the microscope is seen to consist of a feltwork of fine granular fibrils, in the meshes of which are entangled the red and white corpuscles of the blood. In the serum nothing can be seen but a few stray

corpuscles. The fibrils are composed of a substance called *fibrin*. (Fig. 4.) Hence we may speak of the clot as consisting of fibrin and corpuscles; and the act of clotting or coagulation is obviously a conversion of the naturally fluid portion of the blood or plasma into fibrin and serum, followed by separation of the fibrin and corpuscles from the serum.

In man, blood when shed becomes viscid in about two or three minutes, and enters the jelly stage in about five or ten minutes. After the lapse of another few minutes the first drops of serum are seen, and coagulation is generally complete in from one to several hours. The times, however, will be found to vary according to the condition of the individual, the temperature of the air, and the size and form of the vessel into which the blood is shed. Among animals the rapidity of coagulation varies exceedingly in different species. The blood of the horse coagulates with remarkable slowness; so slowly, indeed, that many of the red corpuscles (these being specifically heavier than the plasma) have time to sink before viscidity sets in. In consequence there appears on the surface of the blood an upper layer of colorless plasma, containing in its deeper portions many colorless corpuscles (which are higher than the red). This layer clots like the other parts of the blood, forming the so-called " buffy coat." A similar buffy coat is sometimes seen in the blood of man, in inflammatory conditions of the body.

This buffy coat makes its appearance in horse's blood even at the ordinary temperature of the air. If a portion of horse's blood be surrounded by a cooling mixture of ice and salt, and thus kept at about $0°$ C., coagulation may be almost indefinitely postponed. Under these circumstances a more complete descent of the corpuscles takes place, and a considerable quantity of colorless, transparent plasma free from blood-corpuscles may be obtained. A portion of this plasma removed from the freezing mixture clots exactly as does the entire blood. It first becomes viscid and then forms a jelly, which subsequently separates into a colorless shrunken clot and serum. This shows that the corpuscles are not an essential part of the clot.

If a few cubic centimetres of the same plasma be diluted with 50 times its bulk of a 0.6 per cent. solution of sodium chloride,[1] coagulation is much retarded, and the various stages may be more easily watched. As the fluid is becoming viscid, fine fibrils of fibrin will be seen to be developed in it, especially at the sides of the containing vessel. As these fibrils multiply in number, the fluid becomes more and more of the consistence of a jelly, and

[1] A solution of sodium chloride of this strength will hereafter be spoken of as "normal saline solution."

at the same time somewhat opaque. Stirred or pulled about with a needle, the fibrils shrink up into a small, opaque, stringy mass; and a very considerable bulk of the jelly may by agitation be resolved into a minute fragment of shrunken fibrin floating in a quantity of what is really diluted serum. If a specimen of such diluted plasma be stirred from time to time, as soon as coagulation begins, with a needle or glass rod, the fibrin may be removed piecemeal as it forms, and the jelly stage may be altogether done away with. When fresh blood which has not yet had time to coagulate is stirred or whipped with a bundle of rods (or anything presenting a large amount of rough surface), no jelly-like coagulation takes place, but the rods become covered with a mass of shrunken fibrin. Blood thus whipped until fibrin ceases to be deposited, is found to have entirely lost its power of coagulation.

Putting all these facts together, it is very clear that the phenomena of the coagulation of blood are caused by the appearance in the plasma of fine fibrils of fibrin. As long as these are scanty, the blood is simply viscid. When they become sufficiently numerous, they give the blood the firmness of a jelly. Soon after their formation they begin to shrink; and in their shrinking enclose in their meshes the corpuscles, but squeeze out the fluid parts of the blood. Hence the appearance of the shrunken colored clot and the colorless serum.

Fibrin, whether obtained by whipping freshly shed blood, or by washing either a normal clot, or a clot obtained from colorless plasma, exhibits the same general characters. It belongs to that class of complex, unstable, nitrogenous bodies called *proteids*, which form a large portion of all living bodies and an essential part of all protoplasm.[1] It gives the ordinary proteid reactions. It is insoluble in water and in dilute saline solutions; and though it swells up in dilute hydrochloric acid, it is not thereby appreciably dissolved.[2]

Coagulation, then, is brought about by the appearance in the blood-plasma of a substance, fibrin, which previously did not exist there as such. Such a substance must have antecedents, or an antecedent—What are they, or what is it?

If blood be received direct from the bloodvessels into one-third its bulk of a saturated solution of some neutral salt, such as magnesium sulphate, and the two gently but thoroughly mixed, coagulation, especially at a moderately low temperature, will be deferred for a very long time. If the mixture be allowed to stand, the corpuscles will sink, and a colorless plasma will be obtained similar to the plasma gained from horse's blood by cold, except that it contains an excess of the neutral salt. The presence of the neutral

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[1] See Appendix.   [2] For further details see Appendix.

salt has acted in the same direction as cold; it has prevented the occurrence of coagulation. It has not destroyed the fibrin; for if some of the plasma be diluted with from five to ten times its bulk of water, it will coagulate speedily in quite a normal fashion, with the production of quite normal fibrin.

If some of the colorless, transparent plasma, obtained either by the action of neutral salts from any blood, or by the help of cold from horse's blood, be treated with some solid neutral salt, such as sodium chloride, to saturation, a white, flaky, somewhat sticky precipitate will make its appearance. If this precipitate be removed, the fluid is no longer coagulable (or very slightly so), even though the neutral salt present be removed by dialysis, or its influence lessened by dilution. With the removal of the substance precipitated, the plasma has lost its power of coagulating.

If the precipitate itself, after being washed with a saturated solution of the neutral salt (in which it is insoluble) so as to get rid of all serum and other constituents of the plasma, be treated with a small quantity of water, it readily dissolves,[1] and the solution rapidly filtered gives a clear, colorless filtrate, which is at first perfectly fluid. Soon, however, the fluidity gives way to viscidity, and this in turn to a jelly condition, and finally the jelly shrinks into a clot floating in a clear fluid; in other words, the filtrate clots like plasma. Thus there is present in cooled plasma, and in plasma kept from clotting by the presence of neutral salts, a something, precipitable by saturation with neutral salts, a something which, since it is soluble in very dilute saline solutions, cannot be fibrin itself, but which in solution speedily gives rise to the appearance of fibrin. To this substance its discoverer, Denis, gave the name of *plasmine.* We are justified in saying that the coagulation of blood is the result of the conversion of plasmine or some part of plasmine into fibrin.

But there are reasons for thinking that plasmine is a mixture of at least two bodies. If sodium chloride be carefully added to plasma to an extent of about 13 per cent., a white, flaky, viscid precipitate is thrown down very much like plasmine. If, after the removal of the first precipitate more sodium chloride, and especially if magnesium sulphate be added, a second precipitate is thrown down, less viscid and more granular than the first. The name *fibrinogen* is given to the former, *paraglobulin* to the latter. Both are proteids belonging to the *globulin* family,[2] the

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[1] The substance itself is not soluble in distilled water, but a quantity of the neutral salts always clings to the precipitate, and thus the addition of water virtually gives rise to a dilute saline solution, in which the substance is readily soluble.

[2] See Appendix.

members of which, while insoluble in distilled water, are readily soluble in dilute solutions of neutral salts. According to some authors, solutions of fibrinogen are characterized by their being precipitated, and *coagulated*[1] at a temperature of about 55°–60°, while solutions of paraglobulin are not so changed till the temperature rises to 68°–70°. There are also other differences (see Appendix).

Both these substances are thrown down when plasma is saturated with sodium chloride, so that the plasmine of Denis appears to be a mixture of fibrinogen and paraglobulin, and the question arises, Are both these concerned in the formation of fibrin?

Paraglobulin not only occurs as a constituent of plasma, but is found in considerable quantity in the serum left after clotting; it forms, as we shall see, a large portion of the proteids present in serum. Now, the addition of serum will often bring about coagulation in fluids, which, left to themselves, will not coagulate, the clot so formed being composed of fibrin with normal characters, and the artificial coagulation thus induced being in all other respects exactly like a natural clotting. Thus, for instance, hydrocele fluid, carefully removed without admixture of blood from a hydrocele, will in most cases remain fluid without any disposition to clot.[2] So, also, the serous fluid removed from the pericardial, pleural, or peritoneal cavities some hours after death in most cases shows no disposition to clot.[3] But these fluids, hydrocele or pericardial, though they do not clot spontaneously, will generally, upon the addition of serum or a little whipped blood, clot in a most unmistakable manner.[4] Now, fibrinogen is certainly present in these fluids, and may be thrown down from them by the addition of sodium chloride or by other means; and, since serum contains paraglobulin, it was at first thought that the absence of spontaneous coagulation in the untouched hydrocele or pericardial fluid was due to the absence of paraglobulin, which, as we have seen, is present with fibrinogen in the spontaneously coagulable plasma of blood, and that the coagulating effect of the addition of the serum was due to the paraglobulin it contained, the paraglobulin and fibrinogen acting in some way or other upon each other to produce fibrin. And this view was supported by the fact that paraglobulin precipitated from serum was, like the entire serum, efficacious in giving rise to a coagulation in fibrinogenous pericardial or hydrocele fluids.

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[1] See Appendix for the distinction between the coagulation of proteids by heat, and the coagulation due to the appearance of fibrin.

[2] In some specimens, however, a spontaneous coagulation, generally slight, but in exceptional cases massive, may be observed.

[3] If it be removed immediately after death, it generally clots readily and firmly, giving a colorless clot consisting of fibrin and white corpuscles only.

[4] In a few cases, no coagulation can thus be induced.

It was soon found, however, that certain specimens of pericardial and even hydrocele fluid did not need the addition of the paraglobulin to make them coagulate; that though they would not coagulate spontaneously, they might be made to coagulate by adding to them a constituent of serum which was not paraglobulin, but something else. Thus if serum, or indeed whipped blood, be mixed with a large quantity of alcohol, and allowed to stand some days, the proteids present are in time so changed by the alcohol as to become insoluble in water. Hence, if the copious precipitate, after long standing, be separated by filtration from the alcohol, dried at a low temperature not exceeding 40°, and extracted with distilled water, the aqueous extract contains very little proteid matter—indeed, very little organic matter at all. Nevertheless, even a small quantity of this aqueous extract added alone to certain specimens of hydrocele fluid will bring about a speedy coagulation. The same aqueous extract has also a remarkable effect in hastening the coagulation of fluids which though they will eventually clot, do so very slowly. Thus plasma may, by the careful addition of a certain quantity of neutral salt and water, be reduced to such a condition that it coagulates very slowly indeed, taking perhaps days to complete the process. The addition of a small quantity of the aqueous extract we are describing, will, however, bring about a coagulation which is at once rapid and complete.

The active substance, whatever it be, in this aqueous extract, exists in small quantity only, and its coagulating virtues are at once and forever lost when the solution is boiled. Further, there is no reason to think that the active substance actually enters into the formation of the fibrin to which it gives rise; it seems, without undergoing changes in itself, to act in some way or other on the actual fibrin factors (fibrinogen and paraglobulin or one of them), and to convert them or part of them into fibrin. It appears to belong to a class of bodies playing an important part in physiological processes and called *ferments*, of which we shall have more to say hereafter. We may, therefore, speak of it as the *fibrin-ferment*, the name given to it by its discoverer, Alex. Schmidt.

Fibrin-ferment appears to make its appearance in blood soon after it has been shed, and, like other ferments, is apt to be entangled in and carried down by any precipitates which occur in blood. It is carried down by the plasmine, and hence solutions of plasmine coagulate spontaneously.

It exists in serum, and is carried down with paraglobulin when that substance is precipitated. And hence arises the serious question whether the coagulating effects of serum or prepared paraglobulin on hydrocele or pericardial fluid are not, after all,

due to the ferment present rather than to the paraglobulin ; so that two views may be taken of the nature of coagulation. One[1] teaches that fibrin arises from some mutual action of fibrinogen and paraglobulin induced by the fibrin-ferment; the other[2] that fibrin is formed through the conversion of fibrinogen alone by the agency of the ferment, paraglobulin either having nothing to do with the matter, or merely assisting by its presence in some indirect way.

There can be no doubt that fibrinogen is an essential factor ; that coagulation cannot take place without it, and that it or some part of it actually becomes fibrin. There is equally no doubt that the presence of the fibrin-ferment is absolutely necessary. It is also more than probable that fibrin does not result from the union of fibrinogen and paraglobulin, since the quantity of fibrin formed is not greater than that of either of the two substances used to produce it. But we still need further light as to the exact nature of the change produced by the ferment, the true characters of the ferment itself, and the part played by paraglobulin.

In favor of the view that paraglobulin is not concerned in the matter, it is asserted that fibrinogen cautiously precipitated from plasma by small quantities of sodium chloride, so as to obtain it apart from paraglobulin, and then freed from ferment by repeated washing, will yield a solution not spontaneously coagulable, but clotting freely on the addition of ferment only. In favor of the view that the presence of paraglobulin is essential, may be quoted the striking fact that certain specimens of hydrocele fluid may be met with which will not coagulate either spontaneously or upon the addition of ferment alone, but will coagulate upon the addition of paraglobulin and ferment. Such fluids may be supposed to contain fibrinogen only. And it has been argued that two substances have been confused under the name of fibrinogen ; one coagulating at the same temperature as paraglobulin, and needing the coöperation of paraglobulin to form fibrin, and another body which may be thrown down from solutions of plasmine or from blood at the temperature of $55°-60°$ (the fluids thereby losing the power of coagulating), and which is fibrinogen already on its way to become fibrin—in fact, a sort of nascent fibrin, capable of becoming actual fibrin in the total absence of paraglobulin. Lastly, the presence of a neutral salt, such as sodium chloride, appears to be essential to the process, coagulation not occurring even where all three factors are present, if no neutral salt accompanies them.

Awaiting further investigation, we may for the present con-

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[1] That of Alexander Schmidt, and his pupils and others.
[2] That of Hammarsten, Fredericq, and others.

clude that fibrin is formed by the conversion, through the agency of a ferment, of a substance fibrinogen, which forms part of the plasmine spoken of above, but the exact nature of that conversion and whether paraglobulin has any share in the matter, and if so what, must remain as yet undecided.

This conception of coagulation as a chemical process between certain factors renders easy of comprehension the influence of various conditions on the coagulation of blood. The quickening influence of heat, the retarding effect of cold, the favorable action of motion and of contact with surfaces, and hence the results of whipping and the influence exerted by the form and surface of vessels, become intelligible. The greater the number of points— that, is the larger and rougher the surface presented by the vessels into which blood is shed—the more quickly coagulation comes on, for contact with surfaces favors chemical union. So also the presence of spongy platinum, or of an inert powder like charcoal, quickens the coagulation of tardily clotting fluids, such as many specimens of pericardial fluid.

Having thus arrived at an approximate knowledge of the nature of coagulation, we are in a better position for discussing the question, Why does blood remain fluid in the vessels of the living body and yet clot when shed ?

The older views may be at once summarily dismissed. The clotting is not due to loss of temperature, for cold retards coagulation, and the blood of cold-blooded animals behaves just like that of warm-blooded animals in clotting when shed. It is not due to loss of motion, for motion favors coagulation. It is not due to exposure to air, whereby either an increased access of oxygen or an escape of volatile matters is facilitated, for on the one hand the blood is fully exposed to the air in the lungs, and on the other shed blood clots when received, without any exposure to the atmosphere, in a closed tube over mercury.

All the facts known to us point to the conclusion, that when blood is contained in healthy living bloodvessels, a certain relation or equilibrium exists between the blood and the containing vessels of such a nature that as long as this equilibrium is maintained the blood remains fluid, but that when this equilibrium is disturbed by events in the blood or in the bloodvessels, or by the removal of the blood, the blood undergoes changes which result in coagulation. The most salient facts in support of this conclusion are as follows :

1. After death, when all motion of the blood has ceased, the blood remains for a long time fluid. It is not till some time afterwards, at an epoch when post-mortem changes in the blood and in the bloodvessels have had time to develop themselves, that coagulation begins. Thus some hours after death the blood

in the great veins may be found perfectly fluid. Yet such blood has not lost its power of coagulating; it still clots when removed from the body, and clots, too, when received over mercury without exposure to air, showing that the fluidity of the highly venous blood is not due to any excess of carbonic acid or absence of oxygen. Eventually it does clot even within the vessels, but perhaps never so firmly and completely as when shed. It clots first in the larger vessels, but remains fluid in the smaller veins for a very long time, for many hours in fact, since in these the same bulk of blood is exposed to the influence of, and reciprocally exerts an influence on, a larger surface of the vascular walls than in the larger veins.

2. If the vessels of the heart of a turtle (or any other cold-blooded animal) be ligatured, and the heart be cut out and placed in favorable circumstances so that it may continue to beat for as long a period as possible, the blood will remain fluid within the heart as long as the pulsations go on—*i. e.*, for one or two days (and indeed for some time afterwards), though a portion taken away at any period of the experiment will clot very speedily.

3. If the jugular vein of a large animal, such as an ox or horse, be ligatured when full of blood, and the ligatured portion excised, the blood in many cases remains perfectly fluid, along the greater part of the length of the piece, for twenty-four or even forty-eight hours. The piece so ligatured may be suspended in a framework and opened at the top so as to imitate a living test-tube, and yet the blood will often remain long fluid, though a portion removed at any time into another vessel will clot in a few minutes. If two such living test-tubes be prepared, the blood may be poured from one to the other without coagulation taking place.

The above facts illustrate the absence of coagulation in intact or slightly altered living bloodvessels; the following show that coagulation may take place even in the living vessels.

4. If a needle or piece of wire or thread be introduced into the living bloodvessel of an animal, either during life or immediately after death, the piece will be found encrusted with fibrin.

5. If in a living animal a bloodvessel be ligatured, the ligature being of such a kind as to injure the inner coat, coagulation takes place at the ligature and extends for some distance from it. Thus, if the jugular vein of a rabbit be ligatured roughly in two places, clots will in a few hours be found in the ligatured portion, reaching upwards and downwards from the ligatures, the middle portion being the least coagulated. Clots will also be found on the far side of each ligature. The clots will still appear if the ligature be removed immediately after being applied, provided

that in the process the inner coat has been wounded. If the ligatures be applied in such a way as not to injure the inner coat, coagulation will not take place, though the blood may remain for many hours perfectly at rest between the ligatures.

So, also, when an artery is ligatured a conspicuous clot is formed on the cardiac side of the ligature. The clot is largest and firmest in the immediate neighborhood of the ligature, gradually thinning away from this point and reaching usually to where a branch is given off. Between this branch and the ligature there is stasis; the walls of the artery suffer from the want of renewal of blood, and thus favor the propagation of the coagulation. On the distal side of the ligature, where the artery is much shrunken, the clot which is formed, though naturally small and inconspicuous, is similar.

6. Any injury of the inner coat of a bloodvessel causes a coagulation at the spot of injury. Any treatment of a bloodvessel tending to injure its normal condition causes local coagulation.

7. Disease involving the inner coat of a bloodvessel causes a coagulation at the part diseased. Thus, inflammation of the lining membrane of the valves of the heart in endocarditis is frequently accompanied by the deposit of fibrin. In aneurism the inner coat is diseased, and layers of fibrin are commonly deposited. So, also, in fatty and calcareous degeneration without any aneurismal dilatation there is a tendency to the formation of clots.

Similar phenomena are seen in the case of serous fluids which coagulate spontaneously. If, as soon after death as the body is cold and the fat is solidified, the pericardium be carefully removed from a sheep by an incision round the base of the heart, the pericardial fluid may be kept in the pericardial bag as in a living cup for many hours without clotting, and yet a small portion removed with a pipette clots at once, and a thread left hanging into the fluid soon becomes covered with fibrin.

The only interpretation which embraces these facts is that, so long as a certain normal relation between the lining surfaces of the bloodvessels and the blood is maintained, coagulation does not take place; but when this relation is disturbed by the more or less gradual death of bloodvessels, or by their more sudden disease or injury, or by the presence of a foreign body, coagulation sets in. Two additional points may here be noticed. 1. Stagnation of blood favors coagulation within the bloodvessels, apparently because the bloodvessels, like other tissues, demand a renewal of the blood on which they depend for the maintenance of their vital powers. 2. The influence of surface is seen even in the coagulation within the vessels. In cases of coagulation from gradual death of the bloodvessels, as in the case of an excised

jugular vein, the fibrin, when its deposition is sufficiently slow, is seen to appear first at the sides, and thence gradually, frequently in layers, to make its way to the centre. So in aneurism, the deposit of fibrin is frequently laminated. In cases where coagulation results from disease of the lining membrane, the rougher the interior, the more speedy and complete the clotting. So, also, a rough foreign body, presenting a large number of surfaces and points of attachment, more readily produces a clot when introduced into the living bloodvessels than a perfectly smooth one.

We may perhaps go a step further, for there are certain weighty reasons for believing that in normal circulating blood all the fibrin-factors are not present in the plasma, and that a disturbance of the equilibrium between the blood and the bloodvessels gives rise to coagulation by inducing changes in certain corpuscles, either the ordinary white corpuscles or corpuscles of a special kind, whereby one or more of the fibrin-factors are discharged into the plasma.

1. When blood is received direct from the bloodvessels into alcohol, the aqueous extract of the precipitate contains little or no fibrin-ferment. If the blood be allowed to stand a little while before being thrown into alcohol, some ferment makes its appearance; and the longer, up to clotting, that the blood stands before being treated with alcohol, the more efficacious is the aqueous extract of the precipitate. Fibrin-ferment, therefore, seems to make its appearance in blood after being shed.

2. When blood, kept from clotting by exposure to cold or through being retained by ligatures in a living bloodvessel, is allowed to stand till the corpuscles have sunk, the upper layers of the plasma, free from both red and white corpuscles, exhibit when removed very little power of coagulation, and, upon examination, are found to contain a very small quantity only of fibrin-ferment.

3. We have reasons for thinking that when blood is shed, a certain number of corpuscles, which we may speak of as white corpuscles, leaving it for the present uncertain whether they are to be regarded as a special kind of corpuscles or not, are broken up and disappear.

Putting these facts together, we are led to think that normal blood plasma circulating in the normal bloodvessels contains no fibrin-ferment, but that when the equilibrium of blood is disturbed, either by the shedding of the blood, or by injury to the bloodvessels, or by the introduction of foreign bodies, fibrin-ferment is discharged into the plasma, as the result of changes taking place in certain corpuscles.

With regard to the other fibrin-factors, our knowledge is at

present deficient. As we shall have to state presently, paraglobulin apparently exists in serum, and therefore in plasma, in very considerable quantity; and to say nothing of the doubt as to whether paraglobulin has any share in forming fibrin, it seems extremely unlikely that the whole of this large quantity could have come from disintegrating corpuscles. Fibrinogen is generally supposed to be preëxistent in the plasma; but there do not appear to be adequate reasons for this view; and it is quite possible that it too, like the ferment, comes from the corpuscles. But this is almost tantamount to saying that the whole fibrin comes from the corpuscles, and, indeed, it has been argued that the white corpuscles are in part bodily converted into fibrin.

The whole matter needs further investigation, and when we remember that fibrin-ferment, and even masses of white corpuscles injected into the living bloodvessels do not necessarily bring about coagulation, it is clear that we have much yet to learn. Moreover, we have reason, as we shall see, to think that corpuscles are continually dying in the body, and therefore continually setting free fibrin-factors; and these, unless we suppose that a certain quantity of fibrin can exist scattered, so to speak, in the blood, must be made away with, or at least prevented from giving rise to clots.

Sec. 2.—The Chemical Composition of Blood.

As we have already urged, the chief chemical interests of blood are attached to the changes which it undergoes in the several tissues, and which will be considered in connection with each tissue at the appropriate place. Nevertheless, a brief summary of the main characters of blood as a whole may be introduced here.

The average specific gravity of human blood is 1055, varying from 1045 to 1075, within the limits of health. The reaction of blood as it flows from the bloodvessels is found to be distinctly, though feebly alkaline.

If the corpuscles be supposed to retain the amount of water proper to them, blood may, in general terms, be considered as consisting by weight of from about one-third to somewhat less than one-half of corpuscles, the rest being plasma. As will be insisted on presently, the number of corpuscles in a specimen of blood is found to vary considerably, not only in different animals and in different individuals, but in the same individual at different times.

Conspicuous and striking as are the results of coagulation, massive as appears to be the clot which is formed, it must be

remembered that by far the greater part of the clot consists of corpuscles. The amount by weight of fibrin required to bind together a number of corpuscles in order to form even a large firm clot is exceedingly small. Thus the average quantity by weight of fibrin in human blood is said to be 0.2 per cent., but the amount which can be obtained from a given quantity of plasma varies extremely; the variation being due not only to circumstances affecting the blood, but also to the method employed.

The difficulties, indeed, of acquiring an exact knowledge of the chemical constitution of the plasma, which, as we have seen from the foregoing section, is probably undergoing changes from the moment of being shed, are very great; our information concerning the composition of the serum and of the corpuscles is much more trustworthy.

[Chemical constituents of the blood-plasma, according to Hermann, are:
1. Water, about 90 per cent.
2. Proteids, viz:
    a. Albumin (precipitated by heat).
    b. Sodium albuminate (serum-casein precipitated by acids).
    y. The substances which form fibrin during coagulation of the blood.
The greater portion of the albuminoid substances consists of albumin; altogether they form from 8 to 10 per cent. of the plasma.
3. Creatine, hypoxanthine, and urea; also at times hippuric and uric acids in very small quantities.
4. Grape sugar, in small quantities, varying according to the situation.
5. Fats, soaps, fatty acids, cholesterin, lecithin. The fat is partly dissolved by the soaps, and partly exists as an emulsion, but always in a small, though varying quantity (0.1–0.2 per cent.).
6. An odoriferous principle peculiar to each kind of blood.
7. A *yellow pigment*. (The serum also often contains hæmoglobin, but this may be only an impurity, caused by disintegrated blood-corpuscles.)
8. Salts, with a preponderance of salts of sodium, chlorides, and carbonates; therefore, more especially common salt and carbonate of sodium.
9. Gases.
With the exception of the bodies included under 2, the above-named constituents form also the constituents of the serum—that is, of the liquid obtained after coagulation of the blood or plasma.]

Composition of Serum.—In 100 parts of serum there are in round numbers:

Water	90 parts.
Proteid substances	8 to 9 "
Fats, extractives,[1] and saline matters	2 to 1

[1] This word is used to denote substances of varied origin and nature, occurring in small quantities, and therefore requiring to be " extracted " by special means.

The proteid substances present in serum are:[1] (1) The so-called *serum-albumin*, (2) paraglobulin. The paraglobulin, as has been stated in the preceding section, may be removed from the serum in several ways, viz., by passing carbonic acid through, or by cautiously adding dilute acetic acid to, the diluted serum, or more completely by saturating the undiluted serum with magnesium sulphate. When the whole of the paraglobulin has been removed, a considerable quantity of proteid material is still left in the serum in the form known as serum-albumin, distinguished from paraglobulin among other characters by its being soluble in distilled water, and therefore not requiring for its solution the presence of a neutral salt.[2] From the researches of Hammarsten, it would appear that owing to imperfect methods the amount of paraglobulin in serum has been much underrated. According to him, the quantity, though varying in different animals, is at times equal to, and sometimes even greater than that of the serum-albumin. Even if we were to accept as definitely proved the view that paraglobulin in some form or other is in some way associated with the formation of fibrin, it seems hardly probable that the whole of this large quantity of para-globulin present in serum is fibrinoplastic—*i. e.*, capable of taking part in the formation of fibrin. We cannot at present, however, attach any definite functions to the paraglobulin and serum-albumin respectively, nor do we know much as to what extent they vary in quantity, though the interesting observation has been made that in snakes the serum-albumin disappears during starvation, while the paraglobulin is fairly constant. When serum, after the cautious addition of acetic acid in order to neutralize its alkalinity, is heated to about 75° C., both the serum-albumin and paraglobulin are thrown down in the form known as *coagulated proteids*, substances characterized by their great insolubility. This "coagulation" by heat of these and other proteids is, it perhaps need hardly be repeated, not to be confounded with the coagulation of plasma due to the appearance of fibrin.

The fats, which are scanty, except after a meal, or in certain pathological conditions, consist of the neutral fats, stearin, palmitin, and olein, with a certain quantity of their respective alkaline soaps. Lecithin[3] and cholesterin occur in very small quantities only. Among the extractives present in serum may be put

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[1] There seems no longer any reason to distinguish a serum-casein from para-globulin (see Appendix).

[2] For further details see Appendix.

[3] For detailed accounts of the characters of the several chemical substances mentioned in this and succeeding chapters, consult the Appendix under the appropriate headings.

down all the nitrogenous and other substances which form the extractives of the body and of food, such as urea, creatine, sugar, lactic acid, etc. A very large number of these have been discovered in the blood under various circumstances, the consideration of which must be left for the present. The peculiar odor of blood-serum is probably due to the presence of volatile bodies of the fatty acid series. The faint yellow color of serum is due to a special yellow pigment. The most characteristic and important chemical feature of the saline constitution of the serum is the preponderance of sodium salts over those of potassium. In this respect serum offers a marked contrast to the corpuscles (see p. 54). Less marked, but still striking, is the abundance of chlorides and the poverty of phosphates in the serum as compared with the corpuscles. The salts may, in fact, briefly be described as consisting chiefly of sodium chloride, with some amount of sodium carbonate, or more correctly sodium bicarbonate, and potassium chloride, with small quantities of sodium sulphate, sodium phosphate, calcium phosphate, and magnesium phosphate. And of even the small quantity of phosphates found in the ash, part of the phosphorus exists in the serum itself, not as a phosphate, but as phosphorus in some organic body.

[**Physical Properties of the Red Corpuscles.**—When observed on the stage of a microscope, the red corpuscles appear as minute, circular, flattened, biconcavo convex bodies, depressed in the centre, and surrounded by an elevated rounded margin. If seen a little beyond the focus of the instrument, the centre appears as a dark spot surrounded by an annular light ring; while if the corpuscle is brought a little within focus the converse is observed. This optical effect is due to the impossibility of getting both the biconcave and biconvex portions in focus at the same time. The appearance of the central dark spot was supposed to indicate the existence of a nucleus, but from what has already been said, this supposition must certainly be erroneous. These corpuscles are further observed to be soft, transparent, and ductile. By virtue of their elastic and ductile properties, they are capable of adapting themselves to sudden changes in the direction of the blood-current, or to modifications in the calibre of the capillaries. Thus in their passage through capillary anastomoses they will often be observed to become bent nearly at right angles in going from one capillary to another; occasionally they become lodged in the middle of the blood-current on an intracapillary septum, and are bent nearly double, resuming again their original outline when dislodged. In the minutest

vessels they will often appear elongated, so as to be enabled to pass through the constricted channel.

The color of the corpuscles if *en masse* is a bright red; if seen singly, they appear of a pale amber color. After the blood is drawn from the vessels, they exhibit a remarkable tendency to aggregrate by approximating their sides, and thus forming irregular rows, which, from their appearance to rolls of money,

Fig. 5.
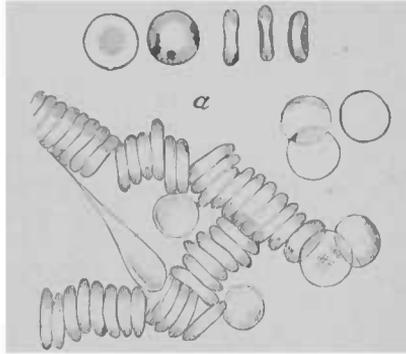
Red Corpuscles of Man. At *a*, the corpuscles are seen flat on edge, and in rolls; the first two corpuscles show the central spot or concavity dark and light; next are shown the bicon-cave and concavo-convex forms; among the rolls, one corpuscle is drawn out by virtue of its viscidity, and would resume its circular shape by virtue of its elasticity.

have been termed *rouleaux*. If the amount of plasma be quite small, so that the corpuscles cannot be floated sufficiently to allow of the approximation of their entire sides, they will over-lap or adhere by their edges.

Another interesting fact observed after the blood is drawn, is that their outline becomes much changed by the development of small nodular projections on their edges. If the corpuscles are now allowed to be somewhat desiccated, they become shrunken and assume a stellate or crenated appearance.

In different animals these corpuscles vary both in size and form. In mammalia (excluding the camel tribe) they exist as circular disks, relatively small, possessing no nucleus. In aves they are oval, nucleated, and larger; while in reptilia they possess the same features as in aves, but are still larger. The different forms and sizes of these corpuscles are beautifully exhibited in Fig. 6.

The size of the corpuscles seems to bear no relation to the size of the body; but, as has been pointed out by Milne-Edwards, there occasionally exists a relation between the size and the muscular activity of the animal. Thus it was found that in

Fig. 6.
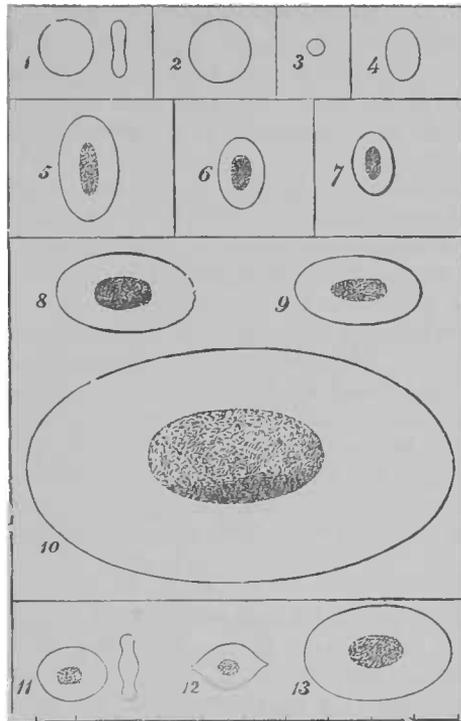
All the corpuscles here shown are drawn to the uniform scale at the bottom of the wood-cut, of 1-4000th of an English inch, and the measurements are expressed in vulgar fractions of that inch. T. D. signifies transverse diameter ; L. D. long diameter ; S. D. short diameter.

	T. D.	L. D.	S. D.
MAMMALIA.			
1. Red Corpuscle of **Man**, seen on the flat surface and also on the edge ; thickness 1-12400	1-3200		
2. Red Corpuscle of **Elephant**	1-2745		
3. Red Corpuscle of **Musk Deer**	1-12325		
4. Red Corpuscle of **Dromedary**, thickness 1-15337		1-3254	1-5921
AVES.			
5. Red Corpuscle of **Ostrich**		1-1649	1-3000
Red Corpuscle of **Nucleus of Ostrich**		1-3200	1-9166
6. Red Corpuscle of **Pigeon**		1-2314	1-3429
7. Red Corpuscle of **Humming-bird**		1-2666	1-4000
REPTILIA.			
8. Red Corpuscle of **Crocodile**		1-1231	1-2286
9. Red Corpuscle of **Python**		1-1440	1-2400
10. Red Corpuscle of **Proteus**		1-400	1-727
PISCES.			
11. Red Corpuscle of **Perch**		1-2161	1-3000
12. Red Corpuscle of **Pike**		1-2000	1-3555
13. Red Corpuscle **of Shark** .		2-1143	1-1684

deer and other fleet-footed animals the corpuscles were relatively
small; in amphibia, which are comparatively sluggish, the cor-
puscles were relatively larger. The relation then that the
diameter of the corpuscle would bear to the muscular activity
would be in an inverse ratio. It has also been found that the
higher the scale of life is advanced the smaller the diameter of
these bodies becomes.

The action of different substances on the corpuscles is very
interesting. Water causes them to swell and become globular.
Acetic acid and alkalies cause them to swell and become decol-
orized. They are also decolorized by freezing and thawing, or
removal of the gases, the addition of chloroform, ether, alcohol,
carbon disulphide, and salts of the bile acids. Tannic acid
causes a nodule to project from the circumference. Electric
shocks temporarily crenate them, which state is followed by their
becoming round and decolorized. In fever they are diminished
in size, and may be restored by quinine or other antipyretics.
Carbonic acid gas renders them biconvex. Sodium chloride
causes numerous thorn-like projections to appear on their cir-
cumference. Boracic acid isolates a nucleated red mass from a
colorless stroma.]

Composition of the Red Corpuscles.—The corpuscles contain
less water than the serum, the amount of solid matter being
variously estimated at from 30 to 40 or more per cent. The
solids are almost entirely organic matter, the inorganic salts in
the corpuscles amounting to less than 1 per cent. Of the or-
ganic matter again, by far the larger part consists of hæmo-
globin. In 100 parts of the dried organic matter of the cor-
puscles of human blood, Hoppe-Seyler and Jüdel found, as the
mean of two observations,

Hæmoglobin	90.54
Proteid substances	8.67
Lecithin	.54
Cholesterin	.25

There are reasons for believing that not only may the number
of red corpuscles vary, but also the quantity of hæmoglobin
present in the red corpuscles differ under different circumstances.
Malassez, by comparing the tint of a quantity of blood, the
number of whose corpuscles had been estimated, with that of a
graduated solution of picrocarminate of ammonia, has been able
to estimate the amount of hæmoglobin present in the corpuscles
under different circumstances. He finds that in anæmia the
poverty of the corpuscles in hæmoglobin is even more striking
than the scantiness of the corpuscles, and is sooner affected by
the administration of iron.

The composition and properties of hæmoglobin will be considered in connection with respiration.

Of the proteid substances which form the stroma of the red corpuscles, this much may be said, that they appear to belong to the globulin family; their exact nature need not be considered here. As regards the inorganic constituents, the corpuscles are distinguished by the relative abundance of the salts of potassium and of phosphates. This at least is the case in man; the relative quantities of sodium and potassium in the corpuscles and serum respectively appear, however, to vary in different animals; in some the sodium salts are in excess even in the corpuscles.

[**Properties of the White Corpuscles.**—The white corpuscles exist in the blood as free masses of protoplasm. They appear as globules with granular contents, frequently containing a nucleus or nuclei. As observed on the stage of the microscope, they are irregularly shaped masses, and are remarkable for their pseudopod prolongations and movements, which, from their resemblance to those of the amœba, have been termed "the amœboid movements."

Fig. 7.
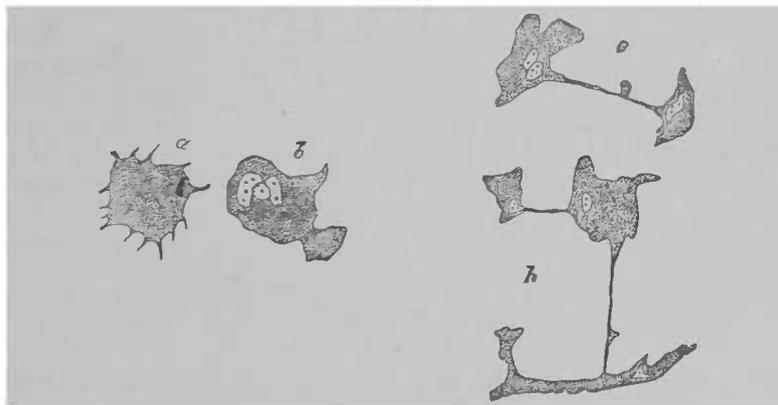
a. Common White Corpuscle, soon after its withdrawal from the vessels (magnified). *b.* The surface become prickly. *h.* Protrusion of larger processes and apparition of nuclei.

In the bloodvessels, they sustain their globular form, and have a tendency to adhere to the sides of the vessels—a tendency directly opposite to that of the red corpuscles. They possess a very remarkable property of migrating through the intercellular interstices of the capillaries into the adjacent tissues. In this act of migration, it is assumed that a prolongation is sent out, which, penetrating the intercellular substance of the vessel-wall, continues to urge its way through, more and

more, until the whole mass of protoplasm has passed; other observers assume that it is a kind of filtration; and still others, that the exit takes place through preëxisting openings (stomata) in the capillary walls.

Through the intervention of vital processes, the corpuscles, after reaching the extravascular tissues, may undergo such changes in the differentiation of the amœbiform units and differentiation of structure that they become component parts of the tissues, and we have "the manifestation of certain only of the fundamental properties of protoplasm, to the exclusion or complete subordination of others."

The corpuscles, as *free* protoplasm, possess all the fundamental properties of protoplasm. As *fixed* protoplasm, they lose certain of the amœbiform units. Free protoplasm is automatic; fixed protoplasm is subservient to the influences exerted through the nervous system. This is probably true of all fixed protoplasm, and we find, in rising the scale of life, that the more differentiated and fixed the protoplasm, the greater proportionately is the development of the nervous system.

The migration of these corpuscles is best seen in points of inflammation, where vast numbers are observed congregated in the bloodvessels and extravascular tissues. Professor Binz and other investigators have proven that quinine has the very interesting power of preventing this migration. He exposed the mesentery of a frog on the stage of a microscope, and found that, after a hypodermic injection of quinine, the migration was immediately checked. He also found that in areas of inflammation, when the migration was most active, it at once ceased after the administration of the drug.

In size they are somewhat larger than the red corpuscles, measuring about 11 mmm. in diameter. Although the red corpuscles vary exceedingly in size in different species of animals, the white corpuscles always retain about the same measurement.]

Composition of the White Corpuscles.—Our knowledge of the exact nature of the proteid matrix of the white corpuscles is at present too uncertain to enable any definite or useful statements to be made, and the probable relation of the corpuscles to coagulation has already been spoken of. The corpuscles are found to contain, in addition to proteid material, lecithin or protagon, glycogen, extractives, and inorganic salts, there being in the ash a preponderance of potassium salts and of phosphates. The nuclei contain nuclein. Upon the death of the corpuscle, the glycogen appears to be converted into sugar.

Both the corpuscles and the plasma (or serum) contain gases. These will be considered in connection with respiration.

The main facts of interest, then, in the chemical composition of the blood are as follows: The red corpuscles consist chiefly of hæmoglobin. The organic solids of serum consist partly of serum-albumin, and partly of paraglobulin. The serum or plasma contrasts in man at least with the corpuscles, inasmuch as the former contains chiefly chlorides and sodium salts, while the latter are richer in phosphates and potassium salts. The extractives of the blood are remarkable rather for their number and variability than for their abundance, the most constant and important being perhaps urea, kreatin, sugar, and lactic acid.

Sec. 3.—The History of the Corpuscles.

In the living body red blood-corpuscles are continually being destroyed, and new ones as continually being produced. The proofs of this are :

1. The number of the red corpuscles in the blood at any given time varies much.

The number of corpuscles in a specimen of blood is determined by mixing a small but carefully measured quantity of the blood with a large quantity of some indifferent fluid, and then actually counting the corpuscles in a known minimal bulk of the mixture.

This may be done either by Vierordt's plan (somewhat modified by Gowers), in which a minimal quantity of the diluted blood, measured in a fine capillary tube, is spread on a surface marked out in square areas, and the number of corpuscles in each square area counted under the microscope ; or by that of Malassez, in which the diluted blood is drawn into a capillary tube with flattened sides, and the number of corpuscles counted *in situ* in the tube by means of an ocular marked out in squares, the microscope being so adjusted that each area of the ocular corresponds to a certain capacity of the capillary tube.

The average number of red corpuscles in mammals generally ranges from 3 to 18 millions ; in human blood it is about 5 millions in a cubic millimetre. The number is increased by meals, and diminished by fasting ; of course, the number of corpuscles present in any given bulk of blood being merely the expression of the proportion of corpuscles to the amount of plasma, variations in the number counted might, and in certain cases are probably caused by an increase or decrease in the quantity of plasma, occurring while the actual number of corpuscles is stationary.   But many of the variations cannot be so accounted for ; they must be due to an increase or decrease of the total number of corpuscles in the body.   After a very large reduction of the total number of red corpuscles, as by hemorrhage or disease (anæmia), the normal proportion may be regained even within a very short time.

2. There are reasons for thinking that the urinary and bile-pigments are derivatives of hæmoglobin. If this be so, an immense number of corpuscles must be destroyed daily (and replaced by new ones) iu order to give rise to the amount of urinary and bile-pigment discharged daily from the body.

3. When the blood of one animal is injected into the vessels of another (*ex. gr.*, that of a bird into a mammal), the corpuscles of the first may for some time be recognized in blood taken from the second; but eventually they wholly disappear. This, of course, is no strong evidence, since the destruction of foreign corpuscles might take place, even though the proper ones had a permanent existence.

That the white corpuscles or leucocytes also are continually being destroyed and replaced is similarly probable from the fact that they vary extremely in number at different times and under various circumstances. Most observers agree that they are very largely increased by taking food. Thus during fasting, they may be seen in a drop of blood to bear to the red the proportion of 1 in 800 or 1000. After a meal, this proportion may rise to 1 in 300 or 400.

The mode of origin of the red corpuscles is so fully dealt with in histological treatises, and at the same time the subject of so many conflicting opinions, that it will be sufficient to remind the reader that the facts at present in our possession seem to show that in the adult the generation of new corpuscles takes place chiefly in the red medulla of bones, but also, at all events in young animals, and especially after great loss or destruction of red corpuscles, in the spleen, and possibly in other places. In the peculiar capillary meshwork of the red medulla are found certain corpuscles which differ, among other characters, from the normal red corpuscles (in mammals) by possessing a nucleus, and from the ordinary leucocytes by having their protoplasm impregnated with a certain quantity of hæmoglobin. These peculiar intermediate corpuscles appear to be transformed into normal red corpuscles, but the exact mode of transformation, whether, for instance, the nucleus is bodily extruded from the cell, or broken up within the cell, or whether indeed, as some think, the nucleus, and not the whole cell, becomes the red corpuscle, is not yet wholly cleared up. Nor are we at present sure whether these peculiar corpuscles themselves arise by a metamorphosis of ordinary leucocytes, or, as Bizzozero urges, represent a special class of cells, whose continual existence is insured by their continually undergoing division. Intermediate cells of this description (which must not be confounded with smaller cells described by Hayem, and called by him hæmatoblasts, but whose nature is doubtful) have been seen in circulating and even shed blood by various observers, and it is this kind of corpuscle which Alex. Schmidt be-

lieves to break up so largely and disappear, with the production of fibrin-factors, when blood is shed. Making every allowance for controverted points, we may conclude that the red medulla of bones has an important function in giving rise to new red corpuscles, and that after unusual loss or destruction of these bodies, the normal activity of this tissue at least is greatly increased.

When we come to treat of respiration, we shall bring forward evidence that the red corpuscles, by virtue of hæmoglobin, have a most important use in carrying oxygen from the lungs to the several tissues. It is through the red corpuscles that the tissues themselves breathe, at least as far as breathing is the taking in of oxygen. We do not know what wear and tear the red corpuscles undergo in this respiratory function; nor have we any evidence as to any other work which they perform in the economy, and which would tend to their being used up. But, as we have already urged, we have reason to think that they are being constantly destroyed, and apparently one place at least where this destruction goes on is the spleen.

In this organ may be seen, as Kölliker long since pointed out, large protoplasmic cells, in which are included a number of red corpuscles: and these red corpuscles may be observed in various stages of apparent disintegration. Moreover, the serum of the blood of the splenic vein, unlike that of blood in general, is said to be tinged with hæmoglobin. It would seem, therefore, probable that a certain amount of hæmoglobin is set free in the spleen from disintegrating red corpuscles, and carried, in part at least, thence through the portal circulation to the liver. Whether any large amount of destruction of red corpuscles goes on elsewhere, we do not know.

Since the serum of blood, with the exception of that from the splenic vein, contains no dissolved hæmoglobin, it is clear that the hæmoglobin of the broken-up corpuscles must speedily be transformed into some other body. Into what other body? In old blood-clots (as in those of cerebral hemorrhage), there are frequently found minute crystals of a body free from iron, which has received the name *hæmatoidin*. There can be no doubt that the hæmatoidin of these clots is a derivative from the hæmoglobin of the escaped blood. We know[1] that hæmoglobin contains, besides a proteid residue, a residue not proteid in nature, called hæmatin. We know, further, that hæmatin may lose the iron which it contains (and which appears to be loosely attached), and yet remain a colored body; so that there is no difficulty in the passage from the proteid-and-iron-containing hæmoglobin to the proteid-and-iron-free hæmatoidin. But hæmatoidin, not only in the form and appearance of its crystals, but also, as far as can be

[1] See chapter on Changes of Blood in Respiration.

ascertained by the analysis of the small quantities at disposal, in its chemical composition, is identical with *bilirubin*, the primary pigment of bile. Moreover, according to some observers, the injection of hæmoglobin, or of dissolved red corpuscles, into the vessels of a living animal, gives rise to a large amount of bile-pigment in the urine, and at the same time increases enormously the relative quantity of *bilirubin* in the bile. Thus, though no one has yet succeeded in producing *bilirubin* artificially from hæmoglobin, and the actual identity of the two cannot as yet, perhaps, be regarded as settled facts, and especially, perhaps, the presence of hæmoglobin in the serum of the splenic vein, and its disappearance after the blood has passed through the liver, point very strongly to the view that the red corpuscles are used up to supply bile-pigment.

Our knowledge of urinary pigments is so imperfect, that little can be said as to their relation to hæmoglobin. We cannot at present definitely trace the normal urinary pigment back to hæmoglobin, however probable such a source may seem.

As regards the white corpuscles of the blood—using this term without prejudice or as to the question whether or no there be more than one distinct kind—these, as we have seen, also come and go.

The fact that in the lymphatic glands, and other adenoid structures, corpuscles, similar to if not identical with white blood-corpuscles, are to be seen of very various sizes, many with double nuclei, and some indeed actually dividing into two corpuscles, suggests that these organs are the birth-places of the white corpuscles. The lymph is continually pouring into the blood a crowd of white corpuscles, which, since they for the most part make their appearance in the lymph-vessels after the latter have traversed the lymphatic glands, probably take origin from those bodies.

At the same time, it is open for us to suppose that any proliferating tissue may give rise to new corpuscles; and Klein states that he has seen them budded off from the reticulum of the spleen. The white corpuscles have also been observed to divide.[1]

We may conclude, therefore, that the white corpuscles probably arise, by division chiefly, from the corpuscles of adenoid tissue, but that other sources may exist.

While we are able to attribute to the numerous red corpuscles an important respiratory function, we are at present, at all events, unaware of any special work carried on by the scantier white corpuscles while they are being hurried along in the blood-current. As far as our present knowledge goes, they seem to tarry

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[1] Klein, Hdb. Phys. Lab., p. 8.

in the blood only on their way either to be broken up or to pass into the tissues.

We have already referred to the probable view that it is not the ordinary white corpuscle, but a special kind of corpuscle which is transformed into the red corpuscle; if this is the case, the keeping up a supply of red corpuscles cannot, as was once thought, be an important end of the existence of white corpuscles in general. We have already (p. 47) dwelt on the probability that the coagulation of shed blood is due to white corpuscles breaking up and discharging certain fibrin-factors into the plasma; but it is uncertain in the first place whether this function is to be attributed to all white corpuscles or to a special kind only, and in the second place whether in normal conditions of the economy any appreciable amount of fibrin-factors is in this way habitually discharged into the blood, and as constantly got rid of without fibrin being formed. It is quite possible that normal circulating plasma may always contain a certain stock, for instance, of fibrinogen, which is continually being drawn upon for the nourishment of the tissues, and as continually replaced by the destruction of corpuscles. But there are no facts at present which absolutely contradict the view that fibrinogen is normally absent from intact circulating plasma, and that the arrangements for the manufacture of fibrin exist only for the purpose of meeting the contingency of fibrin being required under circumstances which may be considered abnormal.

On the other hand, we know that in an inflamed area the white corpuscles migrate in large numbers into the extravascular portions of the tissues, and it has been maintained that not only the pus-corpuscles and " exudation " corpuscles which are the common products of inflammation, but even the new tissue elements (connective-tissue cells and fibres), which make their appearance as the result of the so-called " productive " inflammations, are the descendants, immediate or remote, of such migratory corpuscles. But a discussion of this question would lead us too far away from the purpose of this work.

It would appear, therefore, that with the exception of the respiratory function of the red corpuscles, the physiological interest of the blood is attached rather to the plasma than to the corpuscles. The work done by the corpuscles, even when it is fully understood, will, with the exception of the carrying of oxygen by the red corpuscles, always appear insignificant compared with the incessant labors of the plasma, which is for ever busy as the middle-man between the several tissues, bringing to each tissue what it needs and taking from it that which is useless or even injurious to itself, but necessary to the well-being of some other part.

Sec. 4.—The Quantity of Blood, and its Distribution in the Body.

The total quantity of blood present in an animal body is estimated in the following way : As much blood as possible is allowed to escape from the vessels ; this is measured directly. The vessels are then washed out with water or normal saline solution, and the washings carefully collected, mixed, and measured. A known quantity of blood is diluted with water or normal saline solution until it possesses the same tint as a measured specimen of the washings. This gives the amount of blood (or rather of hæmoglobin) in the measured specimen, from which the total quantity in the whole washings is calculated. Lastly, the whole body is carefully minced and washed free from blood. The washings are collected and filtered, and the amount of blood in them estimated as before by comparison with a specimen of diluted blood. The quantity of blood in the two washings, together with the escaped blood, gives the total quantity of blood in the body.

The method is not free from objections, the most serious of which, perhaps, are attached to the difficulty of obtaining infusions of the minced tissues clear enough to have their tint accurately estimated, and to the fact that the animal must be killed for the purpose ; but other methods—for instance, those in which the quantity is calculated from the proportion of red corpuscles to plasma before and after either diminution of the plasma by sweating or increase by the injection of serum or other fluids free from corpuscles—are open to still graver objections.

From the result of a few observations on executed criminals, it has been concluded that the total quantity of blood in the human body is about $\frac{1}{13}$th of the body weight. But in various animals, the proportion of the weight of the blood to that of the body has been found to vary very considerably ; and probably this holds good for man also, at all events within certain limits.

The blood is in round numbers distributed as follows :

About one-fourth in the heart, lungs, large arteries, and veins.
About one-fourth in the liver.
About one-fourth in the skeletal muscles.
About one-fourth in the other organs.

Since in the heart and great bloodvessels the blood is simply in transit, without undergoing any great changes (and in the lungs, as far as we know, the changes are limited to respiratory changes), it follows that the changes which take place in the blood passing through the liver and skeletal muscles far exceed those which take place in the rest of the body.

CHAPTER II.

THE CONTRACTILE TISSUES.

THE greater number of the movements of the complex animal body are carried on by means of the skeletal striated muscles. A skeletal muscle when subjected to certain influences contracts—*i. e.*, shortens, bringing its two ends nearer together; and the shortening, acting through various bony levers or by help of other mechanical arrangements, produces a movement of some part of the body. The striated tissue of which the skeletal muscles are composed is the chief contractile tissue. The peculiar muscular tissue of the heart is another contractile tissue; under certain influences the fibres into which it is arranged shorten, and thus give rise to the beat of the heart. A similar shortening or contraction of the fusiform fibre-cells of plain muscular tissue, gives rise to movements such as changes of calibre, etc., of the alimentary canal, the urinary bladder, the uterus, the arteries, and the like.

At first sight, "contraction" of any one of these forms of differentiated muscular tissue seems wholly unlike an amœboid movement of an amœba or of a white blood-corpuscle. And yet the transition from the one to the other is very slight. A typical amœba may be regarded as spherical in form, and when it is executing its movements the pseudopodic bulging of its protoplasm may be seen to occur now on this, now on that, part of its circumference, and to take now this and now that direction. The fibre-cell of plain muscular tissue is a nucleated protoplasmic mass of a distinctly fusiform shape, and when it executes its movements—*i. e.*, contracts, the bulging of its protoplasm is always a lateral bulging in a direction at right angles to the long axis of the fibre-cell. Since, as we shall see, there is no change of total bulk, this thickening of the fibre by means of the lateral bulging is necessarily accompanied by a shortening of its length. The contraction of muscular tissue is, in fact, a limited and definite amœboid movement in which intensity and rapidity are gained at the expense of variety.

Besides these movements, which are carried out in the body by means of differentiated muscular tissue, there are others brought about by the peculiar structures known as cilia, among

which we may include the motile tails of spermatozoa; and ordinary amœboid movements are not wanting, being conspicuously shown by the so-called migrating cells. We may include both these under the heading of contractile tissues.

Of all these various forms of contractile tissue, the skeletal striated muscles, on account of the more complete development of their functions, will be better studied first; the others, on account of their very simplicity, are in many respects less satisfactorily understood.

All the ordinary striated skeletal muscles are connected with nerves. We have no reason for thinking that their contractility is called into play, under normal conditions, otherwise than by the agency of nerves.

Muscles and nerves being thus so closely allied, and having besides so many properties in common, it will conduce to clearness and brevity if we treat them together.

[*Physiological Anatomy of the Skeletal or Voluntary Muscles.*

The skeletal muscles compose that portion of the body which is commonly termed flesh. They are made up of bundles, which are subdivided through several gradations into smaller bundles.

FIG. 8.
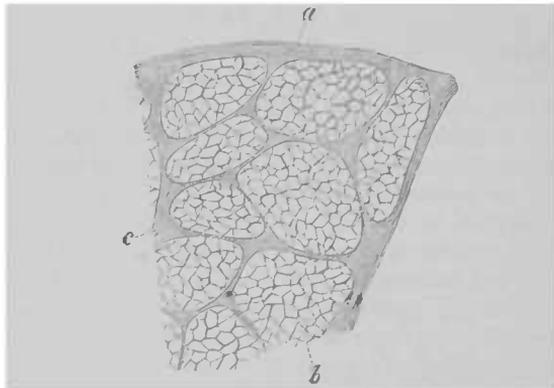
Transverse Section of " Portion of a Muscle (magnified), showing smaller bundles with secondary and primitive fasciculi. *a*, external perimysium; *c*, internal perimysium.

These, in their turn, consist of *secondary* fasciculi closely bound together, and inclosed in a fibro-areolar tissue, called the "internal perimysium." (Fig. 8, *c.*) The internal perimysium is formed by prolongations from the "external perimysium," which envelops the muscle. (Fig. 8, *a.*)

These fasciculi are made up of a number of *primitive* fasciculi,

or *fibres*, placed parallel with each other, enclosed and separated by a delicate, structureless membrane called the sarcolemma. They are more or less flattened on their sides, owing to the pressure of adjacent fibres.   These fibres, which are the contractile

FIG. 9.
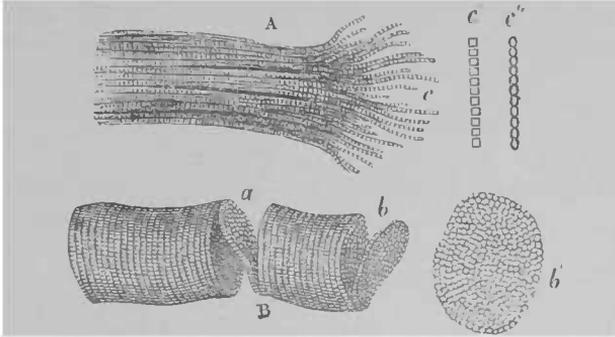
A, a Muscular Fibre showing longitudinal and transverse lines of separation ; *c*, individual fibrillæ, which have been separated in the longitudinal lines ; B, showing the transverse lines of separation ; *b'*, plate detached and more highly magnified, showing sarcous elements more distinctly ; *c'*, *c''*, sarcous elements more highly magnified, showing different appearances.

substance of the organ, are, in their turn, composed of numerous long, cylindriform, thread-like bodies called *fibrillæ* (Fig. 9), which have distinct longitudinal lines of separation, and are marked by transverse striæ, giving them an appearance which has been likened to a number of strings of beads closely bound together.   The transverse striæ mark the divisions between the cells composing the fibrillæ.   These cells, which are called the "sarcous elements," are rectangular in outline, and possess a dark centre, which indicates the presence of a nucleus.

FIG. 10.
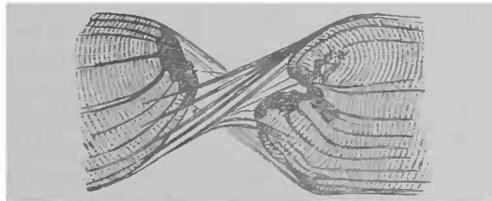
Muscular Fibre torn across ; the sarcolemma still connecting the two parts of the fibre. After TODD and BOWMAN.

When these fibres are torn, the sarcolemma, by virtue of its greater tenacity, often remains intact, and forms a delicate transparent tube, in which are enclosed the ruptured ends of the fibre. (Fig. 10.)

When the muscular fibre is attached to the skin or mucous membrane, it is continuous with the areolar tissue; when attached to a tendon, the sarcolemma becomes joined to the tissue of the tendon, and the fibre ends in a conical extremity, which is received into a depression in the tendon, or else is connected to an adjoining fibre by means of the sarcolemma.

The skeletal muscles are abundantly supplied with nerves and bloodvessels. The nerves are principally supplied by the cerebrospinal system. The capillaries form elongated meshes outside of the sarcolemma.]

Sec. 1.—The Phenomena of Muscle and Nerve.

Muscular and Nervous Irritability.

The skeletal muscles of a frog, the brain and spinal cord of which have been destroyed, do not exhibit any spontaneous movements or contractions, even though the nerves be otherwise quite intact. Left untouched, the whole body may decompose without any contraction of any of the muscles having been witnessed. Neither the skeletal muscles nor the nerves distributed to them possess any power of automatic action.

If, however, a muscle be laid bare and be more or less violently disturbed—if, for instance, it be pinched, or touched with a hot wire, or brought in contact with certain chemical substances, or subjected to the action of galvanic currents—it will contract whenever it is thus disturbed. Though not possessing any automatism, the muscle is (and continues for some time after the general death of the animal to be) *irritable.* Though it remains quite quiescent when left untouched, its powers are then dormant only, not absent. These require to be roused or "stimulated" by some change or disturbance, in order that they may manifest themselves. The substances or agents which are thus able to evoke the activity of an irritable muscle are spoken of as *stimuli.*

But to produce a contraction in a muscle, the stimulus need not be applied directly to the muscle; it may be applied indirectly by means of the nerve. Thus, if the trunk of a nerve he pinched, or subjected to sudden heat, or dipped in certain chemical substances, or acted upon by various galvanic currents, contractions are seen in the muscles to which branches of the nerve are distributed.

The nerve, like the muscle, is irritable; it is thrown into a state of activity by a stimulus; but, unlike the muscle, it does not itself contract. The changes set up in the nerve by the stimulus are not visible changes of form; but that changes of

some kind or other are set up and propagated along the nerve down to the muscle is shown by the fact that the muscle contracts when a part of the nerve at some distance from itself is stimulated. Both nerve and muscle are irritable, but only the muscle is contractile—*i. e.*, manifests its irritability by a contraction. The nerve manifests its irritability by transmitting along itself, without any visible alteration of form, certain molecular changes set up by the stimulus. We shall call these changes thus propagated along a nerve, "nervous impulses."

We have stated above that the muscle is irritable in the sense that it may be thrown into contractions by stimuli applied directly to itself. But it might fairly be urged that the contractions so produced are in reality due to the fact that, although the stimulus is apparently applied directly to the muscle, it is, after all, the fine nerve-branches, so abundant in the muscle, which are actually stimulated. The following facts, however, go far to prove that the muscular fibres themselves are capable of being directly stimulated without the intervention of any nerves. When a frog (or other animal) is poisoned with urari, the nerves may be subjected to the strongest stimuli without causing any contractions in the muscles to which they are distributed; yet even ordinary stimuli applied directly to the muscle readily cause contractions. If, before introducing the urari into the system, a ligature be passed underneath the sciatic nerve in one leg—for instance, the right, and drawn tightly round the whole leg to the exclusion of the nerve, it is evident that the urari when injected into the back of the animal, will gain access to the right sciatic nerve above the ligature, but not below, while it will have free access to the whole left sciatic. If, as soon as the urari has taken effect, the two sciatic nerves be stimulated, no movement of the left leg will be produced by stimulating the left sciatic, whereas strong contractions of the muscles of the right leg below the ligature will follow stimulation of the right sciatic, whether the nerve be stimulated above or below the ligature Now, since the upper parts of both sciatics are equally exposed to the action of the poison, it is clear that the failure of the left nerve to cause contraction is not attributable to any change having taken place in the upper portion of the nerve, else why should not the right, which has in its upper portion been equally exposed to the action of the poison, also fail? Evidently the poison acts on some parts of the nerve lower down. If a single muscle be removed from the circulation (by ligaturing its bloodvessels), previous to the poisoning with urari, that muscle will contract when any part of the nerve going to it is stimulated, though no other muscle in the body will contract when its nerve is stimulated. Here the whole nerve right down to the muscle has been exposed to the action

of the poison; and yet it has lost none of its power over the muscle. On the other hand, if the muscle be allowed to remain in the body, and so be exposed to the action of the poison, but the nerve be divided high up and the part connected with the muscle gently lifted up before the urari is introduced into the system, so that no blood flows to it and so that it is protected from the influence of the poison, stimulation of the nerve will be found to produce no contractions in the muscle, though stimuli applied directly to the muscle at once cause it to contract. From these facts it is clear that urari poisons the ends of the nerve within the muscle long before it affects the trunk, and it is exceedingly probable that it is the very extreme ends of the nerves (possibly the end-plates, for urari poisoning, at least when profound, causes a slight but yet distinctly recognizable effect in the microscopic appearance of these structures) which are affected. The phenomena of urari poisoning, therefore, go far to prove that muscles are capable of being made to contract by stimuli applied directly to the muscular fibres themselves; and there are other facts which support this view.

This question of "independent muscular irritability" was once thought to be of importance. In old times, the swelling of a muscle during contraction was held to be caused by the animal spirits descending into it along the nerves; and when the doctrine of "spirits" was given up, it was still taught that the vital activity of the muscle was something bestowed upon it by the action of the nerve, and not properly belonging to itself. We owe to Haller the establishment of the truth, that the contraction of a muscle is a manifestation of the muscle's own energy, excited it may be by nervous action, but not caused by it. Haller spoke of the muscle as possessing a *vis insita*, while he called the nervous action, which excites contraction, the *vis nervosa*. He used the word irritability as almost synonymous with contractility, a meaning which is still adopted by many authors. In this work we have used it in the wider sense, first employed by Glisson, which includes other manifestations of energy than the change of form which constitutes a contraction.

The Phenomena of a Simple Muscular Contraction.

If the far end of the nerve of a muscle-nerve preparation,[1] Figs. 11 and 12, be laid on the electrodes of an induction-machine,[2]

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[1] By this is meant a muscle dissected out with some length of nerve attached to it, both being in a living condition—*i. e.*, still irritable. The muscle generally used is the gastrocnemius of the frog, the attachment to the femur and a portion of the tendo Achillis, together with a considerable length of the sciatic nerve, being carefully preserved.

[2] It may, perhaps, be worth while to remind the reader of the following facts: In a galvanic battery, the substance (plate of zinc, for instance) which is acted upon and used up by the liquid is called the *positive* element, and the substance which is not so acted upon and used up (plate, etc., of copper, platinum, or carbon, etc.) is called the *negative* element. A galvanic action is set up when

Fig. 11.

DIAGRAM ILLUSTRATING APPARATUS ARRANGED FOR EXPERIMENTS WITH MUSCLE
AND NERVE.

A. The moist chamber containing the muscle-nerve preparation. (The muscle-nerve and electrode-holder are shown on a larger scale in Fig. 12.) The muscle *m*, supported by the clamp *cl.*, which firmly grasps the end of the femur *f*, is connected by means of the S hook *s* and a thread with the lever *l*, placed below the moist chamber. The nerve *n*, with the portion of the spinal column *n′* still attached to it, is placed on the electrode-holder *el*, in contact with the wires *x, y*. The whole of the interior of the glass case *gl.* is kept saturated with moisture, and the electrode-holder is so constructed that a piece of moistened blotting-paper may be placed on it without coming into contact with the nerve.

B. The revolving cylinder bearing the smoked paper on which the lever writes.

C. Du Bois-Reymond's key arranged for short-circuiting. The wires *x* and *y* of the electrode-holder are connected through binding screws in the floor of the moist chamber with the wires *x′, y′*, and these are secured in the key, one on either side. To the same key are attached the wires (*x″* and *y″*) coming from the secondary coils *s. c.* of the induction-machine *D*. This secondary coil can be made to slide up and down over the primary coil *pr. c.*, with which are connected the two wires *x‴* and *y‴*. *x‴* is connected directly with one pole—for instance, the copper pole *c. p.* of the battery *E*. *y‴* is carried to a binding screw, *a*, of the Morse key *F*, and is continued as *y*iv from another binding screw, *b*, of the key to the zinc pole *z. p.* of the battery.

the passage of a single induction-shock, which may be taken as a convenient form of an almost momentary stimulus, will produce

the positive (zinc) and the negative (copper) elements are connected outside the battery by some conducting material, such as a wire, and the current is said to flow in a circuit or circle from the zinc, or positive element, to the copper, or negative element, *inside the battery*, and then from the copper, or negative element, back to the zinc, or positive element, through the wire *outside the battery*. If the conducting wire be cut through, the current ceases to flow; but if the cut ends be brought into contact, the current is reëstablished, and continues to flow so long as the contact is good. The wires, or the ends of the wires, which may be fashioned in various ways, are called *electrodes*. When the electrodes are brought into contact, or are connected by some conducting material, galvanic action is set up, and the current flows through the battery and wires; this is spoken of as " making the current," or " completing or closing the circuit." When the electrodes are drawn apart from each other, or when some non-conducting material is interposed between them, the galvanic action is arrested; this is spoken of as " breaking the current," or " opening the circuit." The current passes from the electrode connected with the negative (copper) element in the battery to the electrode connected with the positive (zinc) element in the battery; hence the electrode connected with the copper (negative) element is called the *positive* electrode, and that connected with the zinc (positive) element is called the *negative* electrode.

In an " induction-machine," the wire connecting the two elements of a battery is twisted at some part of its course into a close spiral, called the *primary coil*. Thus, in Fig. 11 the wire *x‴* connected with the copper or negative plate *c. p.* of the battery *E*, joins the primary coil *pr. c.*, and then passes on as *y‴*, through the " key " *F*, to the positive (zinc) plate *z. p.* of the battery. (In Fig. 19, p. 81, the direction of the current from *x* to *y* through the primary coil *P* is shown by arrows: but in this figure complications are introduced which will be explained hereafter.) Over this primary coil, but quite unconnected with it, slides another coil, the *secondary coil*, *s. c.*; the ends of the wire forming this coil, *y″* and *x″*, are continued on in the arrangement illustrated in the figure as *y′* and *y*, and as *x′* and *x*, and terminate in electrodes. If these electrodes are in contact, or connected with conducting material, the circuit of the secondary coil is said to be closed; otherwise it is open.

In such an arrangement, it is found that at the moment when the primary circuit is closed—*i. e.*, when the primary current is " made," a secondary "in-

no visible change in the nerve, but the muscle will give a short, sharp contraction—*i. e.*, will for an instant shorten itself, becoming

duced" current is, for an exceedingly brief period of time, set up in the secondary coil. Thus, in Fig. 11, when by moving the "key" F, y''' and x''', previously not in connection with each other, are put into connection, and the primary current thus made; at that instant a current appears in the wires y'' and x'', etc , but almost immediately disappears. A similar almost instantaneous current is also developed when the primary current is "broken," but not till then. So long as the primary current flows with uniform intensity, no current is induced in the secondary coil. It is only when the primary current is either made or broken, or suddenly varies in intensity, that a current appears in the secondary coil. In each case the current is of very brief duration—gone in an instant almost—and may therefore be spoken of as "a shock"—an induction-shock; being called a "making shock" when it is caused by the making, and a "breaking shock" when it is caused by the breaking, of the primary circuit. The direction of the current in the making shock is opposed to that of the primary current; thus, in the figure, while the primary current flows from x''' to y''', the induced making shock flows from y to x. The current of the breaking shock, on the other hand, flows in the same direction as the primary current, from x to y, and is, therefore, in direction the reverse of the making shock.

When the primary current is repeatedly and rapidly made and broken, the secondary current being developed with each make and with each break, a rapidly recurring series of alternating currents is developed in the secondary coil and passes through its electrodes. We shall frequently speak of this as the *interrupted* induction-current, or, more briefly, the interrupted current.

FIG. 12.
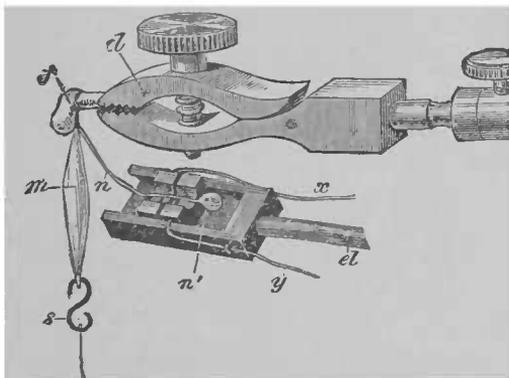
The muscle-nerve preparation of Fig. 11, with the clamp, electrodes, and electrode-holder, are here shown on a larger scale. The letters as in Fig. 11.

The apparatus figured in Figs. 11 and 12 is intended merely to illustrate the general method of studying muscular contraction; it is not to be supposed that the details here given are universally adopted, or, indeed, the best, for all purposes.

Supposing everything to be arranged, and the battery charged, on depressing the handle, ha, of the Morse key, F, a current will be made in the primary coil, *pr. c.*, passing from *c. p.* through x''' to *pr. c.*, and thence through y''' to a, thence to b, and so through y^{iv} to $z. p.$ On removing the finger from the handle of F, a spring thrusts up the handle, and the primary circuit is in consequence immediately broken.

At the instant that the primary current is either made or broken, an induced

thicker the while, and then return to its previous condition. If one end of the muscle be attached to a lever, while the other is fixed, the lever will by its movement indicate the extent and duration of the shortening. If the point of the lever be brought to bear on some rapidly travelling surface, on which it leaves a mark (being for this purpose armed with a pen and ink if the surface be plain paper, or with a bristle or needle if the surface be smoked glass or paper), so long as the muscle remains at rest the lever will describe an even line. When, however, a contraction takes place, as when a single induction-shock is sent through the nerve, some such curve as that shown in Fig. 13 will be described, the lever rising with the shortening of the muscle, and descending as the muscle returns to its natural length. This is known as the "muscle-curve." In order to make the "muscle-curve" complete, it is necessary to mark on the recording surface the exact time at which the induction-shock is sent into the nerve, and also to note the speed at which the recording surface is travelling. These points are best effected by means of the pendulum myograph, Fig. 14.

FIG. 13.
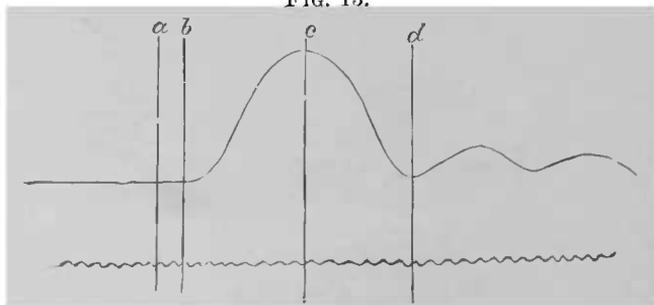
A MUSCLE-CURVE OBTAINED BY MEANS OF THE PENDULUM MYOGRAPH.
To be read from left to right.

a indicates the moment at which the induction-shock is sent into the nerve. *b* the commencement, *c* the maximum, and *d* the close of the contraction.

Below the muscle-curve is the curve drawn by a tuning-fork making 180 double vibrations a second, each complete curve representing, therefore, $\frac{1}{180}$ of a second. It will be observed that the plate of the myograph was travelling more rapidly towards the close than at the beginning of the contraction, as shown by the greater length of the vibration-curves.

current is for the instant developed in the secondary coil *s c*. If the cross-bar, *h* in the Du Bois-Reymond key be raised (as shown in the thick line in the figure), the wires x'', x', x, the nerve between the electrodes and the wires, y, y', y'', form the complete secondary circuit, and the nerve consequently experiences a making or breaking induction-shock whenever the primary current is made or broken. If the cross-bar of the Du Bois-Reymond key be shut down as in the dotted line, h', in the figure, the resistance of the cross-bar is so slight compared with that of the nerve and of the wires going from the key to the nerve, that the whole secondary (induced) current passes from x'' to y'' (or from y'' to x''), along the cross-bar, and practically none passes into the nerve. The nerve being thus " short-circuited," is not affected by any changes in the current.

FIG. 14.
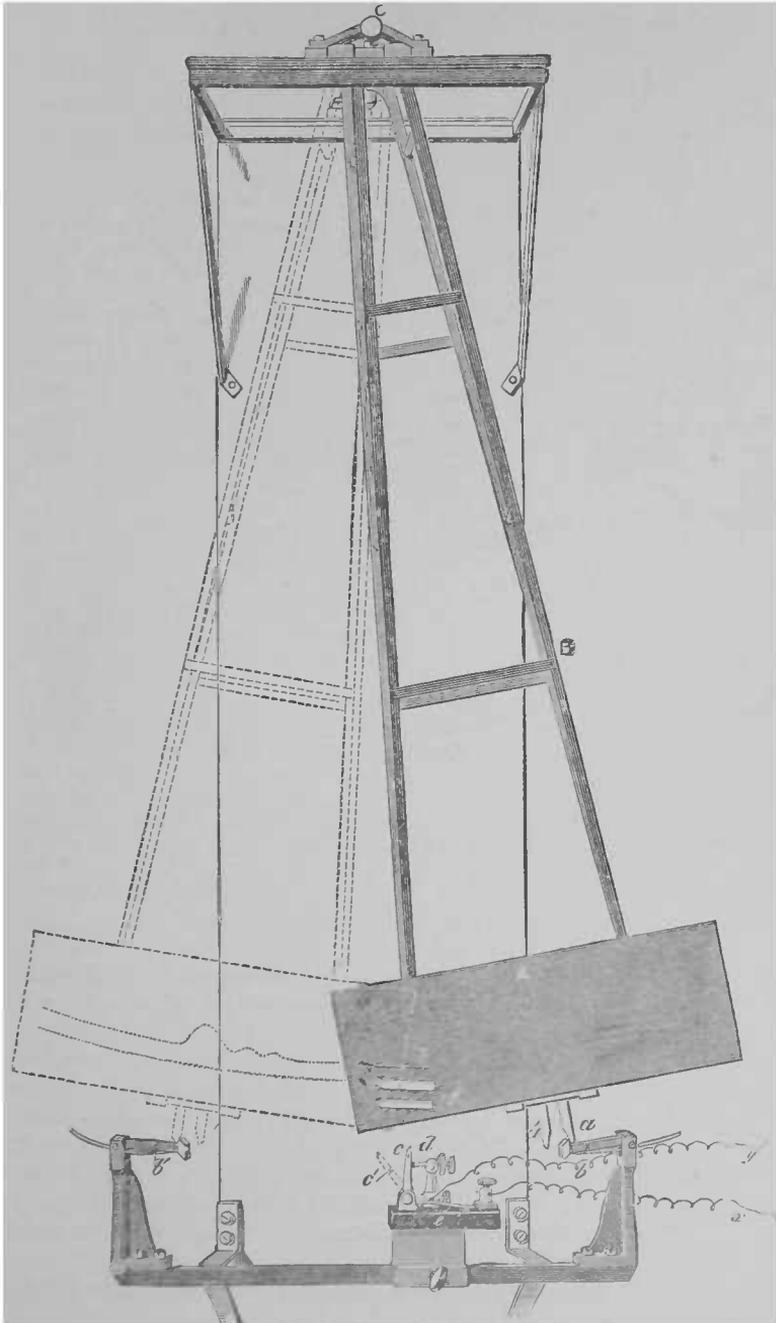
THE PENDULUM MYOGRAPH.

The figure is diagrammatic, the essentials only of the instrument being shown. The smoked-glass plate, *A*, swings with the pendulum, *B*, on carefully adjusted bearings at *.*. The contrivances by which the glass plate can be removed and replaced at pleasure, are not shown. A second glass plate, so arranged that the first glass plate may be moved up and down without altering the swing of the pendulum, is also omitted. Before commencing an experiment the pendulum is raised up (in the figure to the right), and is kept in that position by the tooth, *a*, catching on the spring-catch, *b*. On depressing the catch, *b*, the glass plate is set free, swings into the new position indicated by the dotted lines, and is held in that position by the tooth, *a'*, catching on the catch, *b'*. In the course of its swing the tooth, *a*, coming into contact with the projecting steel rod, *c*, knocks it on one side into the position indicated by the dotted line, *c'*. The rod, *c*, is in electric continuity with the wire, *x*, of the primary coil of an induction-machine. The screw, *d*, is similarly in electric continuity with the wire, *y*, of the same primary coil. The screw, *d*, and the rod, *c*, are armed with platinum at the points in which they are in contact, and both are insulated by means of the ebonite block, *e*. As long as *c* and *d* are in contact the circuit of the primary coil to which *x* and *y* belong is closed. When in its swing the tooth, *a'*, knocks *c* away from *d*, at that instant the circuit is broken, and a "breaking" shock is sent through the electrodes connected with the secondary coil of the machine, and so through the nerve. The lever, *l*, the end only of which is shown in the figure, is brought to bear on the glass plate, and when at rest describes a straight line, or, more exactly, an arc of a circle of large radius. The tuning-fork, *f*, the ends only of the two limbs of which are shown in the figure, placed immediately below the lever, serves to mark the time.

In this instrument a smoked-glass plate, on which a lever writes, forms the bob of a pendulum and consequently swings with it. The pendulum with the glass plate attached being raised up, is suddenly let go. It swings, of course, to the opposite side, the glass plate travels through an arc of a circle, and the lever being stationary, the point of the lever describes an arc on the glass plate. The rate at which the glass plate travels—*i. e.*, the time it takes for the lever-point to describe a line of a given length on the glass plate, may be calculated from the length of the pendulum, but it is simpler and easier to place a vibrating tuning-fork immediately under the point of the lever. If the vibrations of the tuning-fork are known, then the number of vibrations which are marked on the plate between any two points on the line described by the lever gives the time taken by the lever in passing from one point to the other. An easy arrangement permits the exact time at which the shock is sent through the nerve to be marked on the line of the lever. To avoid the confusion of too many markings on the plate, the pendulum, after describing an arc, is caught by a spring-catch on the opposite side.

A complete muscle-curve, such as that shown in Fig. 13, taken from the gastrocnemius of a frog, teaches us the following facts:

1. That although the passage of the induced current from electrode to electrode is practically instantaneous, its effect measured from the entrance of the shock into the nerve to the return of the muscle to its natural length after the shortening, takes an appreciable time. In the figure, the whole curve from *a* to *d* takes up about the same time as eighteen double vibrations of the tuning-fork. Since each double vibration here represents $\frac{1}{180}$ of a second, the duration of the whole curve is $\frac{1}{10}$ of a second.

2. In the first portion of this period, from *a* to *b*, there is no

visible change, no shortening of the muscle, no raising of the lever.

3. It is not until b, that is to say after the lapse of $\dfrac{2\frac{1}{3}}{180}$ — $i.\,e.$,

about $\frac{1}{77}$ of a second, that shortening begins. The shortening as shown by the curve is at first slow, but soon becomes more rapid, and then slackens again until it reaches a maximum at c; the whole shortening occupying about $\frac{1}{20}$ of a second.

4. Arrived at the maximum of shortening, the muscle at once begins to relax, the lever descending at first slowly, then very rapidly, and at last more slowly again, until at d the muscle has regained its natural length; the whole return from the maximum of contraction to the natural length occupying $\frac{7}{180}$—$i.\,e.$, about $\frac{1}{30}$ of a second.

Thus a simple muscular contraction, a simple spasm or twitch, as it is sometimes called, produced by a momentary stimulus, such as a single induction-shock, consists of three main phases:

1. A phase antecedent to any visible alteration in the muscle. This phase, during which invisible preparatory changes are taking place in the nerve and muscle, is called the "latent period."

2. A phase of shortening or, in the more strict meaning of the word, contraction.

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

In the case we are considering, the electrodes are supposed to be applied to the nerve at some distance from the muscle. Consequently the latent period of the curve comprises not only the preparatory actions going on in the muscle itself, but also the changes necessary to conduct the immediate effect of the induction-shock from the part of the nerve between the electrodes, along a considerable length of nerve down to the muscle. It is obvious that these latter changes might be eliminated by placing the electrodes on the muscle itself or on the nerve close to the muscle. If this were done, the muscle and lever being exactly as before, and care were taken that the induction-shock entered into the nerve at the new spot, at the moment when the point of the lever had reached exactly the same point of the travelling surface as before, a curve like that shown by the plain line in Fig. 15 would be gained. It resembles the first curve (indicated in the figure by a dotted line) in all points, except that the latent period is shortened; the contraction begins rather earlier. From this we learn two facts:

1. The greater part of the latent period is taken up by changes in the muscle itself, preparatory to the actual visible shortening, for the two latent periods do not differ much. Of course, even in the second case, the latent period includes the changes going

on in the short piece of nerve still lying between the electrodes and the muscular fibres. To eliminate this with a view of determining the latent period in the muscle itself, the electrodes might be placed directly on the muscle poisoned with urari. If this were done, it would still be found that the latent period was
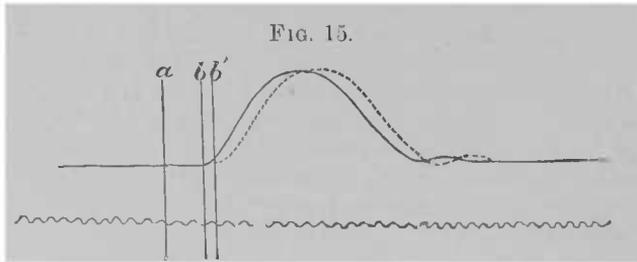
FIG. 15.

CURVES ILLUSTRATING THE MEASUREMENT OF THE VELOCITY OF A NERVOUS IMPULSE. (Diagrammatic.) To be read from left to right.

The same muscle-nerve preparation is stimulated (1) as far as possible from the muscle, (2) as near as possible to the muscle; both contractions are registered by the pendulum myograph exactly in the same way.

In (1) the stimulus enters the nerve at the time indicated by the line a, the contraction, shown by the dotted line, begins at b'; the whole latent period therefore is indicated by the distance from a to b'.

In (2) the stimulus enters the nerve at exactly the same time, a; the contraction, shown by the unbroken line, begins at b; the latent period, therefore, is indicated by the distance between a and b.

The time taken up by the nervous impulse in passing along the length of nerve between 1 and 2 is, therefore, indicated by the distance between b and b', which may be measured by the tuning-fork curve below. N. B.—No value is given in the figure for the vibrations of the tuning-fork, since the figure is diagrammatic, the distance between the two curves, as compared with the length of either, having been purposely exaggerated for the sake of simplicity.

chiefly taken up by changes in the muscular as distinguished from the nervous elements.

2. Such difference as does exist indicates the time taken up by the propagation, along the piece of nerve, of the changes set up at the far end of the nerve by the induction-shock. These changes we shall hereafter speak of as constituting a nervous impulse; and the above experiment shows that it takes some appreciable time for a nervous impulse to travel along a nerve. In the figure the difference between the two latent periods, the distance between b and b', seems almost too small to measure accurately; but if a long piece of nerve be used for the experiment, and the recording surface be made to travel very fast, the difference between the duration of the latent period when the induction-shock is sent in at a point close to the muscle, and that when it is sent in at a point as far away as possible from the muscle, may be satisfactorily measured in fractions of a second. If the length of nerve between the two points be accu-

rately measured, the rate at which a nervous impulse travels along the nerve to a muscle can thus be easily calculated. This has been found to be in the frog about 28, and in man about 33 metres per second.

Thus when a momentary stimulus, such as a single induction-shock, is sent into a nerve connected with a muscle, the following events take place.

1. The generation at the spot stimulated of a nervous impulse, and the propagation of the impulse along the nerve to the muscle. The time taken up by this varies according to the length of the nerve, but is always very short.

2. The setting up of certain molecular changes in the muscle, unaccompanied by any visible alteration in its form constituting the latent period, and occupying on an average about $\frac{1}{100}$ of a second.

3. The shortening of the muscle up to a maximum, occupying about $\frac{4}{100}$ of a second.

4. The return of a muscle to its former length, occupying about $\frac{5}{100}$ of a second.

We have given what may be considered the average duration [1] of each phase chiefly for the sake of showing their relative proportions. But it must be borne in mind that the duration of a contraction differs in different animals and in different muscles of the same animal; in the rabbit the more deeply colored so-called "red" muscles have in their contraction a longer period than have the pale muscles. The duration may also differ in the same muscle under different conditions; moreover, the duration of the several phases may vary independently. Temperature has a marked effect in varying the length of the muscle-curve, a high temperature shortening, and a low temperature prolonging the contraction, and especially the third phase, or relaxation. Fatigue also lengthens the contraction, as do also to a remarkable extent certain poisons, such as veratrin. An increase in the load which the muscle is lifting shortens the descending or return part of the curve, and increases the length of the latent period. All such influences will be better studied when we come to speak more in detail of the changes which take place in a muscle during contraction. Their effects are only mentioned now in order that the reader may thus early learn to conceive of even a simple muscular contraction as a complex act, the several parts of which are variable, so that many differing forms of a muscle-curve may be obtained under different circumstances.

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[1] The curve described in the previous text happened to have a rather long latent period, and the lengthening to be of shorter instead of longer duration than the shortening.

Tetanic Contractions.

If a single induction-shock be followed at a sufficiently short interval by a second shock of the same strength, the first simple contraction or spasm will be followed by a second spasm, the two bearing some such relation to each other as that shown by the curve in Fig 6, where the interval between the two shocks was just long enough to allow the first spasm to have passed its maximum before the latent period of the second was over. It will be observed that the second curve is almost in all respects like the first, except that it starts, so to speak, from the first

Fig. 16.
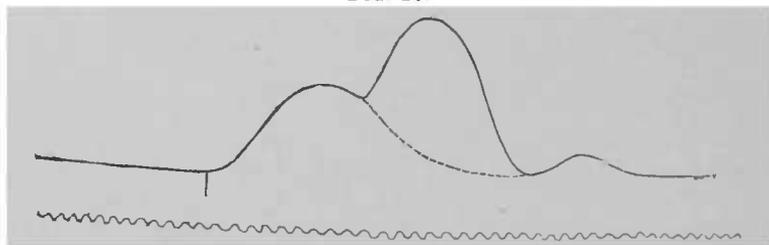
TRACING OF A DOUBLE MUSCLE-CURVE. To be read from left to right.

While the muscle[1] was engaged in the first contraction (whose complete course, had nothing intervened, is indicated by the dotted line), a second induction-shock was thrown in, at such a time that the second contraction began just as the first was beginning to decline. The second curve is seen to start from the first, as does the first from the base-line.

curve instead of from the base-line. The second nervous impulse has acted on the already contracted muscle, and made it contract again just as it would have done if there had been no first impulse and the muscle had been at rest. The two contractions are added together and the lever raised nearly double the height it would have been by either alone. A more or less similar result would occur if the second contraction began at any other phase of the first. The combined effect is, of course, greatest when the second contraction begins at the maximum of the first, being less both before and afterwards. If in the same way a third shock follows the second at a sufficiently short interval, a third curve is piled on the top of the second. The same with a fourth, and so on.

When, however, repeated shocks are given it is found that the height of each contraction is rather less than the preceding one, and this diminution becomes more marked the greater the

[1] In this and the other curves of this section the tracings figured were taken from *frog's* muscle.

number of shocks.   Hence, after a certain number of shocks, the succeeding impulses do not cause any further shortening of the muscle, any further raising of the lever, but merely keep up the contraction already existing.   The curve thus reaches a maximum, which it maintains, subject to the depressing effects of exhaustion, so long as the shocks are repeated.   When these cease to be given, the muscle returns, in the usual way, at first very rapidly, and then more slowly, to its natural length. When the shocks do not succeed each other too rapidly, the individual contractions may readily be traced along the whole curve, as is seen in Fig. 7, where the primary current of the

FIG. 17.
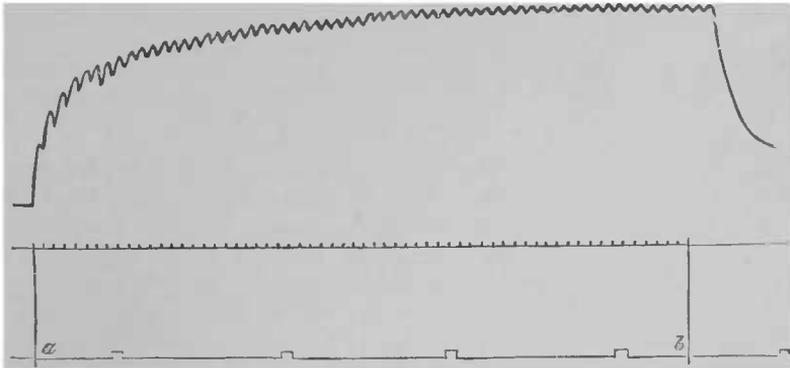
MUSCLE THROWN INTO TETANUS, WHEN THE PRIMARY CURRENT OF AN INDUCTION-MACHINE IS REPEATEDLY BROKEN AT INTERVALS OF SIXTEEN IN A SECOND.

To be read from left to right.

The upper line is that described by the muscle. The lower marks time, the intervals between the elevations indicating seconds.   The intermediate line shows when the shocks were sent in, each mark on it corresponding to a shock.   The lever, which describes a straight line before the shocks are allowed to fall into the nerve, rises almost vertically (the recording surface travelling in this case slowly) as soon as the first shock enters the nerve at a.   Having risen to a certain height, it begins to fall again, but in its fall is raised once more by the second shock, and that to a greater height than before.   The third and succeeding shocks have similar effects, the muscle continuing to become shorter, though the shortening at each shock is less.   After a while the increase in the total shortening of the muscle, though the individual contractions are still visible, almost ceases.   At b, the shocks cease to be sent into the nerve ; the contractions almost immediately disappear, and the lever forthwith commences to descend.   The muscle being lightly loaded, the descent is very gradual ; the muscle had not regained its natural length when the tracing was stopped.

induction-machine was repeatedly broken at intervals of sixteen in a second.   When the shocks succeed each other more rapidly, the individual contractions, visible at first, may become fused together and lost to view as the tetanus continues and the muscle becomes tired.   When the shocks succeed each other still more rapidly (the second contraction beginning in the ascending por-

tion of the first), it becomes difficult or impossible to trace out the single contractions. The curve then described by the lever is of the kind shown in Fig. 18, where the primary current of an induction-machine was rapidly made and broken by the magnetic

FIG. 18.
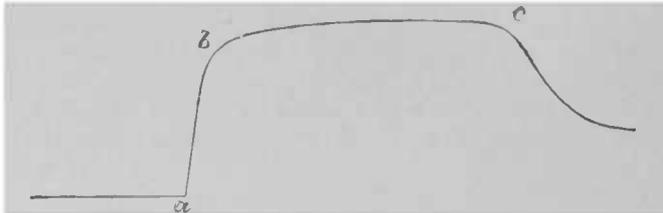
TETANUS PRODUCED WITH THE ORDINARY MAGNETIC INTERRUPTOR OF AN INDUCTION-MACHINE. (Recording surface travelling slowly.) To be read from left to right.

The interrupted current being thrown in at *a* the lever rises rapidly, but at *b* the muscle reaches the maximum of contraction. This is continued till *c*, when the current is shut off and relaxation commences.

interruptor, Fig. 19. The lever, it will be observed, rises at *a* after the latent period (which is not marked), first rapidly, and then more slowly, in an apparently unbroken line to a maximum at about *b*, maintains the maximum so long as the shocks continue to be given, and when these cease to be given, as at *c*, gradually descends to the base-line. This condition of muscle, brought about by rapidly repeated shocks, this fusion of a number of simple spasms into an apparently smooth, continuous effort, is known as *tetanus*, or *tetanic contraction*. The above facts are most clearly shown when induction-shocks, or at least galvanic currents in some form or other are employed. They are seen, however, whatever be the form of stimulus employed. Thus in the case of mechanical stimuli, while a single blow may cause a single spasm, a pronounced tetanus may be obtained by rapidly striking successively fresh portions of a nerve. With chemical stimulation, as when a nerve is dipped in acid, it is impossible to secure a momentary application; hence tetanus, generally irregular in character, is the normal result of this mode of stimulation. In the living body, the contractions of the striated muscles, brought about either by the will or by reflex action, are generally tetanic in character. Even very short, sharp movements, such as a sudden jerk of the limbs, are in reality examples of tetanus of short duration.

When it has once been realized that an ordinary tetanic muscular movement is essentially a vibratory movement, that the apparently rigid and firm muscular mass is really the subject of a whole series of vibrations—a series, namely, of simple spasms—it will be readily understood why a tetanized muscle, like all other

FIG. 19.
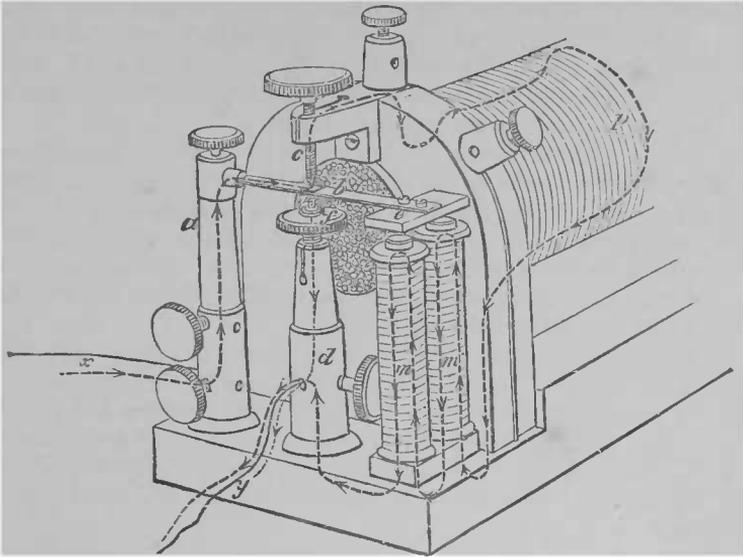
THE MAGNETIC INTERRUPTOR.

The figure is introduced to illustrate the action of this instrument as commonly used by physiologists.

The two wires x and y from the battery are connected with the two brass pillars a and d by means of screws. Directly contact is thus made, the current, indicated in the figure by the *thick* interrupted line, passes in the direction of the arrows, up the pillar a, along the steel spring b, as far as the screw c, the point of which, armed with platinum, is in contact with a small platinum plate on b. The current passes from b through c and a connecting wire into the primary coil p. Upon its entering into the primary coil, an induced (making) current is for the instant developed in the secondary coil (not shown in the figure). From the primary coil p the current passes, by a connecting wire, through the double spiral, m, and, did nothing happen, would continue to pass from m by a connecting wire to the pillar d, and so by the wire y to the battery. The whole of this course is indicated by the thick interrupted line with its arrows.

As the current, however, passes through the spirals m, the iron cores of these are made magnetic. They, in consequence, draw down the iron bar e, fixed at the end of the spring b, the flexibility of the spring allowing this. But, when e is drawn down, the platinum plate on the upper surface of b is also drawn away from the screw c, and a similar platinum plate on the *under* surface of b is brought into contact with the platinum-armed point of the screw f, the screws being so arranged that this takes place. In consequence of this change, the current can no longer pass from b to c. On the contrary, it passes from b to f, and so down the pillar d, in the direction indicated by the *thin* interrupted line, and out to the battery by the wire y. Thus, the current is "short-circuited" from the primary coil; and the instant that the current is thus cut off from the primary coil, an induced (breaking) current is for the moment developed in the secondary coil. But the current is cut off not only from the primary coil, but also from the spirals m; in consequence, their cores cease to be magnetized, the bar e ceases to be attracted by them, and the spring b, by virtue of its elasticity, resumes its former position in contact with the screw c. This return of the spring, however, reëstablishes the current in the primary coil and in the spirals, and the spring is drawn down, to be released once more in the same manner as before. Thus, as long as the current is passing along x, the contact of b is constantly alternating between c and f, and the current is constantly passing into and being shut off from p, the periods of alternation being determined by the periods of vibration of the spring b. With each passage of the current into, or withdrawal from the primary coil, an induced (making and, respectively, breaking) shock is developed in a secondary coil.

vibrating bodies, gives out a sound. That a contracting (tetanized) muscle does give out a sound, the so-called muscular sound, is easily proved by listening with a stethoscope to a contracted biceps, or by stopping the ears and listening to the contractions of one's own masseter and temporal muscles.

When a muscle is thrown into tetanus by interrupted shocks applied directly to the nerve or to the muscle, the note is the same as that of the interruptor determining the number of the shocks. This is naturally the case, since the note of the muscle-sound is determined by the rapidity of the spasms or vibrations which go to make up the tetanus, and these are determined by the rapidity with which the stimulus is repeated.

When a muscle is thrown into tetanus by the will or by reflex action, or by direct stimulation of the spinal cord—in fact, in any way through the action of the central nervous system, the same note is always heard, viz., one of 36 to 40 vibrations per second, which, however, is probably a harmonic of a lower note, indicating that the muscle is really vibrating 19 or 20 times a second.

It need hardly be said that a single muscular contraction, a single vibration, cannot cause a muscular sound.

The general observations which have been described in this section may, when proper precautions are taken, be carried out on a muscle-nerve preparation from a frog for a very considerable time after its removal from the body. After some hours, however, or it may be days, the length of time varying according to circumstances, it will be found that no stimulus, however powerful, will cause any contraction when applied either to the nerve or to the muscle. Both muscle and nerve are then said to have lost their irritability; and a short time afterwards the muscle may be observed to pass into a peculiar condition known as *rigor mortis*, in which it loses all the suppleness and extensibility characteristic of the living irritable muscle. The causes of this loss of irritability, as well as the features and nature of this rigor mortis, we shall study in detail presently.

The muscles and nerves of a mammal, or, indeed, of any warm-blooded animal, lose their irritability, and the muscles become rigid in a very short time (it may be a few minutes) after removal from the body. Hence these are less suitable for experiments than the muscles and nerves of a frog, though their general phenomena are exactly the same.

We must now attempt to study in greater detail the changes which take place in a muscle and nerve during the contraction of the former and the passage of an impulse along the latter, with a view to the better understanding of both events.

Sec. 2.—The Changes in a Muscle during Muscular Contraction.

The Change in Form.

We have seen that at the close of the latent period the muscle shortens—that is, each fibre shortens, at first slowly, then more rapidly, and lastly more slowly again. The shortening (which in severe tetanus may amount to three-fifths of the length of the muscle) is accompanied by an almost exactly corresponding thickening, so that there is hardly any actual change in bulk. [A very delicate and efficient mode of determining that the muscle does not change in bulk by contracting is by suspending a muscle and nerve preparation by electrodes in a tightly stoppered bottle, having a graduated capillary tube projecting above the cork. The bottle is filled with water, and the tube but partially so. Stimulus is then applied to the nerve, which causes the muscle to contract. If the water-line in the tube is observed, no change will be appreciable. (Marey.)] If a muscle be placed horizontally, and a lever laid upon it, the thickening of the muscle will raise up the lever, and cause it to describe on a recording surface a curve exactly like that described by a lever attached to the end of the muscle. There appears to be a minute diminution of bulk not amounting to more than one thousandth.

If a long muscle of parallel fibres, poisoned with urari, so as to eliminate the action of its nerves, be stimulated at one end, the contraction may be seen, almost with the naked eye, to start from the end stimulated, and to travel along the muscle. If two levers be made to rest on, or be suspended from, two points of such a muscle placed horizontally, the points being at a known distance from each other and from the point stimulated, the progress of the contraction may be studied. It is found that the contraction starting from the spot stimulated, passes along the muscle in the form of a wave diminishing in vigor as it proceeds. The velocity with which this contraction wave travels in the muscles of the frog is about 3 or 4 metres a second; and since it takes, in round numbers, from about 0.5 to 0.1 second for the contraction to pass over any point of the fibre, the wavelength of the contraction wave must be from about 200 to 400 mm.

In the muscles of a mammal laid bare for the purposes of experiment the velocity does not seem to be very different from that in the frog; but in the intact muscles in their normal condition in the living body, it is probably somewhat greater, and the

wave also probably travels with undiminished velocity and vigor to the end of the fibre. In general, the velocity with which the contraction wave travels, like the duration and character of the contraction, varies under different circumstances, being much influenced by temperature, by the action of drugs, and especially by those complex intrinsic changes which we speak of as fatigue or exhaustion.

Seeing that the extreme limit of the length of a muscular fibre is about 30 or 40 mm., it is evident that even when the stimulation begins at one end and the wave travels at the more rapid rate, the whole fibre is not only in a state of contraction at the same time, but almost in the same phase of the contraction wave. In an ordinary contraction occurring in the living body the stimulus is never applied to one end of the fibre; the nervous impulse which in such cases acts as the stimulus to the muscle, falls into the fibre at about its middle, where the nerve ends in an end-plate, and the contraction wave starting from the end-plate travels along the muscular fibre in both directions. In such a case, therefore, still more even than in the urarized muscle stimulated artificially at one end, must the whole fibre be occupied at the same time by the wave of contraction.

Changes in Microscopic Structure.—When portions of living irritable muscle are examined under the microscope, contraction waves similar to those just described, but feebler and of shorter length, may be observed passing along the fibres. By appropriate treatment with osmic acid or other reagents, these short contraction waves may be fixed, and the structure of the contracted portion compared at leisure with that of the portions of the fibre at rest. In Fig. 20, representing a fibre of the muscle of an insect (in which these changes can be more satisfactorily studied than in vertebrate muscle), the contraction wave begins near a, and has reached about its maximum at b, while at c the fibre is at rest, the contraction wave not having reached it (or having passed over it, for the beginning and end of the wave are exactly alike). It will be seen that at b, each disk of the fibre is shorter and broader than at c. Further, while at c the dim band x is conspicuous, and the light band y, with its accessory markings y', is together lighter than the dim band x, at b in the fully contracted part of the fibre the dim band appears light as compared with the black line y' occupying the middle of the previously light band. In the contracted muscle then there is a reversal of the state of things in the resting muscle, the light band (or part of the light band) of the latter in contracting becomes dark, and the dim band of the latter becomes by comparison light. Between rest and full contraction there is an

intermediate stage, as at d, in which the distinction between dim and bright bands seems to be largely lost. The subject, however, is one offering peculiar difficulties in the way of investigation, and while most, though not all, observers agree in the broad facts which have just been stated, there is great diversity of opinion concerning further details, and especially as to the interpretation of the various appearances observed. The accessory markings in the middle of the light band have, in particular, been the subject of controversies into which we cannot enter here.

FIG. 20.
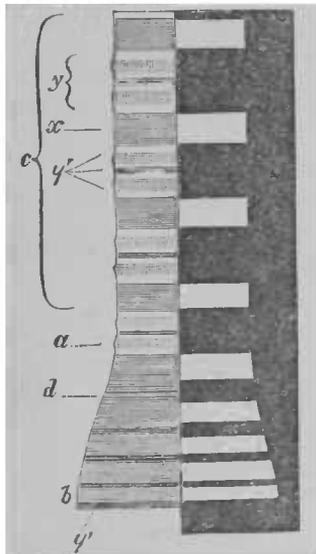
MUSCULAR FIBRE UNDERGOING CONTRACTION.

The muscle is that of *Telephorus melanurus* treated with osmic acid. The fibre at c is at rest, at a the contraction begins, at b it has reached its maximum. The right-hand side of the figure shows the same fibre as seen in polarized light. (After ENGLEMANN.)

When the fibre is examined in polarized light it is seen that the dim band is anisotropic, and the light band isotropic. This is the case during all the phases of the contraction. At no period is there any confusion between the anisotropic and isotropic material; these maintain their relative positions, both become shorter and broader; but it will be observed that the isotropic substance diminishes in height to a much greater extent than does the anisotropic substance. The latter, in fact, appears to increase in bulk at the expense of the former.

Relaxation.—The shortening as we have seen is followed by a relaxation, the muscle returning to its original length. When an

appropriate weight is attached to the muscle this return is generally complete, the curve speedily rejoining, as shown in Fig. 13, the base-line from which it started; but when no load is used and the muscle, therefore, is acted upon by its own weight and that of a very light lever only, the return is incomplete; the curve, though descending near to, fails to touch the base-line and runs nearly parallel to it for some considerable distance. The relaxation is, therefore, obviously assisted by the extending force of the load; but, nevertheless, is in the main the result of intrinsic processes going on in the muscle, the reverse of those leading to the shortening. The return of the muscle to its elongated condition, is not a mere passive stretching, after the causes leading to the shortening have passed away; it like the shortening itself is a manifestation of activity. And hence we find that the completeness of the relaxation is dependent on the complex changes which we speak of as the nutrition of the muscle. Thus in their natural position in the living body, muscles, owing to their vigorous nutrition, assisted by the fact that their anatomical disposition keeps them always on the stretch, return completely to their original length, after even powerful and prolonged contractions. In a muscle out of the body, on the other hand, even when loaded, repeated successive contractions frequently result in the failure to achieve complete relaxation becoming very conspicuous; and the tetanus curves, Figs. 16 and 17, show very strikingly this shortcoming, which is often spoken of as the "contraction remainder."

We may speak of the relaxation as the result of an elastic reaction, but only in the sense that the elastic qualities of the muscle, at any moment, are the expression of deep-seated and continually varying molecular changes going on in the muscular substance. And in this connection attention may be called to a peculiar physical character of contracting muscle. Living muscle at rest is very extensible, but when stretched returns after the extending cause has been removed, rapidly and completely to its former length. In physical language muscle is spoken of as possessing slight but perfect elasticity. It might be imagined that during a contraction this extensibility would be diminished in order that none of the resistance which the muscle had to overcome, no part of the weight for instance which had to be lifted, should be employed in stretching the muscle itself, and thus lead to an apparent waste of energy. On the contrary, we find that during a contraction there is an increase of extensibility; thus if a muscle at rest be loaded with a given weight, say 50 grammes, and its extension observed, and be then while unloaded thrown into tetanus, and the load applied during the tetanus, the extension in the second case will be distinctly greater

than in the first.   During the contraction there is so to speak a greater mobility of the muscular molecules, and though this greater mobility may have its advantages, the loaded muscle has in contracting to overcome its own increased tendency to lengthen on extension before it can produce any effect on the weight which it has to lift.

The elasticity and extensibility of the muscular substance are, however, complicated and difficult subjects, and it will be sufficient to reassert that they are essentially vital properties, being dependent, like the irritability of the muscular substance, on certain nutritive factors.   As the muscular substance becomes weary with too much work or impoverished by scanty nutrition, its elasticity suffers *pari passu* with its irritability.   The exhausted muscle when extended does not return so readily to its proper length as the fresh active muscle, and, as we shall see, the dead muscle does not return at all.

Electrical Changes.

Muscle-currents.—If a muscle be removed in an ordinary manner from the body, and two non-polarizable electrodes,[1] con-

FIG. 21.
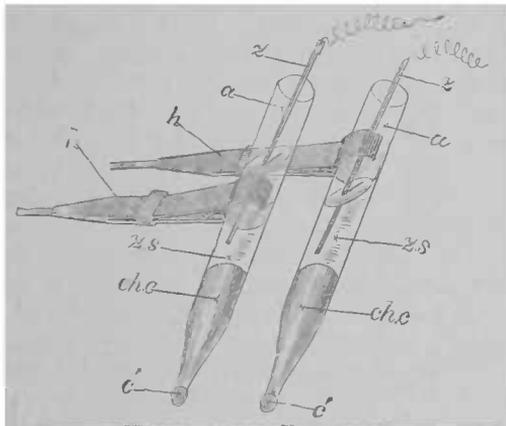
NON-POLARIZABLE ELECTRODES.

a, the glass tube ; *z*, the amalgamated zinc slips connected with their respective wires ; *z s*, the zinc sulphate solution ; *ch c*, the plug of china-clay ; *c'*, the portion of the china-clay plug projecting from the end of the tube ; this can be moulded into any required form.

nected with a delicate galvanometer of many convolutions, be placed on two points of the surface of the muscle, a deflection of

[1] These (**Fig. 21**) consist essentially of a slip of thoroughly amalgamated zinc dipping into a saturated solution of zinc sulphate, which in turn is brought into

the galvanometer will take place, indicating the existence of a current passing through the galvanometer from the one point of the muscle to the other, the direction and amount of the deflection varying according to the position of the points. The "muscle-currents" thus revealed are seen to the best advantage when the muscle chosen is a cylindrical or prismatic one with parallel fibres, and when the two tendinous ends are cut off by clean incisions at right angles to the long axis of the muscle. The muscle then presents a (artificial) transverse section at each end and a longitudinal surface. We may speak of the latter as being divided into two equal parts by an imaginary transverse line on its surface called the "equator," containing all the points of the surface midway between the two ends. Fig. 21 is a diagrammatic representation of a muscle, the line *ab* being the equator. In such a muscle the development of the muscle-currents is found to be as follows.

The greatest deflection is observed when one electrode is placed at the mid-point or equator of the muscle, and the other at either cut end; and the deflection is of such a kind as to show that positive currents are continually passing from the equator through the galvanometer to the cut end—that is to say, the cut end is negative relatively to the equator. The currents outside the muscle may be considered as completed by currents *in the muscle* from the cut end to the equator. In the diagram Fig. 22, the arrows indicate the direction of the currents. If one electrode be placed at the equator, *ab*, the effect is the same at whichever of the two cut ends, *x* or *y*, the other is placed. If one electrode remaining at the equator, the other be shifted from the cut end to a spot, *c*, nearer to the equator, the current continues to have the same direction, but is of less intensity in proportion to the nearness of the electrodes to each other. If the two electrodes be placed at unequal distances, *e* and *f*, one on either side of the equator, there will be a feeble current from the one nearer the equator to the one further off, and the current will be the feebler the more nearly they are equidistant from the equator. If they are quite equidistant, as, for instance, when one is placed on the cut end *x*, and the other on the cut end *y*, there will be no current at all.

If one electrode be placed at the circumference of the transverse section and the other at the centre of the transverse

connection with the nerve or muscle by means of a plug or bridge of china-clay moistened with normal sodium chloride solution; it is important that the zinc should be thoroughly amalgamated. This form of electrodes gives rise to less polarization than do simple platinum or copper electrodes. The clay affords a connection between the zinc and the tissue which neither acts on the tissue nor is acted on by the tissue. Contact of any tissue with copper or platinum is in itself sufficient to develop a current.

section, there will be a current through the galvanometer from the former to the latter ; there will be a current of similar direction but of less intensity when one electrode is at the circumference, *g*, of the transverse section, and the other at some point, *h*, nearer the centre of the transverse section. In fact, the points which are relatively most positive and most negative to each other are points on the equator and the two centres of the transverse sections ; and the intensity of the current between any two

Fig. 22.
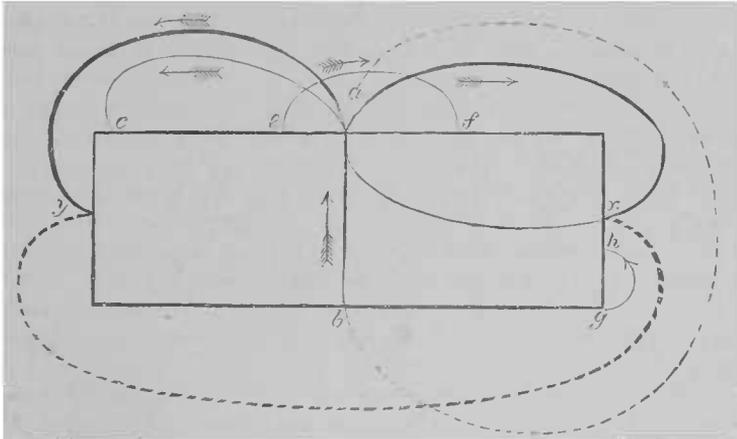
DIAGRAM ILLUSTRATING THE ELECTRIC CURRENTS OF NERVE AND MUSCLE.

Being purely diagrammatic, it may serve for a piece either of nerve or of muscle, except that the currents at the transverse section cannot be shown in a nerve The arrows show the direction of the current through the galvanometer.

ab the equator. The strongest currents are those shown by the dark lines, as from *a*, at equator, to *x* or to *y* at the cut ends. The current from *a* to *c* is weaker than from *a* to *y*, though both, as shown by the arrows, have the same direction A current is shown from *e*, which is near the equator, to *f*, which is further from the equator. The current (in muscle) from a point in the circumference to a point nearer the centre of the transverse section is shown at *gh*. From *a* to *b* or from *x* to *y* there is no current, as indicated by the dotted lines.

points will depend on the respective distance of those points from the equator and from the centre of the transverse section.

Similar currents may be observed when the longitudinal surface is not the natural, but an artificial one ; indeed, they may be witnessed in even a piece of muscle, provided it be of cylindrical shape and composed of parallel fibres.

These "muscle-currents" are not mere transitory currents, disappearing as soon as the circuit is closed ; on the contrary, they last a very considerable time. They must therefore be maintained by some changes going on in the muscle—by continued chemical action, in fact. They disappear as the irritability of the muscle vanishes, and are connected with those

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nutritive so-called vital changes which maintain the irritability of the muscle.

Muscle-currents, such as have just been described, may, we repeat, be observed iu any cylindrical muscle suitably prepared, and similar currents, with variations which need not be discussed here, may be seen in muscles of irregular shape with obliquely or otherwise arranged fibres. And Du Bois-Reymond, to whom chiefly we are indebted for our knowledge of these currents, has been led to regard them as essential and important properties of living muscle. He has, moreover, advanced the theory that muscle may be considered as composed of electro-motive particles or molecules, each of which, like the muscle at large, has a positive equator and negative ends, the whole muscle being made up of these molecules in somewhat the same way (to use an illustration which must not, however, be strained or considered as an exact one), as a magnet may be supposed to be made up of magnetic particles each with its north and south pole.

There are reasons, however, for thinking that these muscle-currents have no such fundamental origin, that they are, in fact, of surface, and indeed of artificial origin. Without entering largely into the controversy on this question, the following important facts may be mentioned :

1. When a muscle is examined while it still retains untouched its natural tendinous terminations, the currents are much less than when artificial transverse sections have been made ; the natural tendinous end is less negative than the cut surface. But the tendinous end becomes at once negative when it is dipped in water or acid—indeed, when it is in any way injured. The less roughly, in fact, a muscle is treated the less evident are the muscle-currents, and it has been maintained that if adequate care be taken to maintain a muscle in an absolutely natural condition, no such currents as those we have been describing exist at all.

2. Englemann has shown that the surface of the uninjured inactive[1] ventricle of the frog's heart is isoelectric—*i. e.*, that no current is obtained when the electrodes are placed on any two points of the surface. If, however, any part of the surface be injured, or if the ventricle be cut across so as to expose a cut surface, the injured spot or the cut surface becomes at once most powerfully negative towards the uninjured surface, a strong current being developed which passes through the galvanometer from the uninjured surface to the cut surface or to the injured spot. The negativity thus developed in a cut surface passes off

[1] The necessity of its being inactive will be seen subsequently.

in the course of some hours, but may be restored by making a fresh cut and exposing a fresh surface.

Now, when a muscle is cut or injured the substance of the fibres dies at the cut or injured surface. And many physiologists, among whom the most prominent is Hermann, have been led by the above and other facts to the conclusion that muscle-currents do not exist naturally in untouched muscles, that the muscular substance is naturally, when living, isoelectric, but that whenever a portion of the muscular substance dies, it becomes *while dying* negative to the living substance, and thus gives rise to currents. They explain the typical currents (as they might be called) manifested by a muscle with a natural longitudinal surface and artificial transverse sections, by the fact that the dying cut ends are negative relatively to the rest of the muscle.

Du Bois-Reymond and those with him offer special explanations of the above facts and of other objections which have been urged against the theory of naturally existing electro-motive molecules. Into these we cannot enter here. We must rest content with the statement that in an ordinary muscle, currents such as have been described may be witnessed, but that strong arguments may be adduced in favor of the view that these currents are not "natural" phenomena but essentially of artificial origin. It will, therefore, be best to speak of them as "currents of rest."

Negative Variations of the Muscle-current.—The controversy whether the "currents of rest" observable in a muscle be of natural origin or not, does not affect the truth or the importance of the fact that an electrical change takes place in a muscle whenever it enters into a contraction. When currents of rest are observable in a muscle these are found to undergo a diminution at the onset of a contraction, and this diminution is spoken of as "the negative variation" of the currents of rest. The negative variation may be seen when a muscle is thrown into a single contraction, but is most readily shown when the muscle is tetanized. Thus, if a pair of electrodes be placed on a muscle, one at the equator, and the other at or near the transverse section, so that a considerable deflection of the galvanometer needle, indicating a considerable current of rest, be gained, the needle of the galvanometer will, when the muscle is tetanized by an interrupted current sent through its nerve (at a point too far from the muscle to allow any escape of the current into the electrodes connected with the galvanometer), swing back towards zero; it returns to its original deflection when the tetauizing current is shut off.

Not only may this negative variation be shown by the galvano-

meter, but it, as well as the current of rest, may be used as a galvanic shock and so employed to stimulate a muscle, as in the experiment known as "the rheoscopic frog." For this purpose the muscles and nerves need to be very irritable and in thoroughly good condition. Two muscle-nerve preparations (A and B) having been made and each placed on a glass plate for the sake of insulation, the nerve of one (B) is allowed to fall on the muscle of the other (A), in such a way that one point of the nerve comes in contact with the equator of the muscle, and another point with one end of the muscle or with a point at some distance from the equator. At the moment the nerve is let fall and contact made, a current, viz., the "current of rest" of the muscle A, passes through the nerve; this acts as a stimulus to the nerve, and so causes a contraction in the muscle connected with the nerve. Thus the muscle A acts as a battery, the completion of the circuit of which by means of the nerve of B serves as a stimulus, causing the muscle B to contract.

If while the nerve of B is still in contact with the muscle of A, the nerve of the latter is tetanized with an interrupted current, not only is the muscle of A thrown into tetanus, but also that of B; the reason being as follows: At each spasm of which the tetanus of A is made up, there is a negative variation of the muscle-current of A. Each negative variation in the muscle-current of A serves as a stimulus to the nerve of B, and is hence the cause of a spasm in the muscle of B; and the stimuli following each other rapidly, as being produced by the tetanus of A they must do, the spasms in B to which they give rise are also fused into a tetanus in B. B, in fact, contracts in harmony with A. This experiment shows that the negative variation accompanying the tetanus of a muscle, though it causes only a single swing of the galvanometer, is really made up of a series of negative variations, each single negative variation corresponding to the single spasms of which the tetanus is made up.

But an electrical change may be manifested even in cases when no currents of rest exist. We have stated (p. 90) that the surface of the uninjured inactive ventricle of the frog's heart is isolectric, no currents being observed when the electrodes of a galvanometer are placed on two points of the surface. Nevertheless a most distinct current is developed whenever the ventricle contracts. This may be shown either by the galvanometer or by the rheoscopic frog. If the nerve of an irritable muscle-nerve preparation be laid over a pulsating ventricle, each beat is responded to by a spasm of the muscle of the preparation. In the case of ordinary muscles, too, instances occur in which it seems impossible to regard the electrical change manifested

during the contraction as the mere diminution of a preëxisting current.

Accordingly Hermann, and those who with him deny the existence of " natural " muscle-currents, speak of a muscle as developing during a contraction a "current of action," occasioned, as they believe, by the muscular substance as it is entering into the state of contraction becoming negative towards the muscular substance, which is still at rest, or has returned to a state of rest. In fact, they regard the negativity of muscular substance as characteristic alike of beginning death and of a beginning contraction. So that in a muscular contraction a wave of a negativity, starting from the end-plate when indirect, or from the point stimulated when direct stimulation is used, passes along the muscular substance to the ends or end of the fibre. We cannot, however, enter more fully here into a discussion of this difficult subject.

Whichever view be taken of the nature of these muscle-currents, and of the electric change during contraction, whether we regard that change as a "negative variation" or as a "current of action," it is important to remember that it takes place entirely during the latent period. It is not in any way the result of the change of form, it is the forerunner of that change of form. Just as a nervous impulse passes down the nerve to the muscle without any visible changes, so a molecular change of some kind, unattended by any visible events, known to us at present only by an electrical change, runs along the muscular fibre from the end-plates to the terminations of the fibre, preparing the way for the visible change of form which is to follow. This molecular invisible change is the work of the latent period, and careful observations have shown that it, like the visible contraction which follows at its heels, travels along the fibre from a spot stimulated towards the ends of the fibres, in the form of a wave having about the same velocity as the contraction, viz., about 3 metres a second.[1]

Chemical Changes.

Before we attack the important problem, What are the chemical changes concerned in a muscular contraction ? we must study in some detail the chemical features of muscles at rest. And here we are brought face to face with the chemical differences between living and dead muscles. All muscles within a certain time after removal from the body, or while still within the body,

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[1] In the muscles of the frog; but, as we have seen, having probably a higher velocity in the intact mammalian muscles, within the living body, and varying according to circumstances.

after "general" death of the body, lose their irritability. The
loss of irritability, even when rapid, is gradual, but is succeeded
by an event which is somewhat more sudden, viz., the entrance
into the condition known as *rigor mortis*, the occurrence of which
is marked by the following features. The muscle, previously
possessing a certain translucency, becomes much more opaque.
Previously very extensible and elastic, it becomes much less
extensible, and at the same time loses its elasticity; the muscle
now requires considerable force to stretch it, and when the force
is removed, does not, as before, return to its natural length. To
the touch it has lost much of its former softness, becomes firmer
and more resistant. The entrance into rigor mortis is charac-
terized by a shortening or contraction, which may, under certain
circumstances, be considerable. The energy of this contraction
is not great, so that when opposed, no actual shortening takes
place. When rigor mortis has been fully developed, no muscle-
currents whatever are observed. The onset of this rigidity may
be considered as the token of the death of the muscle itself.
As we shall see, the chemical features of the dead rigid muscle
are strikingly different from those of the living muscle.

If a **dead muscle,** from which all fat, tendon, fascia, and con-
nective tissue have been as much as possible removed, and
which has been freed from blood by the injection of saline solution,
be minced and repeatedly washed with water, the washings will
contain certain forms of albumin and certain extractive bodies,
of which we shall speak directly. When the washing has been
continued until the wash-water gives no proteid reaction, a large
portion of muscle will still remain undissolved. If this be
treated with a 10 per cent. solution of a neutral salt, ammonium
chloride being the best, a large portion of it will become imper-
fectly dissolved into a viscid fluid which filters with difficulty.
If the viscid filtrate be allowed to fall drop by drop into a large
quantity of distilled water, a white flocculent matter will be
precipitated. This flocculent precipitate is *myosin.* It is a pro-
teid, giving the ordinary proteid reactions, and having the same
general elementary composition as other proteids. It is soluble
in dilute saline solutions, especially those of ammonium chloride,
and may be classed in the globulin family, though it is not so
soluble as paraglobulin. Dissolved in saline solutions it readily
coagulates when heated—*i. e.,* is converted into coagulated pro-
teid,[1] and it is worthy of notice that it coagulates at a lower
temperature, viz., 55°–60° C., than does serum-albumin, para-
globulin, and many other proteids; it is precipitated, and after
long action, coagulated by alcohol, and is precipitated by an

[1] See Appendix.

excess of sodium chloride. By the action of dilute acids it is very readily converted into what is called syntonin or acid albumin,[1] by the action of dilute alkalies into alkali-albumin. Speaking generally, it may be said to be intermediate in its character between fibrin and globulin. On keeping, and especially on drying, its solubility is much diminished.

Of the substances which are left in washed muscle, from which the myosin has thus been extracted by ammonium chloride solution, little is known. If washed muscle be treated directly with dilute hydrochloric acid, the greater part of the material of the muscle passes at once into syntonin. The quantity of syntonin thus obtained may be taken as representing the quantity of myosin previously existing in the muscle. The portion insoluble in dilute hydrochloric acid consists in part of the substance of the sarcolemma, of the nuclei, and of the tissue between the bundles, and in part, probably, of certain structural elements of the fibres themselves.

If **living contractile frog's muscle,** freed as much as possible from blood, be frozen,[2] and, while frozen, minced and rubbed up in a mortar with four times its weight of snow containing 1 per cent. of sodium chloride, a mixture is obtained which, at a temperature just below $0°$ C., is sufficiently fluid to be filtered, though with difficulty. The slightly opalescent filtrate, or *muscle-plasma* as it is called, is at first quite fluid, but will when exposed to the ordinary temperature become a solid jelly, and afterwards separate into a *clot* and *serum.* It will, in fact, coagulate like blood-plasma, with this difference, that the clot is not firm and fibrillar, but loose, granular, and flocculent. During the coagulation, the fluid, which before was neutral or slightly alkaline, becomes distinctly acid.

The clot is myosin. It gives all the reactions of myosin obtained from dead muscle.

The serum contains ordinary serum-albumin, one or more peculiar proteids[3] coagulating at a lower temperature than does serum-albumin, and extractives. Such muscles as are red also contain a small quantity of hæmoglobin, to which, indeed, their redness is due.

Thus, while dead muscle contains myosin, serum-albumin, and other proteids and extractives, with certain insoluble matters and certain gelatinous elements not referable to the muscle-substance

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[1] See Appendix.

[2] Since, as we shall presently see, a muscle may be frozen and thawed again without losing any of its vital powers, we are at liberty to regard the frozen muscle as a still living muscle.

[3] See Appendix.

itself, living muscle contains no myosin, but some substance or substances which bear somewhat the same relation to myosin that the fibrin-factors do to fibrin, and which give rise to myosin upon the death of the muscle.

We may, in fact, speak of rigor mortis as characterized by a coagulation of the muscle-plasma, comparable to the coagulation of blood-plasma, but differing from it inasmuch as the product is not fibrin but myosin. The rigidity, the loss of suppleness, and the diminished translucency appear to be at all events largely, though probably not wholly, due to the change from the fluid plasma to the solid myosin. We might compare a living muscle to a number of fine, transparent, membranous tubes containing blood-plasma. When this blood-plasma entered into the "jelly" stage of coagulation, the system of tubes would present many of the phenomena of rigor mortis. They would lose much of their suppleness and translucency, and acquire a certain amount of rigidity.

There is, however, one very marked and important difference between rigor mortis of muscle and the coagulation of blood ; blood during its coagulation undergoes only a slight change in its reaction ; but muscle during the onset of rigor mortis becomes distinctly acid.

A living muscle at rest is in reaction neutral, or, possibly from some remains of lymph adhering to it, faintly alkaline. If, on the other hand, the reaction of a thoroughly rigid muscle be tested, it will be found to be most distinctly acid. This development of an acid reaction is witnessed not only in the solid untouched fibre, but also in expressed muscle-plasma ; it seems to be associated in some way with the appearance of the myosin.

The exact causation of this acid reaction has not at present been clearly worked out. Since the coloration of the litmus produced is permanent, carbonic acid, which, as we shall immediately state, is set free at the same time, cannot be regarded as the active acid, for the reddening of litmus produced by carbonic acid speedily disappears on exposure. On the other hand, it is possible to extract from rigid muscle a certain quantity of lactic acid, or rather of a variety of lactic acid known as sarcolactic acid ;[1] and it has been thought that the appearance of the acid reaction of rigid muscle is due to a new formation or to an increased formation of this sarcolactic acid. But there is considerable doubt whether any such increase of sarcolactic acid does actually take place in rigor mortis. Hence, though there can be no doubt that an acid reaction is established, we are not yet in a position to affirm positively the exact manner in which that reaction is pro-

[1] See Appendix.

duced, the complex nature of the muscular substance suggesting to the chemist several ways in which it might come about.

Coincident with the appearance of this acid reaction, though, as we have said, not the direct cause of it, a large development of carbonic acid takes place when muscle becomes rigid. Irritable living muscular substance like all living protoplasm is continually respiring, continually consuming oxygen and giving out carbonic acid. In the body, the arterial blood going to the muscle gives up some of its oxygen, and gains a quantity of carbonic acid, thus becoming venous as it passes through the muscular capillaries. Even after removal from the body, the living muscle continues to take up from the surrounding atmosphere a certain quantity of oxygen and to give out a certain quantity of carbonic acid.

At the onset of rigor mortis there is a very large and sudden increase in this production of carbonic acid ; in fact an outburst, as it were, of that gas. This is a phenomenon deserving special attention. Knowing that the carbonic acid, which is the outcome of the respiration of the whole body, is the result of the oxidation of carbon-holding substances, we might very naturally suppose that the increased production of carbonic acid attendant on the development of rigor mortis is due to the fact that during that event a certain quantity of the carbon-holding constituents of the muscle is suddenly oxidized. But such a view is negatived by the following facts. In the first place, the increased production of carbonic acid during rigor mortis is not accompanied by any corresponding increase in the consumption of oxygen. In the second place, a muscle (of a frog, for instance) contains in itself no free or loosely attached oxygen: when subjected to the action of a mercurial air-pump it gives off no oxygen to a vacuum, offering in this respect a marked contrast to blood ; and yet, when placed in an atmosphere free from oxygen, it will not only continue to give off carbonic acid while it remains alive, but will also exhibit at the onset of rigor mortis the same increased production of carbonic acid that is shown by a muscle placed in an atmosphere containing oxygen. It is obvious that in such a case the carbonic acid does not arise from the direct oxidation of the muscle substance, for there is no oxygen present *at the time* to carry on that oxidation. We are driven to suppose that during rigor mortis, some complex body, containing in itself ready formed carbonic acid, so to speak, is split up, and thus carbonic acid is set free, the process of oxidation by which that carbonic acid was formed out of the carbon-holding constituents of the muscle having taken place at some anterior date.

Living resting muscle, then, is alkaline or neutral in reaction, and the substance of its fibres contains a coagulable plasma.

Dead, rigid muscle, on the other hand, is acid in reaction, and no longer contains a coagulable plasma, but is laden with the solid myosin. Further, the change from the living, irritable condition to that of rigor mortis is accompanied by a large and sudden development of carbonic acid.

It is found, moreover, that there is a certain amount of parallelism between the intensity of the rigor mortis, the degree of acid reaction, and the quantity of carbonic acid given out. If we suppose, as we fairly may do, that the intensity of the rigidity is dependent on the quantity of myosin deposited in the fibres, and the acid reaction to the development, if not of lactic acid, at least of some other substance, the parallelism between the three products, myosin, acid-producing substance, and carbonic acid, would suggest the idea that all three are the results of the splitting up of the same highly complex substance. But we have not at present succeeded in isolating, or in otherwise definitely proving the existence of such a body, and though the idea seems tempting, it may in the end prove totally erroneous.

We may now return to the question, What are the chemical changes which take place when a living resting muscle enters into a contraction? These changes are most evident after the muscle has been subjected to a prolonged tetanus; but there can be no doubt that the chemical events of a tetanus are, like the physical events, simply the sum of the results of the constituent single contractions.

In the first place, the muscle becomes acid, not so acid as in rigor mortis, but still sufficiently so, after a vigorous tetanus, to turn blue litmus distinctly red. The cause of the acid reaction, like that of rigor mortis, is doubtful; but is in all probability the same in both cases.

In the second place, a considerable quantity of carbonic acid is set free; and the production of carbonic acid in muscular contraction is altogether similar to the production of carbonic acid during rigor mortis. It is not accompanied by any corresponding increase in the consumption of oxygen. This is evident even in a muscle through which the circulation of blood is still going on, for though the blood passing through a contracting muscle gives up more oxygen than the blood passing through a resting muscle, the increase in the amount of oxygen taken up falls below the increase in the carbonic acid given out; but it is still more markedly shown in a muscle removed from the body. For in such a muscle both the contraction and the increase in the production of carbonic acid will go on in the absence of oxygen. A frog's muscle suspended in an atmosphere of nitrogen will remain irritable for some considerable time, and

at each vigorous tetanus an increase in the production of carbonic acid may be readily ascertained.

Moreover, there seems to be a correspondence between the energy of the contraction and the amount of carbonic acid and the degree of acid reaction produced, so that, though we are now treading on somewhat uncertain ground, we are naturally led to the view that the essential chemical process lying at the bottom of a muscular contraction, as of rigor mortis, is the splitting up of some highly complex substance. But here the resemblance between rigor mortis and contraction ends. We have no evidence of the formation during a contraction of any body like myosin. Now the contracted and rigid muscle differ essentially in the fact that while the former, as compared with living resting muscle, increases in extensibility and loses none of its translucency, the latter becomes less extensible, less elastic, and less translucent. Corresponding to this marked difference, we find myosin formed in the rigid muscle, but we cannot find it in the contracted muscle.

The other chemical changes in muscle during a contraction have not yet been clearly made out. Indeed our whole information concerning the other chemical constituents of muscle is at present imperfect.

The bodies which we have called extractives are numerous and varied. Among the nitrogenous crystalline extractives the most important is creatine, which occurs to the extent of about 0.2 to 0.3 per cent., is an invariable constituent of muscle, and is found elsewhere only in nervous tissue, the kidney, and to a slight extent in the blood. As we shall hereafter see, great interest is attached to this body inasmuch as it readily splits up into urea, and sarcosin, and accordingly has been regarded as one, at least, of the antecedents of urea, which body is conspicuous by its absence from muscular tissue. The alkaline creatinin into which creatine is converted by the action of acids, and which appears in the urine, is apparently absent from muscle. The other nitrogenous crystalline bodies, which need not detain us now, are karnin, hypoxanthin (or sarkin), xanthin, inosinic acid, taurin and possibly uric acid.[1]

Fats are present in considerable quantities both in the adipose tissue between the bundles of fibres, and also as constituents of the muscular substance within the sarcolemma.

The peculiar starch-like body, glycogen, of which we shall have to speak more fully in a later part of this work, is especially abundant in the muscles of the embryo at an early period, and besides, is so continually met with in the muscles of the

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[1] See Appendix.

adult that it may fairly be considered as a normal constituent of muscle to a variable extent, possibly from 0.5 to 1 per cent. A dextrin-like body has also been found, and at times glucose or an allied sugar. The cardiac muscular tissue contains the peculiar sugar, inosit.

The ashes of muscle, like those of the red corpuscles, are characterized by the preponderance of potassium salts and of phosphates; these form, in fact, nearly 80 per cent. of the whole ash.

The general composition of human muscle is shown in the following table of von Bibra.

Water		744.5
Solids		
Myosin and other matters, elastic elements, etc., insoluble in water	155 4	
Soluble proteids	19 3	
Gelatin	20.7	
Extractives and salts	37.1	
Fats	23.0	
		255.5

Concerning the functional importance of these various bodies, we have very little exact knowledge.

Helmholtz showed long ago that the effect of long-continued contraction is to diminish the substances in muscle which are soluble in water, but to increase those which are soluble in alcohol. In other words, during contraction some substance or substances soluble in water are converted into another or other substances insoluble in water but soluble in alcohol. During or after rigor mortis, glycogen is converted into sugar, and it has been contended that a similar change takes place during contraction; but we are not, at present at all events, in a position to affirm that such a conversion is a necessary and integral part of the chemical transformations which lie at the bottom of a muscular contraction.

We shall have occasion to treat more fully and from a different point of view, of the relations between muscular exercise and the quantity of urea discharged by the kidneys. Meanwhile we may state that not only does this all-important nitrogenous crystalline body appear to be absent from normal muscle, both during rest and after contraction, but we have as yet no adequate evidence that the contraction of a muscle is followed by the appearance in the substance of the muscle or in the blood passing through it of any new nitrogenous product, or by any increase in any of the nitrogenous extractives which we have mentioned as normally present in muscle. In fact, all we know at present is that a contraction is followed by an increase in the discharge of carbonic

acid, and by certain changes which lead to an acid reaction. Beyond this we are in the dark.

Thermal Changes.

The view, however, that chemical changes lie at the bottom of a muscular contraction, that the energy which takes on the form of muscular work arises from a metabolism of the muscular substance, is supported by a variety of considerations, and especially perhaps by the fact, that the development of energy as muscular work is accompanied by a development of energy as heat.

Though we shall have hereafter to treat this subject more fully, the leading facts may be given here. Whenever a muscle contracts, its temperature rises, indicating that heat is given out. When a mercury thermometer is plunged into a mass of muscles, such as those of the thigh of the dog, a rise of the mercury is observed upon the muscles being thrown into a prolonged contraction. More exact results, however, are obtained by means of a thermopile, by the help of which the rise of temperature caused by a few repeated single contractions, or indeed by a single contraction, may be observed and the amount of heat given out approximatively measured.

The thermopile may consist either of a single junction in the form of a needle plunged into the substance of the muscle ; or of several junctions either in the shape of a flat surface carefully opposed to the surface of muscle (Heidenhain), the pile being balanced so as to move with the contracting muscle, and thus to keep the contact exact ; or in the shape of a thin wedge (Fick), the edge of which, comprising the actual junctions, is thrust into a mass of muscles and held in position by them. In all cases the fellow junction or junctions must be kept at a constant temperature.

Fick calculated that the greatest heat given out by the muscles of the thigh of a frog in a single contraction was 3.1 micro-units of heat[1] for a gramme of muscle, the result being obtained by dividing by five the total amount of heat given out in five successive single contractions. It will, however, be safer to regard these figures as illustrative of the fact that the heat given out is considerable rather than as data for elaborate calculations. Moreover, we have no satisfactory quantitative determinations of the heat given out by the muscles of warm-blooded animals, though there can be no doubt that it is much greater than that given out by the muscles of the frog.

There can hardly be any doubt that the heat thus set free is the product of chemical changes within the muscle, changes which,

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[1] The micro-unit being a milligramme of water raised one degree Centigrade.

though they cannot for the reasons given above be regarded as simple and direct oxidations, may be spoken of in general terms as a combustion.   So that the muscle may be likened to a steam-engine, in which the combustion of a certain amount of material gives rise to the development of energy in two forms, as heat and as movement, there being certain quantitative relations between the amount of energy set free as heat and that giving rise to movement.   We must, however, carefully guard ourselves against pressing this analogy too closely.   In the steam-engine, we can distinguish clearly between the fuel which, through its combustion, is the sole source of energy, and the machinery, which is not consumed to provide energy and only suffers wear and tear.   In the muscle we can make no such distinction ; though the whole matter is not fully worked out, we have reason to think that the muscular fibre is not to be regarded as a machine which takes, so to speak, a charge of certain substances from the blood, and by inducing an explosion of these substances in itself gives rise to the energy of heat and movement.   On the contrary, the evidence goes to show that it is the living contractile substance as a whole which is continually breaking down in an explosive decomposition and as continually building itself up again out of the material supplied by the blood.   In a steam-engine only a certain amount of the total potential energy of the fuel issues as work, the rest being lost as heat, the proportion varying, but the work rarely exceeding one-tenth of the total energy.   In the case of the muscle, we are not at present in a position to draw up an exact equation between the latent energy on the one hand and the two forms of actual energy on the other.   We have reason to think that the proportion between heat and work varies considerably under different circumstances, the work sometimes rising as high as one-fourth, sometimes possibly sinking as low as one-twenty-fourth of the total energy, and observations seem to show that the greater the resistance which the muscle has to overcome, the larger the proportion of the total energy expended which goes out as work done.   The muscle, in fact, seems to be so far self-regulating that the more work it has to do, the greater, within certain limits, is the economy with which it works.

Lastly, it must be remembered that the giving out of heat by the muscle is not confined to the occasions when it is actually contracting.   When, at a later period, we treat of the heat of the body generally, evidence will be brought forward that the muscles even when at rest are giving rise to heat, so that the heat given out at a contraction is not some wholly new phenomenon, but a temporary exaggeration of what is going on continually at a more feeble rate.

The Changes in a Nerve during the Passage of a Nervous Impulse.

The change in the form of a muscle during its contraction is a thing which can be seen and felt; but the changes in a nerve during its activity are invisible and impalpable. We stimulate one end of a nerve, and since we see this followed by a contraction of the muscle attached to the other end, we know that some changes or other, constituting a nervous impulse, have been propagated along the nerve; but these are changes which we cannot see. Nor have we satisfactory evidence of any chemical events or of any production of heat accompanying a nervous impulse. We may fairly suppose that *some* chemical changes form the basis of a nervous impulse, and that these changes set free a certain amount of heat; but these, if they occur, are too slight to be recognized satisfactorily by the means at present at our disposal. In fact, beyond the terminal results, such as a muscular contraction in the case of a nerve going to a muscle, or some affection of the central nervous system in the case of a nerve still in connection with its nervous centre, there is one event and one event only which we are able to recognize as the objective token of a nervous impulse, and that is the so-called negative variation of the nerve-current. For a piece of nerve removed from the body exhibits nearly the same electric phenomena as a piece of muscle. It has an equator which is electrically positive as compared to its two cut ends. In fact, the diagram Fig. 22, and the description which it was used on p. 88 to illustrate, may be applied to nerve as well as to muscle, except that the currents are in all cases much more feeble in the case of nerves than of muscles, and the special currents from the circumference to the centre of the transverse sections cannot well be shown in a slender nerve; indeed, it is doubtful if they exist at all.

During the passage of a nervous impulse, the " natural nerve-current" undergoes a negative variation, just as the "natural muscle-current" undergoes a negative variation during a contraction. There are, however, difficulties in the case of the nerve similar to those in the case of the muscle, concerning the pre-existence of any such "natural" currents. It is maintained by many, that a nerve in an absolutely natural condition is like a muscle—isoelectric; hence we may say, that in a nerve during the passage of a nervous impulse, as in a muscle during a muscular contraction, a " current of action " is developed.

This "current of action," or "negative variation,' may be shown either by the galvanometer or by the rheoscopic frog. If the nerve of the " muscle-nerve preparation " *B* (see p. 92) be

placed in an appropriate manner on a thoroughly irritable nerve (*A*) (to which, of course, no muscle need be attached)—*i. e.*, touching, say, the equator and one end of the nerve, then single induction-shocks sent into the far end of *A* will cause single spasms in the muscle of *B*, while tetanization of *A*—*i. e.*, rapidly repeated shocks sent into *A*, will cause tetanus of the muscle of *B*.

That this current, whether it be regarded as an independent "current of action," or as a negative variation of a "preëxisting" current, is an essential feature of a nervous impulse, is shown by the fact that the degree or intensity of the one varies with that of the other. They both travel, too, at the same rate. In describing the muscle-curve, and the method of measuring the muscular latent period, we have incidentally shown (p. 76) how the velocity of the nervous impulse is measured also, and stated that the rate in the nerves of a frog is about 28 metres a second. Bernstein, by means of a special and somewhat complicated apparatus finds that the current of action travels along an isolated piece of nerve at the same rate. He also finds that it, like the molecular change in a muscle preceding the contraction, and, indeed, like the contraction itself, passes over any given spot of the nerve in the form of a wave, rising rapidly to a maximum and then more gradually declining again. He has been able to measure the length of the wave, and this he finds to be about 18 mm., taking 0.0007 second to pass over any one point.

When an isolated piece of nerve is stimulated in the middle, the current of action is propagated equally well in both directions, and that whether the nerve be a chiefly sensory or a chiefly motor nerve, or, indeed, if it be a nerve-root composed exclusively of motor or of sensory fibres. Taking the current of action as the token of a nervous impulse, we infer from this that when a nerve-fibre is stimulated artificially at any part of its course, the nervous impulse set going travels in both directions.

We used just now the phrase "tetanization of a nerve," meaning the application to a nerve of rapidly repeated shocks such as would produce tetanus in the muscle to which the nerve was attached, and we shall have frequent occasion to employ the phrase. It will, however, of course, be understood that there is in the nerve, as far as we know, no summation of nervous impulses comparable to the summation of muscular contractions. The matter, perhaps, needs fuller investigation; but, as far as we know at present, we may say that the series of shocks sent in at the far end of the nerve start a series of impulses; these travel down the nerve and reach the muscle as a series of distinct impulses; and the first changes in the muscle, the molecular latent-period changes, also form a series the members of which are

distinct. It is not until these molecular changes become transformed into visible changes of form that any fusion or summation takes place.

Putting together the facts contained in this and the preceding sections, the following may be taken as a brief approximate history of what takes place in a muscle and nerve when the latter is subjected to a single induction-shock. At the instant that the induced current passes into the nerve, changes occur, of whose nature we know nothing certain except that they cause a " current of action," or " negative variation of the natural " nerve-current. These changes propagate themselves along the nerve in both directions as a nervous impulse in the form of a wave, having a wave-length of about 18 mm., and a velocity (in frog's nerve) of about 28 m. per second. Passing down the nerve-fibres to the muscle, flowing along the branching and narrowing tracts, the wave at last breaks on the end-plates of the fibres of the muscle. Here it is transmuted into a muscle-impulse, with a shorter, steeper wave, and a greatly diminished velocity (about 3 m. per second). This muscle-impulse, of which we know hardly more than that it is marked by a current of action, travels from each end-plate in both directions to the end of the fibre, where it appears to be lost—at all events, we do not know what becomes of it. As it leaves the end-plate it is followed by an explosive decomposition of material, leading to a discharge of carbonic acid, to the appearance of some substance or substances with an acid reaction, and probably of other unknown things, with a considerable development of heat. This explosive decomposition gives rise to the visible contraction-wave, which travels behind the invisible muscle-impulse at about the same rate, but with a vastly increased wave-length. The fibre, as the wave passes over it, swells and shortens, bringing its two ends nearer together, its molecules during the change of form arranging themselves in such a way that the extensibility of the fibre is increased.

SEC. 3.—THE NATURE OF THE CHANGES THROUGH WHICH AN ELECTRIC CURRENT IS ABLE TO GENERATE A NERVOUS IMPULSE.

Action of the Constant Current.

In the preceding account, the stimulus applied in order to give rise to a nervous impulse has always been supposed to be an induction-shock, single or repeated. This choice of stimulus has been made on account of the almost momentary duration of the induced current. Had we used a current lasting for some con-

siderable time, the problems before us would have become more complex in consequence of our having to distinguish between the events taking place while the current was passing through the nerve from those which occurred at the moment when the current was thrown into the nerve or at the moment when it was shut off from the nerve. These complications do arise when, instead of employing the induced current as a stimulus, we use *a constant current*—*i. e.*, when we pass through the nerve (or muscle) a current direct from the battery without the intervention of any induction-coil.

Before making the actual experiment, we might, perhaps. naturally suppose that the constant current would act as a stimulus throughout the whole time during which it was applied—that, so long as the current passed along the nerve, nervous impulses would be generated, and thus the muscle thrown into something at all events like tetanus. And under certain conditions this does take place ; occasionally it happens that at the moment the current is thrown into the nerve, the muscle of the muscle-nerve preparation falls into a tetanus which is continued until the current is shut off. But such a result is exceptional. In the vast majority of cases, what happens is as follows. At the moment that the circuit is made—the moment that the current is thrown into the nerve—a single spasm, a simple contraction, the so-called *making contraction*, is witnessed ; but after this has passed away the muscle remains absolutely quiescent in spite of the current continuing to pass through the nerve, and this quiescence is maintained until the circuit is broken—until the current is shut off from the nerve—when another simple contraction, the so-called *breaking contraction*, is observed. The mere passage of a constant current of uniform intensity through a nerve does not, under ordinary circumstances, act as a stimulus generating a nervous impulse ; such an impulse is only set up when the current either falls into or is shut off from the nerve. It is the entrance or the exit of the current, and not the continuance of the current, which is the stimulus.

The quiescence of the nerve and muscle during the passage of the current is, however, dependent on the current remaining uniform in intensity, or at least not being suddenly increased or diminished. Any sufficiently sudden and large increase or diminution of the intensity of the current, will act like the entrance or exit of a current ; and, by generating nervous impulses, give rise to contractions. If the intensity of the current, however, be very slowly and gradually increased or diminished, a very wide range of intensity may be passed through without any contraction being seen. It is the sudden change from one condition to

another, and not the condition itself, which causes the nervous impulse.

In many cases, both a "making" and a "breaking" contraction, each a simple spasm, are observed, and this is perhaps the commonest event; but when the current is very weak, and again when the current is very strong, either the breaking or the making contraction may be absent—*i. e.*, there may be a contraction only when the current is thrown into the nerve, or only when it is shut off from the nerve.

Under ordinary circumstances, the contractions witnessed with the constant current either at the make or at the break, are of the nature of a "simple" contraction; but, as has already been said, the application of the current may give rise to a very pronounced tetanus. Such a tetanus is seen sometimes when the current is made, lasting during the application of the current, sometimes when the current is broken, lasting some time after the current has been wholly removed from the nerve. The former is spoken of as a "making," the latter as a "breaking," tetanus. But these exceptional results of the constant current need not detain us now.

The great interest attached to the action of the constant current lies in the fact, that *during* the passage of the current, in spite of the absence of all nervous impulses, and therefore of all muscular contractions, the nerve is for the time both between and on each side of the electrodes profoundly modified in a most peculiar manner. This modification, important both for the light it throws on the generation of nervous impulses and for its practical applications, is known under the name of electrotonus.

Electrotonus.—The marked feature of the electrotonic condition is that the nerve, though apparently quiescent, is changed in respect to its irritability; and that in a different way in the neighborhood of the two electrodes respectively.

Suppose that on the nerve of a muscle-nerve preparation are placed two (non-polarizable) electrodes (Fig. 23, a, k) connected with a battery and arranged with a key, so that a constant current can at pleasure be thrown into or shut off from the nerve. This constant current, whose effects we are about to study, may be called the "polarizing current." Let a be the positive electrode or anode, and k the negative electrode or kathode, both placed at some distance from the muscle, and also with a certain interval between each other. At the point x let there be applied a pair of electrodes connected with an induction-machine. Let the muscle further be connected with a lever, so that its contractions can be recorded, and their amount measured. Before the polarizing current is thrown into the nerve, let a single induction-

shock of known intensity (a weak one being chosen, or at least not one which would cause in the muscle a maximum contraction) be thrown in at x. A contraction of a certain amount will follow. That contraction may be taken as a measure of the irritability of the nerve at the point x. Now let the polarizing current be thrown in, and let the direction of the current be a *descending* one, with the kathode or negative pole nearest the muscle, as in Fig. 23 (*A*). If while the current is passing, the same induction-

FIG. 23.
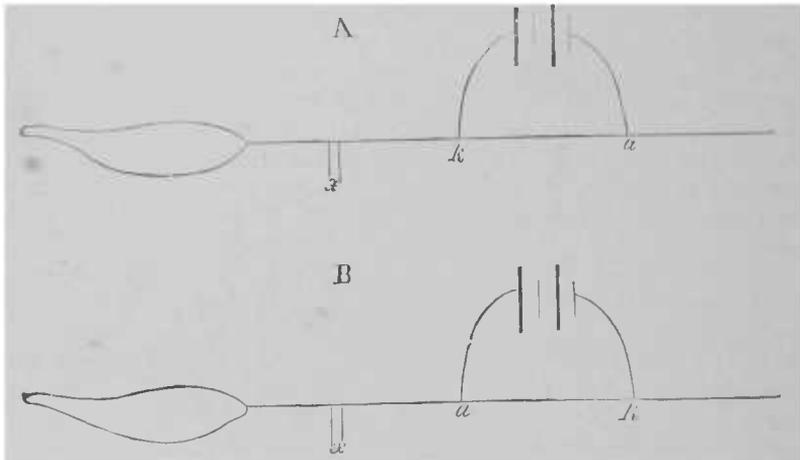
MUSCLE-NERVE PREPARATIONS, with the nerve exposed in *A* to a *descending* and in *B* to an *ascending* constant current.

In each a is the anode, k the kathode of the constant current. x represents the spot where the induction-shocks used to test the irritability of the nerve are sent in.

shock as before be sent through x, the contraction which results will be found to be greater than on the former occasion. If the polarizing current be shut off, and the point x after a short interval again tested with the same induction-shock, the contraction will be no longer greater, but of the same amount, or perhaps not so great, as at first. During the passage of the polarizing current, therefore, the irritability of the nerve at the point x has been temporarily *increased*, since the same shock applied to it causes a greater contraction during the presence than in the absence of the current. But this is only true so long as the polarizing current is a descending one, so long as the point x lies on the side of the kathode. On the other hand, if the polarizing current had been an *ascending* one, with the anode or positive pole nearest the muscle, as in Fig. 23 (*B*), the irritability of the nerve at x would have been found to be *diminished* instead of increased by the polarizing current. That is to say, when a

constant current is applied to a nerve, the irritability of the nerve between the polarizing electrodes and the muscle is, during the passage of the current, increased when the kathode is nearest the muscle (and the polarizing current descending), and diminished when the anode is nearest the muscle (and the polarizing current ascending). Conversely, on the far side of the polarizing electrodes, the irritability, at least with certain strengths of current, is increased with an ascending and diminished with a descending polarizing current. Hence it may be stated generally that during the passage of a constant current through a nerve the irritability of the nerve is increased in the region of the kathode, and diminished in the region of the anode. The changes in the nerve which give rise to this increase of irritability in the region of the kathode are spoken of as *katelectrotonus*, and the nerve is said to be in a katelectrotonic condition. Similarly the changes in the region of the anode are spoken of as *anelectrotonus*, and the nerve is said to be in an anelectrotonic condition. It is also often usual to speak of the katelectrotonic increase, and anelectrotonic decrease of irritability.

This law remains true, whatever be the mode adopted for determining the irritability. The result holds good not only with a single induction-shock, but also with a tetanizing interrupted current, with chemical and with mechanical stimuli. It further appears to hold good not only in a dissected nerve-muscle preparation, but also in the intact nerves of the living body. The increase and decrease of irritability are most marked in the immediate neighborhood of the electrodes, but spread for a considerable distance in either direction in the extrapolar regions. The same modification is not confined to the extrapolar region, but exists also in the intrapolar region. In the intrapolar region there must be, of course, an indifferent point, where the katelectrotonic increase merges into the anelectrotonic decrease, and where, therefore, the irritability is unchanged. When the polarizing current is a weak one, this indifferent point is nearer the anode than the kathode, but as the polarizing current increases in intensity, draws nearer and nearer the kathode (see Fig. 24).

The amount of increase and decrease is dependent: (1) On the strength of the current, the stronger current up to a certain limit producing the greater effect. (2) On the irritability of the nerve, the more irritable, better conditioned nerve being the more affected by a current of the same intensity.

In the experiments just described the increase or decrease of irritability is taken to mean that the same stimulus starts in the one case a larger or more powerful, and in the other case a smaller or less energetic impulse, but we have reason to think that the mere propagation or conduction of impulses started

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elsewhere is affected by the electrotonic condition. At all events, an electrotonus appears to offer an obstacle to the passage of a nervous impulse.

These variations of irritability at the kathode and anode respectively must be the result of molecular changes, brought about by the action of the constant current. They are interesting theoretically because they show that the generation of a nervous impulse as the result of the making or breaking of a constant current is dependent on the change of a nerve from its normal condition into either katelectrotonus or anelectrotonus, or back again from one of these phases into its normal condition. And certain results as to the occurrence or absence of a contraction at the make or at the break, according as the current is strong or weak, ascending or descending (results which need not detain us here, but which have been formulated as the so-called " law of contraction "), go far to show that a nervous
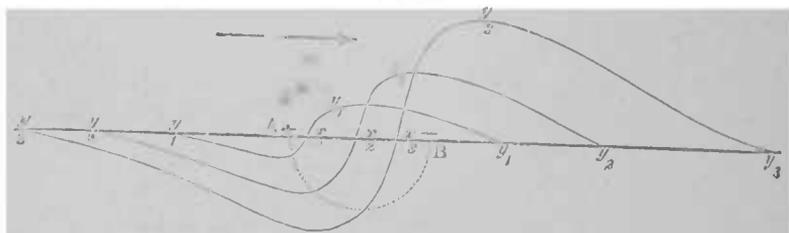
DIAGRAM ILLUSTRATING THE VARIATIONS OF IRRITABILITY DURING ELECTROTONUS, WITH POLARIZING CURRENTS OF INCREASING INTENSITY.   (FROM PFLÜGER.)

The anode is supposed to be placed at A, the kathode at B; AB is consequently the intrapolar district. In each of the three curves, the portion of the curve below the base-line represents diminished irritability, that above, increased irritability. y_1 represents the effect of a weak current ; the indifferent point, x_1, is the anode, A. In y_2, a stronger current, the indifferent point, x_2, is nearer the kathode, B, the diminution of irritability in anelectrotonus and the increase in katelectrotonus being greater than in y_1 ; the effect also spreads for a greater distance along the extrapolar regions in both directions. In y_3 the same events are seen to be still more marked.

impulse is generated only when a nerve passes suddenly from a normal condition into the phase of katelectrotonus (making contraction) or returns from the phase of anelectrotonus to a normal condition (breaking contraction) ; in other words, when it passes suddenly from a phase of lower to a phase of higher irritability.

The phenomena of electrotonus are also interesting practically, inasmuch as they show that in the constant current appropriately applied we have the means of changing at will the irritability of this or that nerve, decreasing it when we wish to lessen pain or spasm, increasing it when we wish to heighten sensibility or muscular action. For the increase or decrease is

observed in the case of nervous impulses passing towards the central nervous system as well as in those passing to muscles.

Electrotonic Currents.—During the passage of a constant current through a nerve, variations in the electric currents of the nerve analogous in some respects to the variations of the irritability of the nerve may be witnessed. Thus if a constant current supplied by the battery P (Fig. 25), be applied to a piece of nerve by means of two non-polarizable electrodes, p, p', the "currents of rest" obtainable from various points of the nerve will be different during the passage of the polarizing current from those which were manifest before or after the current was applied; and, moreover, the changes in the nerve-currents produced by the polarizing current will not be the same in the neighborhood of the anode, p, as those in the neighborhood of the kathode, p'. Thus let G and H be two galvanometers so connected with the two ends of the nerve as to obtain good and clear evidence of the "currents of rest." Before the polarizing current is thrown into the nerve, the needle H will occupy a position indicating the passage of a current of a certain intensity from h to h', through the galvanometer (from the positive longitudinal surface to the negative cut end of the nerve), the circuit being completed by a current *in* the nerve from h' to h—*i. e.*, the current will flow in the direction of the arrow. Similarly the needle of G will by its deflection indicate the existence of a current flowing from g to g' through the galvanometer, and from g' to g through the nerve, in the direction of the arrow.

At the instant that the polarizing current is thrown into the nerve at pp', the currents at gg', hh' will suffer a "current of action" corresponding to the nervous impulse, which, at the making of the polarizing current, passes in both directions along the nerve, and may cause a contraction of the attached muscle. The current of action is, as we have seen, of extremely short duration, it is over and gone in a small fraction of a second. It, therefore, must not be confounded with a permanent effect which in the case we are dealing with, is observed in both galvanometers. This effect, which is dependent on the direction of the polarizing current, is as follows: Supposing that the polarizing current is flowing in the direction of the arrow in the figure, that is, passes in the nerve from the positive electrode or anode, p, to the negative electrode or kathode, p', it is found that the current through the galvanometer, G, is increased, while that through H is diminished. We may explain this result by saying that the polarizing current has caused the appearance in the nerve outside the electrodes of a new current, the "electrotonic" current, having the same direction as itself, which adds to or takes away from the natural nerve-current or "current of rest" according as it is flowing in the same or in an opposite direction.

The strength of the electrotonic current is dependent on the strength of the polarizing current, and on the length of the intrapolar region which is exposed to the polarizing current. When a strong polarizing current is used, the electromotive force of the electrotonic current may be much greater than that of the natural nerve-current.

The strength of the electrotonic current varies with the irritability, or vital condition of the nerve, being greater with the more irritable nerve; and a dead nerve will not manifest electrotonic currents. Moreover, the propagation of the current is stopped by a ligature, or by crushing the nerve.

We may speak of the conditions which give rise to this electrotonic current as a *physical* electrotonus analogous to that *physiological* electro-

tonus which is made known by variations in irritability.   The physical
electrotonic current is probably due to the escape of the polarizing current
along the nerve under the peculiar conditions of the living nerve; but
we must not attempt to enter here into this disputed and difficult subject,
or into the allied question as to the exact connection between the physical
and the physiological electrotonus, though there can be little doubt that
the latter is dependent on the former.

FIG. 25.
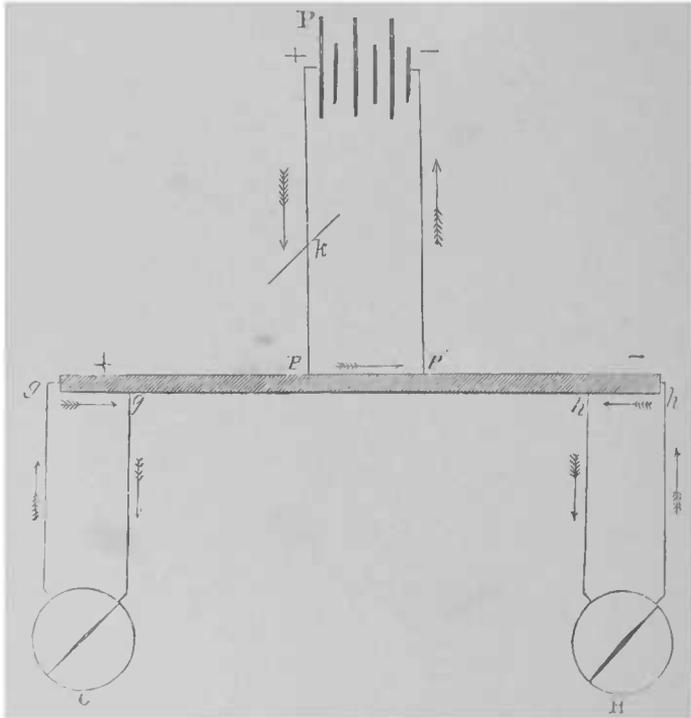
DIAGRAM ILLUSTRATING ELECTROTONIC CURRENTS.

P the polarizing battery, with *k* a key, *p* the anode, and *p′* the kathode.   At the left end of
the piece of nerve the natural current flows through the galvanometer *G* from *g* to *g′*, in the
direction of the arrows; its direction, therefore, is the same as that of the polarizing current;
consequently it appears increased, as indicated by the sign +.   The current at the other end
of the piece of nerve, from *h* to *h′*, through the galvanometer *H*, flows in a contrary direction
to the polarizing current; it consequently appears to be diminished, as indicated by the
sign —.

N. B.—For simplicity's sake, the polarizing current is here supposed to be thrown in at the
middle of a piece of nerve, and the galvanometer placed at the two ends.   Of course, it will be
understood that the former may be thrown in anywhere, and the latter connected with any
two pairs of points which will give currents.

An induction-shock is a current of very short duration, de-
veloped very suddenly and disappearing more gradually.   Hence,

when it falls into a nerve, the nerve undergoes sudden transition from its normal condition to the katelectrotonic phase, and, consequently, a nervous impulse giving rise to a contraction is the result. The return from the anelectrotonic phase to the normal condition appears, from a number of considerations, to be less effective as a generator of nervous impulses than the change from the normal condition to the katelectrotonic phase. Hence in the induced current we have to deal with a "making" contraction only, the breaking contraction being absent. This is true whether the induced current be generated by the making or by the breaking of a constant current.

The constant current applied directly to a muscle from which the purely nervous element has been eliminated by urari poisoning, has effects similar to and yet somewhat different from those which it has upon a nerve. The efficacy of the rise of katelectrotonus and the fall of anelectrotonus respectively in producing contraction is the same as in a nerve. In one respect the muscle is more striking, and offers a support of the hypothesis mentioned above. The making contraction may, under favorable circumstances, be seen to start from the kathode, and the breaking contraction from the anode. Besides the make and break spasm, a partial tetanus during the whole time of the passage of the current through a muscle is very often seen. Another marked difference between muscle and nerve, is that in muscle the current must act for a much longer time upon the tissue before it can call forth a contraction. This is what we might expect from the more sluggish nature of the muscular impulse-wave. Hence, muscular tissue which has lost its nervous elements, or does not possess them, is far less readily affected by the almost momentary induction-shocks than are nerves.

Sec. 4.—The Muscle-nerve Preparation as a Machine.

The facts described in the foregoing sections show that a muscle with its nerve may be justly regarded as a machine which, when stimulated, will do a certain amount of work. But the actual amount of work which a muscle-nerve preparation will do is found to depend on a large number of circumstances, and consequently to vary within very wide limits. These variations will be largely determined by the condition of the muscle and nerve in respect to their nutrition; in other words, by the degree of irritability manifested by the muscle or by the nerve, or by both. But, quite apart from the general influences affecting its nutrition, and thus its irritability, a muscle-nerve preparation is affected as regards the amount of its work by a variety of other

circumstances, which we may briefly consider here, reserving to a succeeding section the study of variations in irritability.

The nature and mode of application of the stimulus as affecting the amount and character of the contraction.

We have seen that a nervous impulse is a molecular disturbance travelling along the nerve in the form of a wave. We saw further, that the velocity with which this wave travels is in the frog about 28 metres per second, and in the mammal somewhat higher; but that it varies according to circumstances, being especially dependent on temperature. The wave-length—that is the total length of nerve along which the disturbance is at any one instant taking place, from the point nearer the muscle which the disturbance has just reached, to the point further from the muscle which the disturbance has just left, may, we have seen be put down (in the frog) as 18 mm.; but possibly this, too, varies somewhat. The greatest and most important variations, however, are those of the energy of the nervous impulse, of the amount of disturbance which takes place in the nerve or in the nerve-fibre as the wave of the nervous impulse passes over it this we might designate as the height of the wave. Thus, a weak stimulus gives rise to a small disturbance—that is, a weak nervous impulse; and a strong stimulus gives rise to a large disturbance—that is, a powerful nervous impulse.

We are not in a position at present to speak definitely as to the occurrence of other differences in the characters of nervous impulses. As far as we know at present, nervous impulses, whatever their origin, are alike in nature;[1] the impulses generated in a natural way, by the brain or spinal cord, or produced artificially by mechanical stimuli, as by cutting or pinching, or by thermal stimuli, as by touching the nerve with a red-hot wire, or by chemical stimuli, or by electrical stimuli, may differ in intensity, and in the rapidity with which they succeed each other, but as far as we know at present, not otherwise. Thus, a drop of acid placed on a nerve gives rise to tetanus in the muscle, which differs from the tetanus produced by repeated induction-shock applied to the nerve, only so far as the tetanus is generally irregular, the individual nervous impulses generated by the acid forming an irregular series, not following each other at equal intervals, and not being all of the same intensity, whereas the impulses generated by the "interrupted current" are generally

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[1] It will be observed, that we are speaking now exclusively of the nerve of a muscle-nerve preparation—*i. e.*, of what we shall hereafter term a motor nerve. Whether sensory impulses differ essentially from motor impulses will be considered later on.

of the same intensity, and follow each other at equal intervals. So, also, we are led at present to believe that when muscles are thrown into action in a natural way in the living body by the agency of the spinal cord, what goes on in the nerve differs from what goes on in the same nerve when the interrupted current is brought to bear on it, only in so far as in the former case the impulses follow each other at a fixed rate (nineteen a second), whereas in the latter, the rate of repetition varies according to the rapidity with which in the induction-machine the shocks follow each other ; the individual impulses, as far as we know at present, have the same characters in the two cases, save only that they may differ in intensity.

Supposing that the irritability of a nerve-muscle preparation remains for the period of the experiment fairly constant, care being taken to avoid the effects of exhaustion, and that the stimulus be applied to the same part of the nerve, we find that the intensity of the nervous impulse generated (as measured by the muscular contraction) varies up to a certain limit, according to what we may call the strength of the stimulus. Thus, taking a single induction-shock as the most manageable stimulus, we find that if, before we begin, we slide the secondary coil (Fig. 11, *sc.*) a certain distance from the primary coil *pr. c.*, no visible effect at all follows upon the discharge of the induction-shocks. The passage of the momentary weak current is either unable to produce any nervous impulse at all, or the weak nervous impulse to which it gives rise is unable to stir the sluggish muscular substance to a visible contraction. As we slide the secondary coil towards the primary, sending in an induction-shock at each new position, we find that at a certain distance between the secondary and primary coils, the muscle responds to each induction-shock[1] with a contraction which makes itself visible by the slightest possible rise of the attached lever. This position of the coils, the battery remaining the same and other things being equal, marks the *minimal* stimulus giving rise to the minimal contraction. As the secondary coil is brought nearer to the primary, the con-tractions increase in height corresponding to the increase in the intensity of the stimulus. Very soon, however, an increase in the stimulus caused by continuing to slide the secondary coil over the primary fails to cause any increase in the contraction. This indicates that the *maximal* stimulus giving rise to the maximal contraction has been reached ; though the shocks increase in intensity as the secondary coil is pushed further and further over the primary, the contractions remain of the same height, until

[1] In these experiments either the breaking or making shock must be used, not sometimes one and sometimes the other, for the two kinds of shock differ in efficiency, the breaking being the most potent.

fatigue lowers them.   Sometimes, however, after the contraction
have for some time remained of the same height, in spite of th
stimulus, at each fresh stimulation, being increased in strength
a point is reached at which, with a further increase in the strengt
of the stimulus, a new increase of contraction sets in ; but we mus
not attempt to explain here this paradoxical *super-maximal* con
traction, as it is called.

With single induction-shocks then the muscular contraction—
and, by inference, the nervous impulse—increases with an in
crease in the intensity of the stimulus, between the limits of th
minimal and maximal stimuli ; and this dependence of th
nervous impulse, and so of the contraction, on the strength of th
stimulus, may be observed not only in electric, but in all kind
of stimuli.

It may here be remarked, that in order for a stimulus to b
effective, a certain abruptness in its action is necessary.   Thus
we have seen that the constant current, when it is passing throug
a nerve with uniform intensity, does not give rise to a nervou
impulse, and that it may be increased or diminished to almos
any extent without generating nervous impulses, provided tha
the change be made gradually enough ; it is only when there i
a sudden change that the current becomes effective as a stimulus
The current which is induced in the secondary coil of an induc
tion-machine, at the breaking of the primary circuit, is mor
rapidly developed, and has a steeper rise than the current whic
appears when the primary circuit is made ; and, accordingly, w
find that the breaking induction-shock is more potent as a stimulu
than the making shock.   Similarly, a sharp tap on a nerve wi
produce a contraction, when a gradually increasing pressure wi
fail to do so ; and, in general, the efficiency of a stimulus of an
kind will depend in part on the suddenness or abruptness of it
action.

A stimulus, in order that it may be effective, must have a
action of a certain duration, the time necessary to produce a
effect varying according to its strength, and being different i
nerve from what it is in muscle.   It would appear that an electri
current applied to a nerve must have a duration of at least abou
0.0015 second to cause any contraction at all, and needs longe
than this to produce its full effect.   When the current is applie
directly to a muscle, whose nervous elements are placed *hors c
combat* by the action of urari, or by degeneration of the nerv
fibres, this period of necessary duration seems to be still longe
and to be especially increased by deficient nutrition.   And th
may be offered as an explanation of the well-known clinical fac
that in various cases of paralysis, muscles which have, by deger
eration of their nerves, lost their nervous supply, more readil

respond to the break and make of the constant current than to induction-shocks, the duration of the former as stimuli being much greater than that of the latter.

In the case of electric stimuli, the strength of the contraction—and, by inference, of the nervous impulse—depends on the manner in which the current flows into the nerve. Though the matter has been disputed, it appears that the current must pass along some appreciable length of nerve-fibre in order to produce an effect; a current which passes through a nerve in an absolutely transverse direction being powerless to generate impulses; and, further, there is a connection between the efficiency of the current and the angle at which it falls into the nerve.

It would also appear—at all events up to certain limits, and as a general rule—that the longer the piece of nerve through which the current passes, the greater is the effect of the stimulus.

When two pairs of electrodes are placed on the nerve of a long and perfectly fresh and successful nerve-preparation, one near to the cut end, and the other nearer the muscle, it is found that the same stimulus produces a greater contraction when applied through the former pair of electrodes than through the latter. Two interpretations of this result are possible. Either the nerve at the part further away from the muscle is more irritable—*i. e.*, that the stimulus gives rise *at the spot stimulated* to a larger nervous impulse; or the impulse started at the further electrodes gathers strength, like an avalanche, in its progress to the muscle. The latter view has been strongly urged by Pflüger, and is generally known under the name of the "avalanche theory." Against it may be urged that, as far as we know, the progress of the current of action along a nerve is marked by no such increase. It is probable, that the larger contraction produced by stimulation of the portions of the nerve near the spinal cord is due to the stimulus setting free a larger impulse—*i. e.*, to this part of the nerve being more irritable. It is possible that the irritability of a nerve may vary considerably at different points of its course.

We have in a preceding section discussed at length the manner in which a stimulus repeated sufficiently rapidly produces a complete and uniform tetanus, during which the constituent single contractions cannot be recognized either by the appearance of the muscle itself or by any features in the curve which it may be made to describe, though the "muscular sound" shows that the muscle is really in a state of vibration. If the frequency of the stimulus be reduced, the tetanus becomes incomplete, and a flickering of the muscle becomes obvious; and upon further reduction of the frequency, the flickering gives place to a rhythmic series of single contractions. Since the height to which the lever is raised—*i. e.*, the amount of total shortening resulting from any

second contraction—is greater when that contraction starts from
the summit of the preceding curve than when it starts from the
decline, it is obvious that the amount of total contraction will, up
to a certain limit, increase with the frequency of repetition of the
stimulus. Thus a stimulus repeated rapidly will produce a teta-
nus, shortening the muscle and raising the weight to a greater
extent than will the same stimulus less rapidly repeated. The
exact frequency of repetition required to produce complete teta-
nus varies according to the condition of the muscle, and is not
the same for all muscles, being dependent on the rapidity with
which the muscle executes each single contraction. In those
animals which possess two kinds of skeletal muscles, red and pale,
the red muscles the single contractions of which are slow and
long-drawn) are thrown into complete tetanus with a repetition
of much less frequency than that required for the pale muscles.
Thus, ten stimuli in a second are quite sufficient to throw the red
muscles of the rabbit into complete tetanus, while the pale mus-
cles require at least twenty stimuli in a second.

When the stimulus is repeated more frequently than is re-
quired to bring about a complete tetanus, the constituent con-
tractions are still proportionately increased in frequency. This
is shown by the increased pitch of the muscular sound. How
far the increase in the frequency of the constituent contractions
can be carried by increasing the frequency of the stimulus, is a
question which presents considerable difficulties, and cannot be
discussed here.

*The value of the muscle as a machine is also in part dependent
on the load.* It might be imagined that a muscle, which, when
loaded with a given weight, and stimulated by a current of a given
intensity, had contracted to a certain extent, would only contract
to half that extent when loaded with twice the weight and stimu-
lated with the same stimulus. Such, however, is not the case; the
height to which the weight is raised may be in the second instance
as great, or even greater, than in the first. That is to say, the
resistance offered to the contraction actually augments the con-
traction, the tension of the muscular fibre increases the facility
with which the explosive changes resulting in a contraction take
place. And it has been observed by Heidenhain that the degree
of acid reaction, the amount of carbonic acid given off, and the
rise of temperature are greater in a muscle contracting against
resistance than when the resistance is removed; that is to say,
the tension increases the metabolism. There is, of course, a
limit to this favorable action of the resistance. As the load con-
tinues to be increased, the height of the contraction is diminished,
and at last a point is reached at which the muscle is unable (even

when the stimulus chosen is the strongest possible) to lift the load at all.

In a muscle viewed as a machine, we have to deal not merely with the height of the contraction—that is, with the amount of shortening, but with the work done. And this is measured as the height to which the load is raised multiplied into the weight of the load. Hence it is obvious from the foregoing observations that the work done must be largely dependent on the weight itself. Thus there is a certain weight of load with which in any given muscle, stimulated by a given stimulus, the most work will be done.

Since mere tension affects the changes going on in the muscular fibres, it is desirable in experiments in which muscles are loaded that the weight should not bear upon the lever until the contraction actually begins. This is easily managed by interposing between the end of the muscle and the weight a lever with a support so arranged that, before contraction takes place, the weight only extends the muscle to the length natural to it during rest; but that the muscle directly it shortens at once begins to pull on the weight. The muscle is then said to be *after-loaded*.[1]

The value of a muscle as a machine is further determined by the size and form of the muscle. Since all known muscular fibres are much shorter than the wave-length of a contraction, it is obvious that the longer the fibre, the greater the height of the contraction with the same stimulus. Hence in a muscle of parallel fibres, the height to which the load is raised as the result of a given stimulus applied to its nerve, will depend on the length of the fibres, while the maximum weight of load capable of being lifted will depend on the number of the fibres, since the load is distributed among them. Of two muscles therefore of equal length (and of the same quality), the most work will be done by that which has the greater sectional area; and of two muscles with equal sectional areas, the most work will be done by that which is the longer. If the two muscles are unequal both in length and sectional area, the work done will be the greater in the one which has the larger bulk, which contains the greater number of cubic units. In speaking, therefore, of the work which can be done by a muscle, we may use as a standard a cubic unit of bulk, or, the specific gravity of the muscle being the same, a unit of weight.

Absolute power of a muscle. We have seen that with a given weight a stimulus (induction-shock) may be chosen of such a strength that a contraction is only just visible. In such a case a very slight increase of the weight would prevent even that minimal contraction. Upon increasing the stimulus the minimal contraction would reappear and vanish again upon a further

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[1] This is perhaps the best equivalent of the German *überlastet*.

increase of the weight. Increasing the stimulus and weight in this way we should be able to find out the weight which, with a maximal stimulation, is just sufficient to prevent any visible contraction from taking place, a very slight diminution of weight at once allowing a minimum contraction to make its appearance. Such a weight is taken as a measure of what is called the "absolute power" of the muscle; and from what has been said in the previous paragraph, it is obvious that this will depend on the number of fibres in, or more correctly, on the sectional area of, the muscle. The absolute power of a square centimetre of a frog's muscle has been in this way estimated at about 2800 to 3000 grms.: of a square centimetre of human muscle at 6000 to 8000.

It may be worth while to mention in this connection the following interesting fact.

If the weight be determined which will stop a contraction when applied directly the contraction begins, and also that which stops any further contraction when applied at a moment when the contraction is already partly accomplished, it will be found that the second weight is much less than the first. It appears, in fact, that the forces which cause the change in the form of the muscle are at their maximum at the beginning of the shortening, and thenceforwards decline until they become nothing when the shortening is complete.

The work done. We learn then from the foregoing paragraphs that the work done — *i. e.*, the weight of the load multiplied into the height of the lift, will depend, not only on the activity of the nerve and muscle as determined by their own irritability, but also on the character and mode of application of the stimulus, on the kind of contraction (whether a single spasm, or a slowly repeated tetanus or a rapidly repeated tetanus), on the load itself, and on the size and form of the muscle. Taking the most favorable circumstances, viz., a well-nourished, lively preparation, a maximum stimulus causing a rapid tetanus and an appropriate load, we may determine the maximum work done by a given weight, say one gramme, of muscle. This, in the case of the muscles of the frog has been estimated at about four grammetres for one gramme of muscle.

Sec. 5.—The Circumstances which Determine the Degree of Irritability of Muscles and Nerves.

A muscle-nerve preparation, at the time that it is removed from the body, possesses a certain degree of irritability, it responds by a contraction of a certain amount to a stimulus of a

certain strength, applied to the nerve or to the muscle. After a while, the exact period depending on a variety of circumstances, the same stimulus produces a smaller contraction—*i. e.*, the irritability of the preparation has diminished. In other words, the muscle or nerve or both have become partially "exhausted;" and the exhaustion subsequently increases, the same stimulus producing smaller contractions until at last all irritability is lost, no stimulus however strong producing any contraction whether applied to the nerve or directly to the muscle; and eventually the muscle, as we have seen, becomes rigid. The progress of this exhaustion is more rapid in the nerves than in the muscles, for some time after the nerve-trunk has ceased to respond to even the strongest stimulus, contractions may be obtained by applying the stimulus directly to the muscle. It is much more rapid in warm-blooded than in cold-blooded animals. The muscles and nerves of the former lose their irritability, when removed from the body, after a period varying according to circumstances from a few minutes to two or three hours; those of cold-blooded animals (or at least of an amphibian or a reptile) may, under favorable conditions, remain irritable for two, three, or even more days. The duration of irritability in warm-blooded animals may, however, be considerably prolonged by reducing the temperature of the body before death.

If, with some thin body, a sharp blow be struck across a muscle which has entered into the later stages of exhaustion, a wheal lasting for several seconds is developed. This wheal appears to be a contraction-wave limited to the part struck, and disappearing very slowly, without extending to the neighboring muscular substance. It has been called an "idio-muscular" contraction, because it may be brought out even when ordinary stimuli have ceased to produce any effect. It may, however, be accompanied at its beginning by an ordinary contraction. It is readily produced in the living body on the pectoral and other muscles of persons suffering from phthisis and other exhausting diseases.

This natural exhaustion and diminution of irritability in muscles and nerves removed from the body, may be modified both in the case of the muscle and of the nerve, by a variety of circumstances. Similarly, while the nerve and muscle still remain in the body, the irritability of the one or of the other may be modified either in the way of increase or of decrease by various events. We have already seen (p. 109) how the constant current produces the variations in irritability known as katelectrotónus and anelectrotonus. We have now to study the effect of more general influences, of which the most important are, severance from the central nervous system, and variations in temperature, in blood-supply, and in functional activity.

The Effects of Severance from the Central Nervous System.

When a nerve—such, for instance, as the sciatic—is divided *in situ* in the living body, there is first of all observed a slight increase of irritability, noticeable especially near the cut end; but after a while the irritability diminishes, and gradually disappears. Both the slight initial increase and the subsequent decrease begin at the cut end and advance centrifugally towards the peripheral terminations. This centrifugal feature of the loss of irritability is often spoken of as the Ritter-Valli law. In a mammal it may be two or three days, in a frog, as many, or even more, weeks, before irritability has disappeared from the nerve-trunk. It is maintained in the small (and especially in the intramuscular) branches for still longer periods.

This centrifugal loss of irritability is the forerunner in the peripheral portion of the divided nerve of structural changes which proceed in a similar centrifugal manner. The medulla suffers changes similar to those seen in nerve-fibres after removal from the body. Its double contour and its characteristic indentations become more marked, it breaks up into small irregular fragments, or drops, a separation apparently taking place between its proteid and its fatty constituents. The latter are soon absorbed, but the former remain for a longer time within the sheath of Schwann, being in some cases scarcely, if at all, to be distinguished from the swollen axis-cylinder. Meanwhile the nuclei which occur, one in each segment of the nerve between each two nodes of Ranvier, divide and multiply rapidly. Lastly the axis-cylinder breaks up and disappears, so that nothing remains of the original fibre but the sheath of Schwann enclosing a proteid mass with many nuclei. If no regeneration takes place, these nuclei eventually disappear.

In the central portion of the divided nerve, similar changes may be traced as far only as the next node of Ranvier. Beyond this, the nerve usually remains in a normal condition.

Regeneration, when it occurs, is apparently carried out by the peripheral growth of the axis-cylinders of the intact central portion. When the cut ends of the nerve are close together, the axis-cylinders growing out from the central portion run into and between the sheaths of Schwann of the peripheral portion; but much uncertainty still exists as to the exact parts which the proliferated nuclei referred to above, the proteid remnants of the medulla, and the old axis-cylinders of the peripheral portion, respectively, play in giving rise to the new structures of the regenerated fibre.

This degeneration may be observed to extend down to the very endings of the nerve in the muscle, including the end-plates, but

does not at first affect the muscular substance itself. The muscle, though it has lost all its nervous elements, still remains irritable towards stimuli applied directly to itself: an additional proof of the existence of an independent muscular irritability.

For some time the irritability of the muscle, as well towards stimuli applied directly to itself as towards those applied through the impaired nerve, seems to be diminished; but after a while a peculiar condition (to which we have already alluded on p. 116) sets in, in which the muscle is found to be not easily stimulated by single induction-shocks, but to respond readily to the make or break of a constant current. In fact, it is said to become even more sensitive to the latter mode of stimulation than it was when its nerve was intact and functionally active. At the same time it also becomes more irritable towards direct mechanical stimuli; and very frequently fibrillar contractions, more or less rhythmic and apparently of spontaneous origin, though their causation is obscure, make their appearance. This phase of heightened sensitiveness of a muscle, especially to the constant current, appears to reach its maximum in man at about the seventh week after nervous impulses, from injury to the nerves or nervous centre, have ceased to reach the muscle.

If the muscle thus deprived of its nervous elements be left to itself, its irritability, however tested, sooner or later diminishes; but if the muscle be periodically thrown into contractions by artificial stimulation with the constant current, the decline of irritability and attendant loss of nutritive power may be postponed for some considerable time. But, as far as our experience goes at present, the artificial stimulation cannot fully replace the natural one, and sooner or later the muscle like the nerve suffers degeneration, loses all irritability, and ultimately becomes replaced by connective tissue.

The Influence of Temperature.

We have already seen that sudden heat applied to a limited part of a nerve or muscle, as when the nerve or muscle is touched with a hot wire, will act as a stimulus, and the same might be said of cold when sufficiently intense. It is, however, much more difficult to generate nervous or muscular impulses by exposing a whole nerve or muscle to a gradual rise of temperature. Thus according to most observers a nerve belonging to a muscle[1] may either be cooled to $0°$ C. or below, or heated to $50°$ or even $100°$ C., without discharging any nervous impulses, as shown by the absence of contraction in the attached muscle. The contractions moreover may be absent even when the heating has not been very gradual.

[1] The action of cold and heat on sensory nerves will be considered in the later portion of the work.

A muscle may be cooled to 0° C or below, without any contraction being caused, but when it it is heated to a limit, which in the case of frogs' muscles is about 45°, of mammalian muscles about 50°, a sudden change takes place; the muscle falls, at the limiting temperature, into a rigor mortis, which is initiated by a forcible contraction or at least shortening. The rigor mortis thus brought about by heat is often spoken of as rigor caloris.

Moderate warmth—*ex. gr.*, in the frog an increase of temperature up to somewhat below 45° C., favors both muscular and nervous irritability. All the molecular processes are hastened and facilitated; the contraction is, for a given stimulus, greater and more rapid—*i. e.*, of shorter duration, and nervous impulses are generated more readily by slight stimuli. Owing to the quickening of the chemical changes, the supply of new material may prove insufficient; hence muscles and nerves removed from the body lose their irritability more rapidly at a high than at a low temperature.

The gradual application of cold to a nerve, especially when the temperature is thus brought near to 0°, slackens all the molecular processes, so that the wave of nervous impulse is lessened and prolonged, the velocity of its passage being much diminished—*e. g.*, from 28 m. to 1 m. per second. At about 0° the irritability of the nerve disappears altogether.

When a muscle is exposed to similar cold—*e. g.*, to a temperature very little above zero, the contractions are remarkably prolonged; they are diminished in height at the same time, but not in proportion to the increase of their duration. Exposed to a temperature of zero or below, muscles soon lose their irritability, without, however, undergoing rigor mortis. After an exposure of not more than a few seconds to a temperature not much below zero, they may be restored, by gradual warmth, to an irritable condition, even though they may appear to have been frozen. When kept frozen, however, for some few minutes, or when exposed for a less time to temperatures several degrees below zero, their irritability is permanently destroyed. When thawed, they enter into rigor mortis of a most pronounced character.

The Influence of Blood-supply.

When a muscle still within the body is deprived by any means of its proper blood-supply, as when the bloodvessels going to it are ligatured, the same gradual loss of irritability and final appearance of rigor mortis are observed as in muscles removed from the body. Thus, if the abdominal aorta be ligatured, the muscles of the lower limbs lose their irritability and finally become rigid. So also in systemic death, when the blood-supply

to the muscles is cut off by the cessation of the circulation, loss of irritability ensues, and rigor mortis eventually follows. In a human corpse the muscles of the body enter into rigor mortis in a fixed order; first, those of the jaw and neck, then those of the trunk, next those of the arms, and lastly those of the legs. The rapidity with which rigor mortis comes on after death varies considerably, being determined both by external circumstances and by the internal conditions of the body. Thus external warmth hastens and cold retards the onset. After great muscular exertion, as in hunted animals, and when death closes wasting diseases, rigor mortis in most cases comes on rapidly. As a general rule, it may be said that the later it is in making its appearance, the more pronounced it is, and the longer it lasts; but there are many exceptions, and when the state is recognized as being fundamentally due to a coagulation, it is easy to understand that the amount of rigidity—*i. e.*, the amount of the coagulum, and the rapidity of the onset—*i. e.*, the quickness with which coagulation takes place, may vary independently. The rapidity of onset after muscular exercise and wasting disease is apparently dependent on an increase of acid reaction, being produced under those circumstances in the muscle, for this seems to be favorable to the coagulation of the muscle-plasma. When rigor mortis has once become thoroughly established in a muscle through deprivation of blood, it cannot be removed by any subsequent supply of blood. Thus where the abdominal aorta has remained ligatured until the lower limbs have become completely rigid, untying the ligature will not restore the muscles to an irritable condition, it simply hastens the decomposition of the dead tissues by supplying them with oxygen, and in the case of the mammal, with warmth also. A muscle, however, may acquire as a whole a certain amount of rigidity on account of some of the fibres becoming rigid, while the remainder, though they have lost their irritability, have not yet advanced into rigor mortis. At such a juncture, a renewal of the blood-stream may restore the irritability of those fibres which were not yet rigid, and thus appear to do away with rigor mortis; yet it appears that in such cases the fibres which have actually become rigid never regain their irritability, but undergo degeneration.

Mere loss of irritability, even though complete, if stopping short of the actual coagulation of the muscle-substance, may be with care removed. Thus, if a stream of blood be sent artificially through the vessels of a separated (mammalian) muscle, the irritability may be maintained for a very considerable time. On stopping the artificial circulation, the irritability diminishes, and in time entirely disappears; if, however, the stream be at once resumed, the irritability will be recovered. By regulating the

flow, the irritability may be lowered and (up to a certain limit) raised at pleasure. From the epoch, however, of interference with the normal blood-stream there is a gradual diminution in the responses to stimuli, and ultimately the muscle loses all its irritability and becomes rigid, however well the artificial circulation be kept up. This failure is, probably, in great part due to the blood sent through the tissue not being in a perfectly normal condition; but we have at present very little information on this point. Indeed, with respect to the *quality* of blood thus essential to the maintenance or restoration of irritability, our knowledge is definite with regard to one factor only, viz., the oxygen. If blood deprived of its oxygen be sent through a muscle removed from the body, irritability, so far from being maintained, seems rather to have its disappearance hastened. In fact, if venous blood continues to be driven through a muscle, the irritability of the muscle is lost even more rapidly than in the entire absence of blood. It would seem that venous blood is more injurious than none at all. If exhaustion be not carried too far, the muscle may, however, be revived by a proper supply of oxygenated blood.

The influence of blood-supply cannot be so satisfactorily studied in the case of nerves as in the case of muscles; there can, however, be little doubt that the effects are analogous.

The Influence of Functional Activity.

This, too, is more easily studied in the case of muscles than of nerves.

When a muscle within the body is unused, it wastes; when used, it (within certain limits) grows. Both these facts show that the nutrition of a muscle is favorably affected by its functional activity. Part of this may be an indirect effect of the increased blood-supply which occurs when a muscle contracts. When a nerve going to a muscle is stimulated, the bloodvessels of the muscle dilate. Hence at the time of the contraction more blood flows through the muscle, and this increased flow continues for some little while after the contraction of the muscle has ceased. But, apart from the blood-supply, it is probable that the exhaustion caused by a contraction is immediately followed by a reaction favorable to the nutrition of the muscle; and this is a reason, possibly the chief reason, why a muscle is increased by use—that is to say, the loss of substance and energy caused by the contraction is subsequently more than made up for by increased metabolism during the following period of rest.

Whether there be a third factor—whether muscles, for instance, are governed by so-called trophic nerves which affect their

nutrition directly in some other way than by influencing either their blood-supply or their activity—must at present be left undecided.

A muscle, even within the body, after prolonged action is fatigued—*i. e.*, a stronger stimulus is required to produce the same contraction ; in other words, its irritability may be lessened by functional activity. Whether functional activity, therefore, is injurious or beneficial, depends on its amount in relation to the condition of the muscle. It may be here remarked that, as a muscle becomes more and more fatigued, stimuli of short duration, such as induction-shocks, sooner lose their efficacy than do stimuli of longer duration, such as the break and make of the constant current.

The sense of fatigue of which, after prolonged or unusual exertion, we are conscious in our own bodies, is probably of complex origin ; and its nature, like that of the normal muscular sense of which we shall have to speak hereafter, is at present not thoroughly understood. It seems to be, in the first place, the result of changes in the muscles themselves ; but is possibly also caused by changes in nervous apparatus concerned in muscular action, and especially in those parts of the central nervous system which are concerned in the production of voluntary impulses. In any case it cannot be taken as an adequate measure of the actual fatigue of the muscles ; for, a man who says he is absolutely exhausted may, under excitement, perform a very large amount of work with his already weary muscles. The will, in fact, rarely if ever calls forth the greatest contractions of which the muscles are capable.

Absolute (temporary) exhaustion of the muscles, so that the strongest stimuli produce no contraction, may be produced even within the body by artificial stimulation ; recovery takes place on rest. Out of the body absolute exhaustion takes place readily. Here, also, recovery may take place. Whether, in any given case, it does occur or not, is determined by the amount of contraction causing the exhaustion, and by the previous condition of the muscle. In all cases recovery is hastened by renewal (natural or artificial) of the blood-stream. The more rapidly the contractions follow each other, the less the interval between any two contractions, the more rapid the exhaustion. A certain number of single induction-shocks repeated rapidly—say every second, or oftener—bring about exhaustive loss of irritability more rapidly than the same number of shocks repeated less rapidly, for instance every five or ten seconds. Hence, tetanus is a ready means of producing exhaustion.

In exhausted muscles the elasticity is much diminished ; the

tired muscle returns less readily to its natural length than does the fresh one.

The exhaustion due to contraction may be the result, either of the consumption of the store of really contractile material present in the muscle, or of the accumulation in the tissue of the products of the act of contraction, or of both of these causes.

The restorative influence of rest may be explained by supposing that during the repose, either the internal changes of the tissue manufacture new explosive material out of the comparatively raw material already present in the fibres, or the directly hurtful products of the act of contraction undergo changes by which they are converted into comparatively inert bodies. A stream of fresh blood may exert its restorative influence not only by quickening the above two events, but also by carrying off the immediate waste products, while at the same time it brings new raw material. It is not known to what extent each of these parts is played. That the products of contraction are exhausting in their effects, is shown by the facts that the injection of a solution of the muscle-extractives into the vessels of a muscle produces exhaustion, and that exhausted muscles are recovered by the simple injection of inert saline solutions into their bloodvessels; moreover, lactic acid—and, indeed, other acids—injected into a muscle, cause rapid exhaustion; and we may suppose that carbonic acid, with the other substances which, after a contraction, tend to give rise to an acid reaction, when generated too rapidly to be neutralized by the alkaline lymph in which the fibres are bathed, in part at least determine the exhaustion. But the matter has not yet been fully worked out.

One important element brought by fresh blood is oxygen. This, as we have seen, is not necessary for the carrying out of the actual contraction, and yet is essential to the maintenance of irritability. It is probably of use as what may be called "intra-molecular oxygen" in preparing the explosive material whose decomposition gives rise to the carbonic acid, and other products of contraction.

SEC. 6.—THE ENERGY OF MUSCLE AND NERVE, AND THE NATURE OF MUSCULAR AND NERVOUS ACTION.

We may briefly recapitulate some of the chief results arrived at in the preceding pages as follows:

A muscular contraction itself is essentially a translocation of molecules—a change of form, not of bulk. We cannot say, however, anything definite as to the nature of this translocation, or as to the way in which it is brought about. Though it would

appear that the dim doubly refractive bands increase in bulk at the expense of the bright singly refractive bands, we cannot satisfactorily explain the connection between the striation of a muscular fibre and a muscular contraction. Nearly all rapidly contracting muscles are striated, and we must suppose that the striation is of some use; but it is not essential to the carrying out of a contraction, for many muscles are not striated. But, whatever be the exact way in which the translocation is effected, it is fundamentally the result of a chemical change—of an explosive decomposition of certain parts of the muscle-substance. The energy which is expended in the mechanical work done by the muscle has its source in the latent energy of the muscle-substance set free by that explosion. Concerning the nature of that explosion, we only know at present that it results in the production of carbonic acid and in an increase of the acid reaction, and that heat is set free as well as the specific muscular energy. There is a general parallelism between the extent of metabolism taking place and the amount of energy set free. The greater the development of carbonic acid, the larger is the contraction and the higher the temperature.

It has not been possible hitherto to draw up a complete equation between the latent energy of the material and the two forms of actual energy set free. The proportion of energy given out as heat to that taking on the form of work, probably varies under different circumstances; and it would appear that, on the whole, a muscle would be no more economical than a steam-engine in respect to the conversion of chemical action into mechanical work, were it not that in warm-blooded animals the heat given out is not, as in the steam-engine, mere loss, but by keeping up the animal temperature serves many subsidiary purposes. It might be supposed that when in a contraction work is actually done, the increase of temperature is less than when the same contraction takes place without doing actual work—that is to say, that the mechanical work is done at the expense of energy which otherwise would go out as heat. Probable as this may seem, it has not yet been experimentally verified.

Of the exact nature of the chemical changes which underlie a muscular contraction, we know very little; the most important fact being, that the contraction is not the outcome of a direct oxidation, but the splitting up or explosive decomposition of some complex substance. The muscle does consume oxygen, and the products of muscular metabolism are in the end products of oxidation, but the oxygen appears to be introduced not at the moment of explosion, but at some earlier date. There is no evidence of nitrogenous products being given off as waste; such nitrogenous crystalline bodies as are present in muscle, creatine,

etc., may be regarded rather as the wear-and-tear of the machine
than as products of the material consumed in the work. Yet it
is hardly consonant with what we know elsewhere, to suppose
that the contraction of a muscular fibre has for its essence the
decomposition of a non-nitrogenous substance; and we may sup-
pose that the explosion does involve some nitrogenous products,
which, however, are retained within the tissue, and used up again.
We may even go so far as to entertain, with Hermann, the view
that a single complex substance, an hypothetical *inogen*, splits
up partly into nitrogenous, partly into non-nitrogenous, factors;
the former, possibly of the nature of myosin, being rapidly built
up again into new inogen, while the latter, such as the carbonic
acid, are discharged at once from the muscle. But our knowl-
edge of these matters is not yet ripe enough for the construction
of an adequate and wholly satisfactory theory. It may be worth
while to point out that, during even the most complete repose,
muscle is undergoing chemical changes which, as far as we know,
are the same in kind, and only differ in degree from those char-
acteristic of a contraction. Thus, carbonic acid is constantly
being produced, as are probably other substances, all being got
rid of as they form, just as they are got rid of in larger quantities
during the repose which follows contraction. Supposing the ex-
istence of a substance which splits up into these various products,
and which we may speak of as the true contractile material, it is
evident that this material, being thus constantly used up, must
be as constantly repaired. Thus, a stream of chemical substances
may be conceived of as flowing through muscle, the raw material
brought by the blood being gradually converted into true con-
tractile stuff, the breaking-down again of which is gentle and
gradual so long as the muscle is at rest, but becomes excessive
and violent when a contraction takes place. When rigor mortis
sets in, the whole remaining contractile material is decomposed.

While in muscle the chemical events are so prominent that
we cannot help considering a muscular contraction to be essen-
tially a chemical process, with electrical changes as attendant
phenomena only, the case is different with nerves. Here the
electrical phenomena completely overshadow the chemical. Our
knowledge of the chemistry of nerves is at present of the scantiest,
and the little we know as to the chemical changes of nervous
substance is gained by the study of the central nervous organs
rather than of the nerves. We find that the irritability of the
former is closely dependent on an adequate supply of oxygen,
and we may infer from this that in nervous as in muscular sub-
stance a metabolism—of, in the main, an oxidative character—
is the real cause of the development of energy; and the axis-
cylinder (which is probably the active element of a nerve-fibre,

the medulla being useful for its nutrition and protection only) undoubtedly resembles in many of its chemical features the substance of a muscular fibre. But we have, as yet, no satisfactory experimental evidence that the passage of a nervous impulse along a nerve is the result, like the contraction of a muscular fibre, of chemical changes, and, like it, accompanied by an evolution of heat.

On the other hand, the electric phenomena are so prominent that some have been tempted to regard a nervous impulse as essentially an electrical change. But it must be remembered that the actual energy set free in a nervous impulse is, so to speak, insignificant, so that chemical changes, too slight to be recognized by the means at present at our disposal, would amply suffice to provide all the energy set free. On the other hand, the rate of transmission of a nervous impulse, putting aside other features, is alone sufficient to prove that it is something quite different from an ordinary electric current.

The curious disposition of the end-plates, and their remarkable analogy with the electric organs which are found in certain animals, have suggested the vew that the passage of a nervous impulse from the nerve-fibre into the muscular substance is of the nature of an electric discharge. But these matters are too difficult and too abstruse to be discussed here.

It may, however, be worth while to remind the reader that in every contraction of a muscular fibre, the actual change of form is preceded by invisible changes propagated all over the fibre and occupying the latent period, and that these changes resemble in their features the nervous impulse of which they are, so to speak, the continuation rather than the contraction of which they are the forerunners and to which they give rise. So that a muscle, even putting aside the visible terminations of the nerve, is fundamentally a muscle and a nerve besides.

Sec. 7.—Other Forms of Contractile Tissue.

[Physiological Anatomy of the Unstriated Muscles.

The unstriated muscles consist of flattened bands or layers, which are made up of bundles of fibres. These fibres are composed of elongated, fusiform, protoplasmic cells, containing an elongated nucleus—or nuclei,—which is usually surrounded by a small amount of granular protoplasm. (Figs. 26 and 27.)

They do not possess a sheath, or sarcolemma, like the skeletal fibres, and when ruptured have somewhat irregularly squared ends.

The unstriated muscles are almost entirely distributed to the viscera, and are disposed as flattened bands or layers, which cross each other at various angles. Generally they appear as two layers—a superficial or longitudinal, and a deep or circular layer.

This form of muscular fibre is found in the skin, where the fibres are seen to have an oblique course, running from the

Fig. 27.
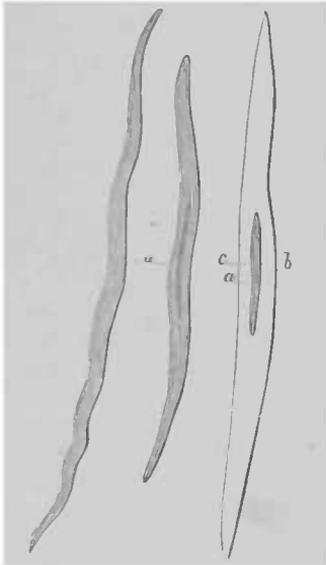
Three Unstriped Muscular Fibre-cells from Human Arteries. *a* and *b* show cells with nuclei; *b* is a cell treated with acetic acid, making nuclei more distinct.
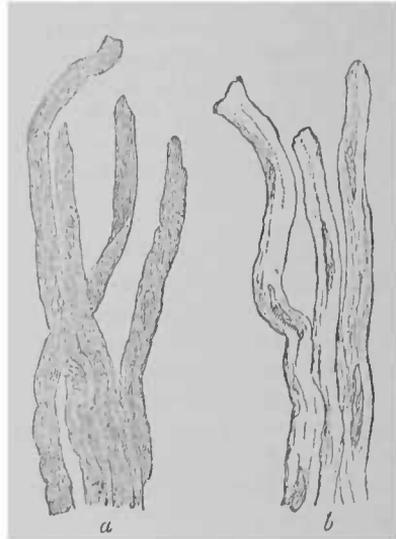
Muscular Fibre-cells from the Bladder. *a* shows them in a normal condition; *b*, treated with acetic acid, which dissolves the granular contents, leaving the nuclei.

superficial layers of the corium to the hair-follicles, where they are inserted (Fig. 28). Unstriped muscular tissue is also abundant in the superficial layers of the corium, at the basis of the papillæ. When these fibres contract, they cause numerous papillary elevations to appear on the skin, which give the surface the appearance of what is commonly termed "goose-skin."

The unstriated muscles appear to be more intimately connected with the sympathetic nervous system, and controlled chiefly by them, while the skeletal muscles are animated by the cerebro-spinal system. According to some observers, the fibres of the intestines are almost exclusively supplied by the sympathetic

nerves. In the former class of fibres, from the fact of their being generally uninfluenced by the will, and of their principal distribution being to the organs of nutrition and growth, they have been termed the muscles of *organic* life. In the latter class, because of their being presided over by the cerebro-spinal system,

FIG. 28.
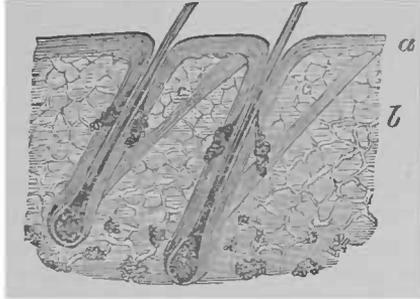
Perpendicular Section through the Scalp, with two Hair-sacs. *a*, epidermis; *b*, cutis; *c*, muscles of the hair-follicles. After KOLLIKER.

their more intimate connection with the animal functions, and their volitional character, are termed the muscles of *animal* life.]

Unstriated Muscular Tissue.—Our knowledge of the phenomena of these structures is very imperfect, since (in vertebrates) they do not exist in isolated masses like the striated muscles, but occur as constituents of complex organs, such as the intestine, ureter, uterus, etc. They undergo rigor mortis; and what little information we do possess concerning their chemical and physical features leads us to believe that the processes which take place in them are fundamentally identical with those occurring in striated muscle, the two differing in degree rather than in kind. When stimulated, they contract. If a stimulus, mechanical or electrical, be applied to the intestine or ureter of a mammal, a circular contraction is seen to take place at the spot stimulated. The contraction, which is preceded by a very long latent period, lasts a very considerable time—in fact, several seconds—after which relaxation slowly takes place—that is to say, over the circularly dispersed fibres of the intestine (or ureter), at the spot in question, there has passed a contraction-wave remarkable for its long latent period and for the slowness of its development. From the spot so directly stimulated, the contraction may pass as a wave (with a length of 1 centimetre and a velocity of from 20 to 30 millimetres a second in the ureter) along the circular coat both upwards and downwards. The longitudinal fibres at the spot stimulated are also thrown into contractions of altogether similar

character, and a wave of contraction may also travel longitudinally along the longitudinal coat both upwards and downwards. It is evident, however, that the wave of contraction of which we are now speaking is in one respect different from the wave of contraction treated of in dealing with striated muscle. In the latter case, the contraction-wave is a simple wave propagated along the individual fibre; in the case of the intestine or ureter, the wave is complex, being the sum of the contraction-waves of several fibres engaged in different phases, and is propagated from fibre to fibre, both in the direction of the fibres, as when the whole circumference of the intestine is engaged in the contraction, or when the wave travels longitudinally along the longitudinal coat, and also in a direction at right angles to the axes of the fibres, as when the contraction-wave travels lengthways along the circular coat of the intestine, or when it passes across a breadth of the longitudinal coat. Moreover, it is obvious that the contraction-wave which passes along a single unstriated fibre differs from that passing along a striated fibre, in the very great length both of its latent period and of the duration of its contraction.

Waves of contraction thus passing along the circular and longitudinal coats of the intestine, constitute what is called peristaltic action.

Like the skeletal muscles, whose nervous elements have been rendered functionally incapable, unstriated muscles are much more sensitive to the making and breaking of a constant current than to induction-shocks.

The unstriated muscles seem to be remarkably susceptible to the influences of temperature. Thus the unstriated muscles of the trachea are said not to contract at a temperature below 12° C., and are most active at a temperature above 21° C. So, also, the movements of the intestine cease at a temperature below 19° C.

[The muscles are, furthermore, variously affected by different poisons. Narcotics generally, nitrite of amyl, nitrite of potassium, apomorphine, hydrocyanic acid, and numerous other drugs depress or paralyze them. Physostigma and caffein stimulate them if directly applied. Veratria first stimulates and afterwards paralyzes them. Ergot seems to possess a remarkable power in causing contraction of the muscles of the uterus, and its chief therapeutic use is for this purpose. When they are placed in certain gases, such as carbonic acid, carbonic oxide, hydrogen, etc., they soon lose their irritability. In an atmosphere of oxygen they will remain irritable for a very long period.]

In striking contradistinction to what takes place in the striated muscles, automatic movements are exceedingly common in structures built up of non-striated muscles; these, moreover, exhibit a great tendency to rhythmic action. Thus, the peristaltic action

of the intestine and ureters, and the corresponding movements of the uterus, are at once rhythmic and largely automatic. What share the nervous elements take in the automatism and the rhythm is uncertain.

Cardiac Muscles.—The most important features of this form of contractile tissue will be studied when we come to deal with the heart. It will be seen that they are intermediate between ordinary skeletal and non-striated muscles.

Cilia.—Ciliary movement consists in the rapid flexion (into a sickle or hook-form) of the cilium and its less rapid return to its previous straight form. The diminished velocity of the return leads to the force of the ciliary action being exerted in the same direction as the flexion. The cause of the flexion seems to be the contraction of the cilium; and that of the return, an elastic re-action. In the lower animals, however, many varieties in the mode of movement of cilia may be observed.

Various attempts to explain the movement by the presence of special mechanisms at the base of the cilia have hitherto failed. Some authors have attributed the movement to a protoplasmic contraction of the cell itself, the cilium acting merely as a minute elastic rod; and some such view as this is supported by the fact that no movement has ever been observed in an isolated cilium. It is difficult, however, to understand how the peculiar sickle-like flexion of the cilium can be brought about unless the contractile material is continued up into the cilium itself; and the tail of a spermatozoon, which is practically a single cilium, may contract even when separated from the head.

Ciliary movement appears, therefore, to differ from ordinary muscular contraction chiefly in the size of the apparatus concerned. The movement is rapid : thus, Englemann has estimated that in the frog the flexions are repeated at least twelve times in a second. The movement, in fact, is too rapid to be visible; it can only be seen at a time when exhaustion and coming death have begun to retard the action. Englemann found that he was first able to count them when their rapidity declined to eight in a second.

In the vertebrate animal, cilia are, as far as we know, wholly independent of the nervous system, and their movement is probably ceaseless. In such animals, however, as Infusoria, Hydrozoa, etc., the movements in a ciliary tract may often be seen to stop and go on again—to be now fast, now slow, according to the needs of the economy, and, as it almost seems, according to the will of the creature; indeed, in some of these animals the ciliary movements are clearly under the influence of the nervous system.

Observations with galvanic currents, constant and interrupted, have not led to any satisfactory results; and, as far as we know

at present, ciliary action is most affected by changes of tempera-
ture and chemical media.   Moderate heat quickens the move-
ments, but a rise of temperature beyond a certain limit (about
$40°$ C. in the case of the pharyngeal membrane of the frog) be-
comes injurious ; cold retards.   Very dilute alkalies are favorable,
acids are injurious.   An excess of carbonic acid or an absence of
oxygen diminishes or arrests the movements, either temporarily
or permanently, according to the length of the exposure.   Chloro-
form or ether in slight doses diminishes or suspends the action
temporarily, in excess kills and disorganizes the cells.

Migrating Cells.—We have already urged the view that an
amœboid movement of a white corpuscle is essentially a form of
contraction.

All the circumstances which affect muscular contraction—
heat, absence or presence of oxygen and carbonic acid, etc., also
affect protoplasmic movements.   The white corpuscles, like
muscular fibres, suffer rigor mortis, in which state they become
spherical.

CHAPTER III.

THE FUNDAMENTAL PROPERTIES OF NERVOUS TISSUES.

In its simplest, and probably earliest form, a nerve is nothing more than a thin strand of irritable protoplasm, forming the means of vital communication between a sensitive ectodermic cell

Fig. 29.
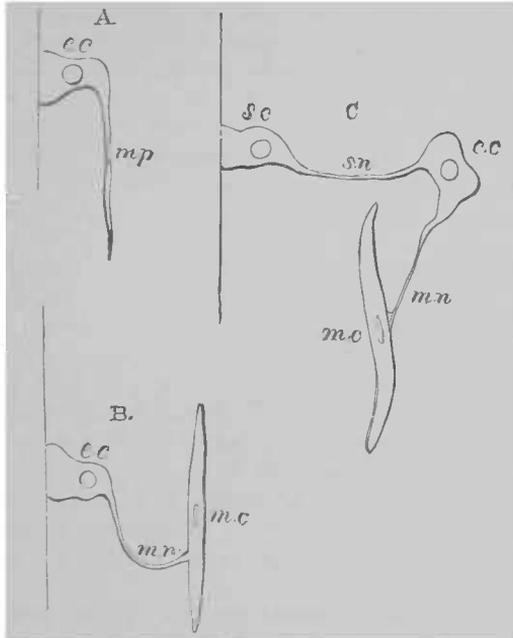
DIAGRAM TO ILLUSTRATE THE SIMPLEST FORMS OF A NERVOUS SYSTEM.

A. An ectoderm-cell *e. c.*, with its muscular process *m. p* , as in Hydra.

B. The ectoderm-cell *e. c.* is connected with the muscle-cell *m. c.* by means of the primary motor nerve *m. n.*

C. The differentiated sensitive cell *s c* is connected by means of the sensory nerve *s. n.* with the central cell *c. c.*, which is again connected by means of the motor nerve *m. n.* with the muscle-cell *m. c.*

exposed to extrinsic accidents, and a muscular, highly contractile cell (or a muscular process of the same cell) buried at some dis-

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tance from the surface of the body, and thus less susceptible to external influences. (Fig. 29, A, B.) If in Hydra, we imagine the junction of the ectodermic muscular process with the body of its cell to be drawn out into a thin thread (as is said to be the case in some other Hydrozoa), we should have just such a primary nerve. Since there would be no need for such a means of communication to be contractile and capable of itself changing in form, but on the other hand an advantage in its remaining immobile, and in its dimensions being reduced as much as possible consistent with the maintenance of irritability, the primary nerve would, in the process of development, lose the property of contractility in proportion as it became more irritable—i. e., more apt in the propagation of the waves of disturbance arising in the ectodermic cell.

We have already seen that automatism—i. e., the power of initiating disturbances or vital impulses, independent of any immediate disturbing event or stimulus from without, is one of the fundamental properties of protoplasm. In simpler, but less exact language, such a mass of protoplasm as an amœba, though susceptible in the highest degree to influences from without, " has a will of its own;" it executes movements which cannot be explained by reference to any changes in surrounding circumstances at the time being. A hydra has also a will of its own ; and seeing that all the constituent cells (beyond the distinction into ectoderm and endoderm) are alike, we have no reason for thinking that the will resides in one cell more than in another, but are led to infer that the protoplasm of each of the cells (of the ectoderm, at least) is automatic, the will of the individual being the coördinated wills of the component cells. In both Hydra and Amœba the processes concerned in automatic or spontaneous impulses, though in origin independent of, are subject to, and largely modified by, influences proceeding from without. Indeed, the great value of automatic processes in a living body depends on the automatism being affected by external influences, and on the simple effects of stimulation, being profoundly modified by automatic action.

The next step of development beyond Hydra, is evidently to differentiate the single (ectodermic) cell into two cells, of which one, by division of labor, confines itself chiefly to the simple development of impulses as the result of stimulation, leaving to the other the task of automatic action, and the more complex transformation of the impulses generated in itself. The latter, which we may call the eminently automatic cell (though much of the work which it has to do is of the kind we shall presently speak of as reflex action), will naturally be withdrawn from the surface of the body ; while the other, which we may call the eminently

sensitive cell, will still retain its superficial position, so that it may most readily be affected by all changes in the world without (Fig. 29, C). And just as a primary *motor* nerve arises as a retained thread of communication between a sensitive cell and its muscular process, so a primary *sensory* nerve may be conceived of as arising as a thread of communication between an eminently sensitive cell and its twin the eminently automatic or central cell. By this arrangement the sensitive cell, relieved of the heavy burden of spontaneous action, is enabled to devote itself with greater vigor to the reception of external influences; while the automatic cell, no longer hampered by the physical necessities of being which are imposed on the superficial cell, exposed as this is to every wind and wave, but secure in its internal retreat, is able, with similar increased energy, to devote itself either to the production of spontaneous impulses, or to modifying profoundly the impulses which it receives from the sensitive cell. Naturally the muscular process or muscular fibre would, on the splitting of the original single cell, remain in connection with the more eminently automatic. We thus arrive at that triple fundamental arrangement of a nervous system in its simplest form, viz., a sensitive cell on the surface of the body connected by means of a sensory nerve with the internal automatic central nervous cell, which, in turn, is connected by means of a motor nerve with the muscular fibre-cell.

We have already seen that the physiology of the motor nerve cannot without inconvenience be separated from that of the muscular fibre. In the same way the physiology of the sensory nerve cannot well be separated from those modifications of superficial sensitive cells which constitute the organs of sense. We may add that the special physiology of the central nervous cells can only profitably be studied in connection with the sensory organs. In the present chapter, therefore, we purpose to confine ourselves to the consideration of the simplest and most general properties of the central nervous cells.

These are arranged in the vertebrate body in two great systems: the cerebro-spinal axis, and the various ganglia scattered over the body; we shall deal with such properties only as are more or less common to the two systems. We may premise that, as far as our knowledge at present goes, the processes which are concerned in the propagation of nervous impulses along a sensory nerve-trunk are identical with those which take place in a motor nerve-trunk. The phenomena of the natural nerve-current, of the currents of action during the passage of an impulse and of electrotonus (and these facts mark out, as we have seen, the limits of our information on this matter) are exactly the same, whether the piece of nerve-trunk experimented on be a mixed nerve-

trunk, or an almost purely motor, or an almost purely sensory nerve-trunk, or an anterior or posterior nerve-root, or the special sensory nerve of a particular sense, such as the optic nerve.   In both sensory and motor nerves the changes accompanying a nervous impulse are transmitted equally well in both directions.

We seem justified in concluding that the events which occur in a sensory nerve when it is an instrument of sensation, differ from those which take place in a motor nerve when that is an instrument of movement, only so far as the sensory impulses are generated by particular processes which bear the stamp of the sensory cell in which they originated, while the motor impulses are generated by particular processes which bear the stamp of the central nervous cells in which they in turn originated.   All sensory impulses appear to be tetanic in nature—*i. e.*, to be composed of a series of constituent simple impulses; and it is probable that while the motor impulses which proceed from the central nervous system to the muscles are composed of simple impulses repeated with the same rapidity, and thus giving rise to the same muscular note (p. 82), the sensory impulses which proceed from the peripheral sense organs to the central nervous system vary exceedingly as to the way in which their constituent simple impulses are combined.   It is indeed possible that the complex sensory impulses which give rise, for instance, to sight and touch respectively, may differ only in the wave-length, so to speak, of their constituent simple impulses, much in the same way as red light differs from blue light.

In the scheme sketched out above, the same central nervous cell is supposed to be engaged at once, both in originating automatic actions and in modifying sensory impulses (*i. e.*, impulses proceeding from the superficial sensitive cells) previous to these being passed on to the muscular fibre.   It is evident that where two or more central nervous cells occur together, a further differentiation would be of advantage—a differentiation into cells which though still susceptible of being influenced from without, should be more especially restricted to automatic action, and into cells which should forego their automatism for the sake of being more efficient in modifying sensory impulses, with a view of transmuting them into motor impulses, and so of giving rise to appropriate movements.   We thus gain the fundamental and primary differentiation of the work of a central nervous system into automatic and into reflex operations.   These are very clearly manifested by the brain and spinal cord, and probably also, though this is less certain, by the sporadic ganglia.

Automatic Actions.—In the vertebrate animal the highest form of automatism, individual volition, with which conscious

intelligence is associated, is a function of certain parts of the brain. There are evidences of the existence in the brain of other forms of automatism. All these will be considered in detail hereafter.

In the spinal cord separated from the brain by section of the medulla oblongata, it becomes difficult to draw a line between purely automatic and reflex actions. Thus, when we come to deal with respiration; we shall see that while there can be no doubt that the muscular respiratory apparatus is kept at work by impulses proceeding, in a rhythmic manner, from a group of nerve-cells, or respiratory nervous centre, in the medulla oblongata it is an open question whether those impulses, whose generation is certainly modified by centripetal impulses passing to the centre along various nerves, are absolutely automatic—*i. e..* whether they can continue to make their appearance when no influences whatever from without are brought to bear upon the centre. Similar doubts hover round other automatic functions of the spinal cord. We shall see hereafter reasons for speaking of the existence in the medulla oblongata of a vaso-motor centre, that is of a group of nerve-cells, whence impulses habitually proceed along the so-called vaso-motor nerves to the muscular coats of the small arteries, and keep these vessels in a state of semi-contraction or tone. Here, too, it is doubtful whether these motor or efferent impulses can be generated in the absence of all sensory or afferent impulses. The posterior lymphatic hearts of the frog are connected by the small tenth pair of spinal nerves with the gray matter of the termination of the spinal cord, in such a manner that destruction of that part of the spinal cord or section of the tenth nerves apparently puts an end to the rhythmic pulsations of the lymphatic hearts. Here it would seem as if rhythmic impulses were automatically generated in the lower end of the cord, and proceeded along the efferent nerves to the hearts, thus determining their rhythmic pulsations. But if it be true, as asserted, that the rhythmic pulsations, though arrested for a time by severance of the nerves, or destruction of the lower end of the cord, are after a while resumed, then these, too, can be no longer counted among the automatic phenomena of the cord. And so in other instances which we shall meet with in the course of this book. The existence of automatism, then, even of this comparatively simple character, is at least doubtful. That all higher automatism comparable at least to that of the cerebral hemispheres is absent, may be regarded as certain.

In the sporadic ganglia the evidence of automatic action seems more clear, and yet is by no means absolutely decisive. The beat of the heart is a typical automatic action, and since

the heart will continue to beat for some time when isolated from
the rest of the body (that of a cold-blooded animal continuing
to beat for hours, or even days), its automatism must lie in its
own structures.   When, however, we come to discuss the beat of
the heart in detail, we shall find that it is still an open question
whether the automatism is confined to the ganglia (either of the
sinus venosus, auricles, or auriculo-ventricular boundary), or
shared in by the muscular tissue—whether, in fact, the automat-
ism like that of a ciliated cell, or the automatism of a differen-
tiated nerve-cell.   And yet the heart is the case where the
automatism of the ganglia seems clearest.

The peristaltic contractions of the alimentary canal are auto-
matic movements; we cannot speak of them as being simply ex-
cited by the presence of food in the canal, any more than we can
say that the beat of the heart is caused by the presence of blood
in its cavities.   When absent they may be set agoing, and when
present may be stopped without any change in the contents of
the canal.   They may, of course, be influenced by the contents,
just as the beat of the heart is influenced by the quantity of blood
in its cavities.   Throughout the intestines are found the nerve-
plexus of Auerbach and that of Meissner; to each or both of
these the automatism of the peristaltic movements has been re-
ferred.   Yet in the ureter, whose peristaltic waves of contraction
closely resemble that of the intestine, automatism is evident in
the middle third of its length, even when completely isolated; in
which region (in the rabbit, at least), according to Englemann,
ganglia—and, indeed, nerve-cells—are entirely absent.

Thus, while in the spinal cord there is doubt whether purely
automatic, as stringently distinguished from reflex, actions take
place, in the case of the sporadic ganglia, the uncertainty is
whether the clearly automatic movements of the organs with
which the ganglia are associated are due to the nerve-cells of the
ganglia, or to the muscular tissue itself.

Reflex Actions.—The spinal cord offers the best and most
numerous examples of reflex action.   In fact, reflex action may
be said to be, *par excellence,* the function of the spinal cord; and
the gray matter of the spinal cord may be broadly considered as
a multitude of reflex centres.   We have here to consider the cord
merely in its general aspects; and must postpone the special
consideration of the particular forms of reflex action which it
exhibits, as they come before us in various connections, or until
we have to deal with it as part of the great central nervous
machinery.

In its simplest form a reflex action is as follows: All the ma-
chinery it demands is (S) a sentient surface (external or internal),

connected by a sensory, or—to adopt the more general and better term—afferent nerve, with (G) a central nerve-cell or group of connected nerve-cells, which is in relation by means of a motor, or efferent, nerve, or nerves, with (M) a muscle, or muscles, or some other irritable tissue-elements, capable of responding by some change in their condition, to the advent of efferent impulses. (Fig. 30.) The afferent impulses started in S, passing

[FIG. 30.
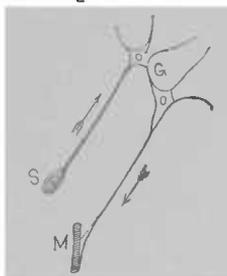
Diagram illustrating Simplest Form of Reflex Apparatus.]

along an afferent nerve reach the centre G, are there transmuted into efferent impulses, which finally reach M, and there produce a cognizable effect. The essence of a reflex action consists in the transmutation, by means of the irritable protoplasm of a nerve-cell, of afferent into efferent impulses. As an approach to a knowledge of the nature of that transmutation, we may lay down the following propositions:

The number, intensity, character, and distribution of the efferent impulses are determined chiefly by the events which take place in the protoplasm of the reflex centre. It is not that the afferent impulse is simply *reflected* in the nerve-cell, and so becomes with but little change an efferent impulse. On the contrary, an afferent impulse passing along a single sensory fibre may give rise to efferent impulses passing along many motor nerves, and call forth the most complex movements. An instance of this disproportion of the afferent and efferent impulses is seen in the case where the contact with the glottis of a foreign body so insignificant as a hair causes a violent fit of coughing. Under such circumstances a slight contact with the mucous membrane, such as could not possibly give rise to anything more than few and feeble impulses, may cause the discharge of so many efferent impulses along so many motor nerves, that not only all the respiratory muscles, but almost all the muscles of the body, are brought into action. Similar, though less striking, instances of how incommensurate are afferent and efferent impulses may be seen in most reflex actions. In fact, the afferent impulse, when it reaches the protoplasm of the nerve, produces there a series of changes—of

explosive disturbances—which, except that the nerve-cell does not in any way change its form, may be likened to the explosive changes in a muscle on the arrival of an impulse along its motor nerve.[1]   The changes in a nerve-cell during reflex action—we might say during any form of activity—far more closely resemble the changes during a muscular contraction than those which accompany the passage along a nerve of either an afferent or efferent impulse.   The simple passage along a nerve is accompanied by little expenditure of energy; it neither gains nor loses force to any great extent as it progresses.   The transmutation in a nerve-cell is most probably (though the direct proofs are, perhaps, wanting) accompanied by a large expenditure of energy, and a simple nervous impulse in suffering the transmutation in a central nervous organ may accumulate in intensity to a very remarkable extent, as in the case of strychnia poisoning.

The nature of the efferent impulses is, however, determined also by the nature of the afferent impulses.   The nerve-centre remaining in the same condition, the stronger or more numerous impulses will give rise to the more forcible or more comprehensive movements.   Thus, if the flank of a brainless frog be very lightly touched, the only reflex movement which is visible is a slight twitching of the muscles lying immediately underneath the spot of skin stimulated.   If the stimulus be increased, the movements will spread to the hind-leg of the same side, which frequently will execute a movement calculated to push or wipe away the stimulus.   By forcibly pinching the same spot of skin, or otherwise increasing the stimulus, the resulting movements may be led to embrace the fore-leg of the same side, then the opposite side, and, finally, almost all the muscles of the body.   In other words, the disturbance set going in the central nerve-cells, confined, when the stimulus is slight, to a few nerve-cells and to a few nerve-fibres, *overflows*, so to speak, when the stimulus is increased, on to a number of adjoining and, we must conclude, connected cells, and thus throws impulses into a larger and larger number of efferent nerves.

Certain relations may be observed between the sentient spot stimulated and the resulting movement.   In the simplest cases of reflex action this relation is merely of such a kind that the muscles thrown into action are those governed by a motor nerve which is the fellow of the sensory nerve, the stimulation of which calls forth the movement.   In the more complex reflex actions of the brainless frog, and in other cases, the relation is of such a kind that the resulting movement bears *an adaptation* to the

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[1] The question as to how far these processes in the central cells are connected with the development of consciousness is here purposely passed over.

stimulus : the foot is withdrawn from the stimulus, or the movement is calculated to push or wipe away the stimulus. In other words, a certain *purpose* is evident in the reflex action.

Thus, in all cases, except, perhaps, the very simplest, the movements called forth by a reflex action are exceedingly complex, compared with those which result from the direct stimulation of a motor trunk. When the peripheral stump of a divided sciatic nerve is stimulated with the interrupted current, the muscles of the leg are at once thrown into tetanus, continue in the same rigid condition during the passage of the current, and relax immediately on the current being shut off. When the same current is applied for a second only, to the skin of the flank of a brainless frog, the leg is drawn up and the foot rapidly swept over the spot irritated, as if to wipe away the irritation ; but this movement is a complex one, requiring the contraction of particular muscles in a definite sequence, with a carefully adjusted proportion between the amounts of contraction of the individual muscles. And this complex movement, this balanced and arranged series of contractions, may be repeated more than once as the result of a single stimulation of the skin. When a deep breath is caused by a dash of cold water, the same coördinated and carefully arranged series of contractions is also seen to result, as part of a reflex action, from a simple stimulus. And many more examples might be given.

In such cases as these, part of the complexity may be due to the fact that the stimulus is applied to terminal sensory organs, and not directly to a nerve-trunk. As we shall see, in speaking of the senses, the impulses which are generated by the application of a stimulus to a sensory organ are more complex than those which result from the direct stimulation of a sensory nerve-trunk. Nevertheless, reflex actions of great, if not of equal, complexity may be induced by stimuli applied directly to a nerve-trunk. We are, therefore, obliged to conclude that in a reflex action, the processes which are originated in the central nerve-cells by the arrival of even simple impulses along afferent nerves may be highly complex ; and that it is the constitution and condition of the nerve-cells which determine the complexity and character of the movements which are affected. In other words, the central nerve-cells concerned in reflex actions are to be regarded as constituting a sort of molecular machinery, the character of the resulting movements being determined by the nature of the machinery set going and its condition at the time being, the character and amount of the afferent impulses determining exactly what parts of and how far the central machinery is thrown into action.

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Actions of Sporadic Ganglia.—Seeing that in the spinal cord the nerve-cells undoubtedly are the central structures concerned in the production of reflex action, it is only natural to infer that the nerve-cells of the sporadic ganglia possess similar functions. Yet the evidence of this is at present of very limited extent. With regard to the ganglia on the posterior roots of the spinal nerves, all the evidence goes to show that these possess no power whatever of reflex action. Of the larger ganglia visible to the naked eye, such as the ciliary, otic, etc., we have indications of reflex action in one only, viz., the submaxillary; and these indications are, as we shall see in treating of the salivary glands, disputed. We have no exact proof that the ganglia of the sympathetic chain, or of the larger sympathetic plexuses, are capable of executing reflex actions.

In fact, in searching for reflex actions in ganglia, we are reduced to the small microscopic groups of cells buried in the midst of the tissues to which they belong, such as the ganglia of the heart, of the intestine, the bladder, etc. When a quiescent frog's heart is stimulated by touching its surface, a beat takes place. This beat is, as we shall see, a complex, coördinated movement, very similar to a reflex action brought about by means of the spinal cord; and in its production it is probable that the cardiac ganglia are in some way concerned. When a quiescent intestine is touched or otherwise stimulated, peristaltic action is set up. Here again the ganglia present in the intestinal walls may be supposed to play a part; but this movement is much more simple than the beat of the heart, and as regards it, and more especially as regards the similar peristaltic action of the ureter, it becomes difficult to distinguish between a movement governed by ganglia, and one produced by direct stimulation of the muscular fibres. We have seen that the great distinction between a reflex action and a movement caused by direct stimulation of a nerve or of a muscle lies in the greater complexity of the former; and we may readily imagine, that by continued simplification of the central nervous machinery, the two might in the end become so much alike as to be almost indistinguishable.

In the vertebrate animal, then, the chief seat of reflex action is the spinal cord and brain. We say, "and brain," because, as we shall see later on, the brain, in addition to its automatism, is as busy a field of reflex action as the spinal cord.

Inhibition.—In speaking of reflex action, we took it for granted that the spinal cord was, at the moment of the arrival of the afferent impulses at the central nerve-cells, in a quiescent state; that the nerve-cells themselves were not engaged in any automatic action. We were justified in doing so because, as far as

the muscles generally of the body are concerned, the spinal cord is in a brainless frog perfectly quiescent; an afferent impulse reaching an ordinary nerve-cell of the spinal cord does not find it preoccupied in discharging efferent impulses to the muscles with which by means of nerve-fibres it is connected. But what happens when afferent impulses reach a nerve-cell or a group of nerve-cells already engaged in automatic action?

We heve already referred to an automatic respiratory centre in the medulla oblongata. We may here premise what we shall show more in detail hereafter, that the pneumogastric nerve is peculiarly associated as an afferent nerve with this respiratory centre. Now if the central end of the divided pneumogastric be stimulated at the time when the respiratory centre is engaged in its accustomed rhythmic action, sending out complex coördinated impulses of inspiration (and of expiration) at regular intervals, one of two things may happen, the choice of events being determined by circumstances which need not be considered here.

The most striking event, and the one which interests us now, is that the respiratory rhythm *is slowed or stopped altogether*. That is to say, afferent impulses which, under ordinary conditions, would, on reaching a quiescent nervous centre, give rise to movement, may, under certain conditions, when brought to bear on an already active automatic nervous centre, check or stop movement by interfering with the production of efferent impulses in that centre. This stopping or checking an already present action is spoken of as an "inhibition;" and the effect of the pneumogastric in this way on the respiratory centre is spoken of as "the inhibitory action of the pneumogastric on the respiratory centre."

The other event is that the respiratory rhythm is accelerated. We shall hereafter discuss the explanation of the two events. We may, however, state that according to one view the pneumogastric contains among its afferent fibres two sets, which are either of a different nature from each other, or are so differently connected with the respiratory centre, that impulses arriving along one stop, while those arriving along the other quicken the action of that centre. Hence, the one set is called "inhibitory," the other "accelerating" or "augmenting" fibres. But we are concerned at present only with the fact that the stimulation of a nerve may produce either inhibitory or augmentative effects.

Similarly the vaso-motor centre in the medulla may, by impulses arriving along various afferent tracts, be inhibited, during which the muscular walls of various arteries are relaxed; or augmented, whereby the tonic contraction of various arteries is increased.

The most striking instance of inhibition is offered by the heart. If when the heart is beating well and regularly, the pneumogastric be divided, and the peripheral portion be stimulated even for a very short time with an interrupted current, the heart is immediately brought to a standstill. Its beats are arrested, it lies perfectly flaccid and motionless, and it is not till after some little time that it recommences its beat. Here, again, it is usually said that the pneumogastric contains efferent cardio-inhibitory fibres, impulses passing along which from the medulla stop the automatic actions of the cardiac ganglia; the respiratory inhibitory fibres of the same nerve are afferent—*i. e.*, impulses pass along them up to the medulla. [Recent experiments seem to indicate that quinine diminishes reflex action mainly by a stimulation of the cardiac peripheries of the pneumogastric nerves.]

Though inhibition is most clearly seen in the case of automatic actions, other actions may be similarly inhibited. Thus, as we shall see later on, the reflex actions of the spinal cord may, by appropriate means, be inhibited.

To sum up, then, the most fundamental properties of nervous tissues.

Nerve-fibres are concerned in the propagation only, not in the origination or transformation of nervous impulses. As far as is at present known, impulses are propagated in the same manner along both sensory and motor nerves. Sensory impulses differ from motor impulses inasmuch as the former are generated in sensory organs, and pass up to the central nervous cells, while the latter pass from the central nervous cells to the muscles or to some other peripheral organs.

The operations of the nerve-cells are either automatic or reflex. In both an automatic and a reflex action, the diversity and the coördination of the impulses are determined by the condition of the nerve-cells. During the passage of an impulse along a nerve-fibre, there is no augmentation of energy; in passing through a nerve-cell, the augmentation may be, and generally is, most considerable.

When afferent impulses reach a centre already in action, the activity of that centre may, according to circumstances, be either depressed or exalted, may be "inhibited" or "augmented."

CHAPTER IV

THE VASCULAR MECHANISM.

In order that the blood may be a satisfactory medium of communication between all the tissues of the body, two things are necessary. In the first place, there must be through all parts of the body a flow of blood, of a certain rapidity and general constancy. In the second place, this flow must be susceptible of both general and local modifications. In order that any tissue or organ may readily adapt itself to changes of circumstances (action, repose, etc.), it is of advantage that the quantity of blood passing to it should be not absolutely constant, but capable of variation. In order that the material equilibrium of the body may be maintained as exactly as possible, it is desirable that the loading of the blood with substances proceeding from the unwonted activity of any one tissue, should be accompanied by a greater flow of blood through some excretory or metabolic tissue by which these substances may be removed. Similarly it is of advantage to the body that the general flow of blood should in some circumstances be more energetic, and in others less so, than normal.

The first of these conditions is dependent on the mechanical and physical properties of the vascular mechanism; and the problems connected with it are almost exclusively mechanical or physical problems. The second of these conditions depends on the intervention of the nervous system; and the problems connected with it are essentially physiological problems.

I. THE PHYSICAL PHENOMENA OF THE CIRCULATION.

The apparatus concerned in the maintenance of the normal flow is composed of the following factors:

1. The heart, beating rhythmically by virtue of its contractility and intrinsic mechanisms, and at each beat discharging a certain quantity of blood into the aorta. For simplicity's sake we omit for the present the pulmonary circulation. [For the physiological anatomy of the heart, see subsequent pages.]

2. The arteries, highly elastic throughout, with a circular

muscular element increasing in relative importance as the arteries diminish in size. It must not be forgotten that the muscular element is also elastic.

[The walls of the arteries consist of three coats, called respectively the internal, middle, and external. The *inner*, or serous coat, consists of an internal layer of ovoid or fusiform, nucleated epithelial cells, resting upon a longitudinal layer of elastic fibres, which, on account of its reticulated appearance, is termed the *fenestrated membrane.* In the middle-sized arteries the inner coat is increased in thickness by the addition of connective tissue and elastic fibres between the epithelium layer and the fenestrated membrane.

The *middle* or muscular coat varies both in character and thickness according to the size of the vessel. In the smallest arteries this coat may be altogether absent, or merely exist as a delicate muscular layer. In large arteries there may be three or four muscular layers. In still larger vessels, like the femoral, numerous alternate layers of elastic and muscular tissues are present. In the great vessels of the heart the elastic tissue much predominates, the muscular element being proportionately less. The general arrangement of the fibres of the middle coat is in a transverse direction.

The *external* coat, or *tunica adventitia*, is composed principally of connective tissue, having intermingled with it a greater or less proportion of elastic fibres. In arteries of medium size, the external coat is composed of two layers, an internal elastic and a superimposed connective tissue. In smaller arteries, the elastic tissue entirely disappears, and the connective tissue alone forms the coat.

The arteries are generally enclosed in a fibro-areolar envelope, which is termed a sheath. The sheath is generally a prolongation or continuation of the fascia of the particular part through which the vessel runs or is distributed.

After an artery is ligated, if the ligature be severed and the vessel opened, it will be seen that the internal and middle coats have been ruptured, and that the external coat alone remains intact, by reason of its comparative toughness.

The principal interest to the physiologist in the anatomy of the arteries lies in the middle coat, which, on account of its muscular and elastic element, plays a very important part in the pulse, and in the passage of the current of blood through the body of the capillaries.]

When an artery divides, the united sectional area of the branches is, as a rule, larger than the sectional area of the stem. Thus, the collective capacity of the arteries is continually (and rapidly) increasing from the heart towards the capillaries. If

all the arterial branches were fused together, they would form a funnel, with its apex at the aorta. The united sectional area of the capillaries has been calculated by Vierordt to amount to several (eight?) hundred times that of the aorta.

3. The capillaries, channels of exceedingly small but variable size. [They average about the $\frac{1}{100}$ of a mm. in diameter, and pervade nearly all portions and tissues of the body, forming a

FIG. 31.
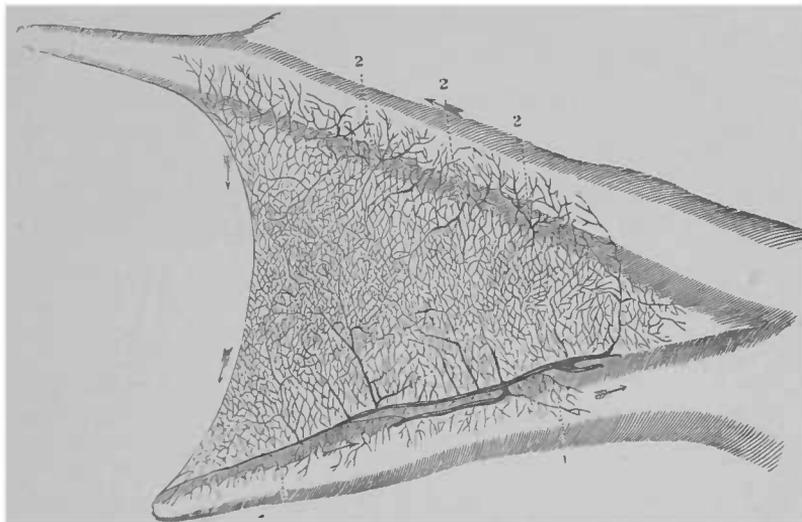
WEB OF A FROG'S FOOT.

Showing arterioles (2, 2, 2), beginnings of veins (1, 1, 1); with intermediate capillaries with their anastomoses. Arrows indicate the direction of the blood-current.

complex interlacement of anastomoses which are found between the terminal ends of the arterioles and the beginnings of the veins. (Fig. 31.)

In structure, the minutest capillaries are composed of a simple wall of ovoid, fusiform, or irregularly shaped nucleated epithelial cells. (Fig. 32.) In larger capillaries they have also a delicate, transparent, structureless basement-membrane. The lines of juncture of these epithelium cells can be brought out in a microscopical preparation with silver nitrate, which stains them black.

The form and intricacy of the capillary plexuses in the different tissues depend principally upon the functional relation which the blood bears to the part, and to the molecular arrangement of the cells composing the organ or tissue. Thus, where respiratory changes in the blood are most active, the plexuses are relatively

more intricate.   This is also the case in the glands, where the
blood-supply is necessarily very great.   Where the vessels merely
convey blood for nutritive purposes, the plexuses are much sim-
plified.   Four of the different forms of capillary meshes, which

FIG. 32.
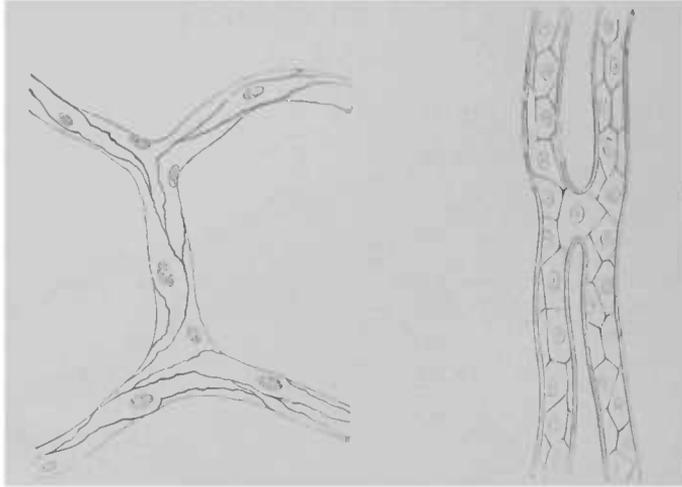
A. Fine capillaries from the mesentery.   B. Capillaries of larger size and with thicker walls,
from the pecten of the eye of a bird.

are dependent principally upon peculiarities in the molecular
arrangement of the tissue elements, are shown in the accompany-
ing Figs. 33, 34, 35, 36.   Thus, around the follicles of mucous
membrane, the capillary meshes are very much elongated; in

FIG. 33.
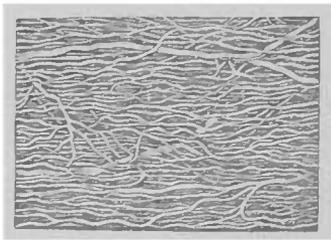
Distribution of Capillaries in Muscle.

FIG. 34.
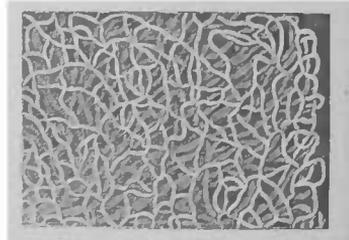
Capillary Network around Fat-cells.

the skin of the finger they are more or less rounded, etc.]   Their
walls are elastic as shown by their behavior during the passage
of blood-corpuscles through them), exceedingly thin and per-
meable.   They are permeable both in the sense of allowing fluids

to pass through them by osmosis, and also in the sense of allow-
ing white and red corpuscles to traverse them. The small arteries
and veins, which gradually pass into and from the capillaries
properly so called, are similarly permeable—the more so, the
smaller they are.

4. [*The Veins.*—The coats of the veins are three in number,
similar to those of the arteries, the principal difference to the

FIG. 35.
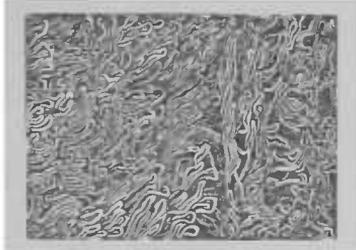
Distribution of Capillaries on the Surface of
the Skin of the Finger.

FIG. 36.
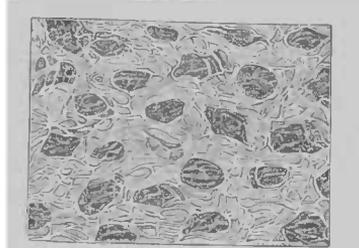
Distribution of Capillaries around Follicles
of Mucous Membrane.

physiologist being in the component parts of the middle coat.
This coat in the veins contains a larger proportion of connective
tissue, with a smaller proportion of muscular and elastic fibres.
An artery, when empty, retains its rounded form; a vein imme-
diately collapses. This is due to the abundance or deficiency of
the yellow elastic tissue element, as the case may be.

The arteries are active agents in the circulation of the blood;
the veins are passive, and serve as channels to convey the blood
from the capillaries to the internal organs.

At intervals, on the internal surface of most of the veins pro-
jecting semicircular pouches are seen, arranged in pairs, opposite
each other. These pouches are the *valves* (Figs. 37, 38) of the
veins, and are formed by reduplications of the internal and
middle coats. Their function is to prevent a reflux of blood.
The veins form numerous anastomoses; if, therefore, a vessel
becomes filled, and the current stagnated, the blood will take a
different channel, as is shown in Fig. 38. These bloodvessels
are all lined with pavement-epithelium.

The walls of the arteries and veins are supplied with nourish-
ment by small vessels, which are termed the *vasa vasorum*. These
vessels form capillary plexuses in the middle and external coats.
The portion of the inner coat upon which the epithelial lining
rests, as well as the epithelium, probably receives its nourishment
from the blood which courses the vessel. The arteries are sup-
plied with nerves from both the sympathetic and cerebro-spinal

systems; principally from the former.   As a general rule, nerves have not been found in the venous walls.]

The veins, less elastic than the arteries (the difference being especially marked when both sets of vessels become distended), and with a very variable muscular element.   The united sectional area of the veins diminishes from the capillaries to the

[FIG. 37.   [FIG. 38.
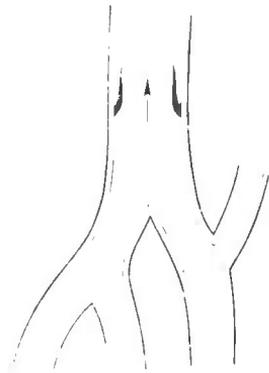
Vein with valves open.   After DALTON.]   Vein with valves closed ; stream of blood passing
                                              off by lateral channel.   After DALTON.]
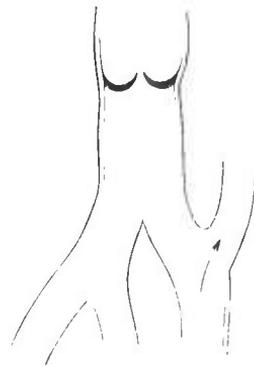
heart, thus resembling the arteries ; but the united sectional area of the venæ cavæ at their junction with the right auricle is greater than that of the aorta at its origin.   (The proportion is nearly two to one.)   The total capacity of the veins is similarly much greater than that of the arteries.   The veins alone can hold the total mass of blood which in life is distributed over both arteries and veins.   Indeed, nearly the whole blood is capable of being received by what is merely a part of the venous system, viz., the vena portæ and its branches.   Such veins as are, for various reasons, liable to a reflux of blood from the heart towards the capillaries are provided with valves.

SEC. 1.—MAIN GENERAL FACTS OF THE CIRCULATION.

1. *The Capillary Circulation.*

If the web of a frog's foot be examined with a microscope, the blood, as judged of by the movements of the corpuscles, is seen to be passing in a continuous stream from the small arteries through the capillaries to the veins (Fig. 39).   The velocity is greater in the arteries than in the veins, and greater in both

than in the capillaries. In the arteries faint pulsations, synchronous with the heart's beat, are occasionally visible, and not unfrequently variations in velocity and in the distribution of the blood, due to causes which will be hereafter discussed, are witnessed from time to time.

The flow through the smaller capillaries is very variable. Sometimes the corpuscles are seen passing through the channel

[FIG. 39.
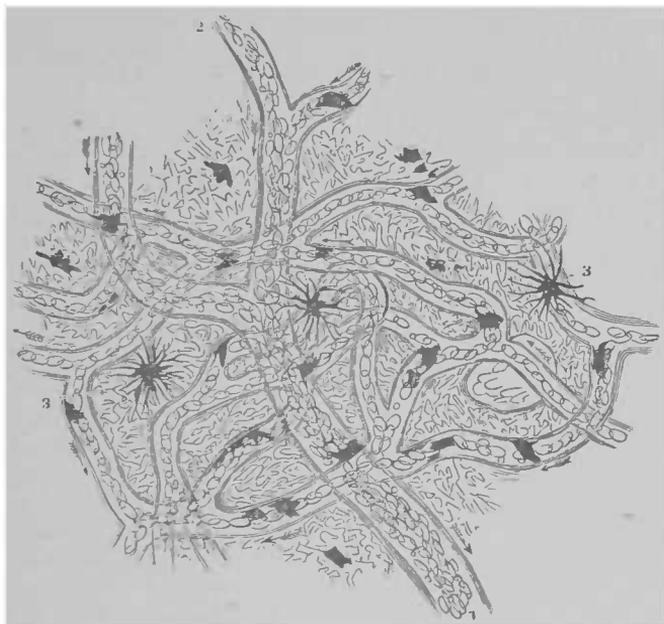
Capillary Plexus in a portion of the Web of a Frog's Foot, magnified 110 diameters; 1, trunk of vein ; 2, 2, 2, its branches arising from the arterial capillaries ; 3, 3, pigment-cells.]

in single file with great regularity ; at other times they may be few and far between. Sometimes the corpuscle may remain stationary at the entrance into a capillary, the channel itself being for some little distance entirely free from corpuscles. Any one of these conditions readily passes into another, and especially with a somewhat feeble circulation, instances of all of them may be seen in the same field of the microscope. It is only when the vessels of the web are unusually full of blood that all the capillaries can be seen equally filled with corpuscles. The long oval red corpuscle moves with its long axis parallel to the stream, frequently rotating on its long axis and sometimes on its short axis. The flexibility and elasticity of a corpuscle are well seen

when it is being driven into a capillary narrower than itself, or
when it becomes temporarily lodged at the angle between two
diverging channels.   The small mammalian corpuscles rotate
largely as they are driven along.

In the web of the frog's foot the average velocity with which
the corpuscles move may be put down as about half a millimetre
in a second.   In the human retina, the velocity of the capillary
flow has, by indirect methods, been estimated at 0.75 mm. per
second.   The movement of the blood in the capillaries is very
slow, compared with that in the arteries or even in the veins.

In the larger capillaries, and especially in the small arteries
and veins which permit the passage of several corpuscles abreast,
it is observed that the red corpuscles run in the middle of the
channel, forming a colored core, between which and the sides of
the vessel all round is a layer, which has been called the "inert
layer," or better, the "plasmatic layer," containing no red cor-
puscles.   This division into a plasmatic layer and an axial
stream is due to the fact that in any stream passing through a
closed channel the friction is greatest at the immediate sides,
and diminishes towards the axis.   The corpuscles pass where
the friction is least, in the axis.   A quite similar axial core is
seen when any fine particles are driven with a sufficient velocity
in a stream of fluid through a narrow tube.   As the velocity is
diminished the axial core becomes less marked and disappears.
In the plasmatic layer, especially in that of the veins, are fre-
quently seen white corpuscles, sometimes clinging to the sides of
the vessel, sometimes rolling slowly along, and in general moving
irregularly, and often in jerks.   The greater the velocity of the
flow of blood, the fewer the white corpuscles in the plasmatic
layer, and with a very rapid flow they, as well as the red cor-
puscles, may be all confined to the axial stream.   The presence
of the white corpuscles in the plasmatic layer has been attributed
to their being specifically lighter than the red corpuscles, it
being affirmed that when fine particles of two kinds, one lighter
than the other, are driven through a narrow tube, the heavier
particles flow in the axis, and the lighter in the more peripheral
portions of the stream.   This, however, has been disputed, and
the phenomenon explained by the white corpuscles being dis-
tinctly more adhesive than the red, as is seen by the manner in
which they become fixed to the glass slide and cover-slip when
a drop of blood is mounted for microscopical examination.   By
reason of this adhesiveness which possibly may vary with the
varying nutritive conditions of the corpuscles and of the blood-
vessels, the white corpuscles, it is urged, become temporarily
attached to the walls of the vessel, and consequently appear in
the plasmatic layer.
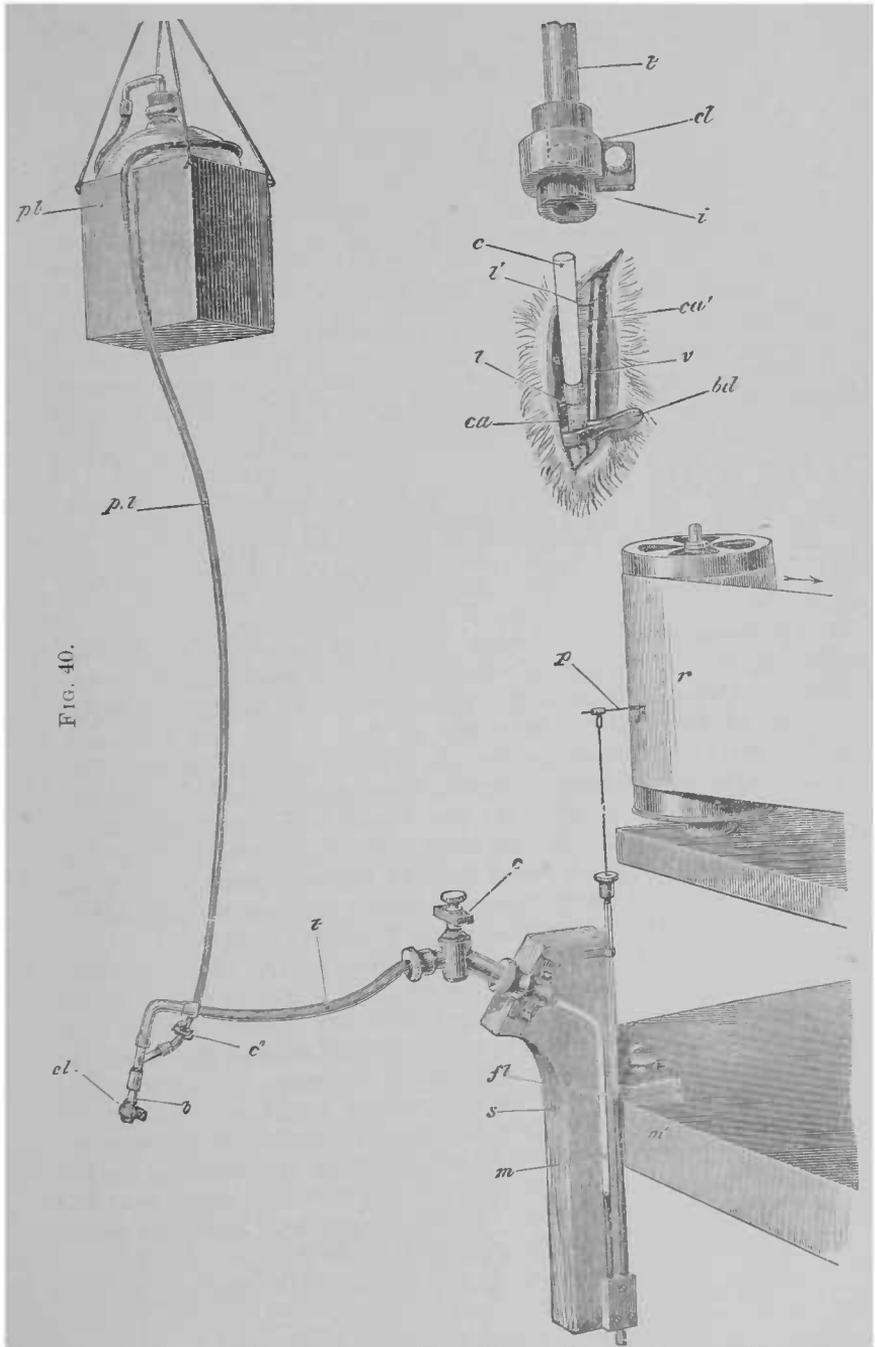
FIG. 40.

At the upper right-hand corner is seen, on an enlarged scale, the carotid artery, clamped by the forceps *bd*, with the vagus nerve = lying by its side. The artery has been ligatured at *l'* and the glass canula *c* has been introduced into the artery between the ligature *l'* and the forceps *bd*, and secured in position by the ligature *l*. The shrunken artery on the distal side of the canula is seen at *ca'*.

p.b. is a box containing a bottle holding a saturated solution of sodium carbonate or a solution of sodium bicarbonate of sp. gr. 1083, and capable of being raised or lowered at pleasure. The solution flows by the tube *p.t.* regulated by the clamp *c''*, into the tube *t*. A syringe, with a stopcock, may be substituted for the bottle, and attached at *c''*. This, indeed, is in many respects a more convenient plan. The tube *t* is connected with the leaden tube *t*, and the stopcock *c* with the manometer, of which *m* is the descending and *m'* the ascending limb, and *s* the support. The mercury in the ascending limb bears on its surface the float *fl.*, a long rod attached to which is fitted with the pen *p*, writing on the recording surface *r*. The clamp *cl.*, at the end of the tube *t*, has an arrangement shown on a larger scale at the right-hand upper corner.

The descending tube *m* of the manometer, and the tube *t* being completely filled along its whole length with fluid to the exclusion of all air, the canula *c* is filled with fluid, slipped into the open end of the thick-walled India-rubber tube *i* until it meets the tube *t* (whose position within the India-rubber tube is shown by the dotted lines), and is then securely fixed in this position by the clamp *cl.*

The stopcocks *c* and *c''* are now opened, and the pressure-bottle raised or fluid driven in by the syringe until the mercury in the manometer is raised to the required height. The clamp *c''* is then closed, and the forceps *bd* removed from the artery. The pressure of the blood in the carotid *ca* is, in consequence, brought to bear through *t* upon the mercury in the manometer.

The resistance to the flow of blood thus caused by the friction generated in so many minute passages, is one of the most important physical facts in the circulation. In the large arteries the friction is small; it increases as they divide, and receives a very great addition in the minute arteries and capillaries. We may speak of it, therefore, as the "peripheral friction" and the resistance which it offers, as the "peripheral resistance." It need perhaps hardly be said that this peripheral friction not only opposes the flow of blood through the capillaries themselves, but working backwards along the whole arterial system, has to be met by the heart at each systole of the ventricle.

It is well known that when any portion of the skin is pressed upon, it becomes pale and bloodless; this is due to the pressure driving the blood out of the capillaries and minute vessels, and preventing any fresh blood entering into them. By carefully investigating the amount of pressure necessary to prevent the blood entering the capillaries and minute arteries of the web of the frog's foot, or of the skin beneath the nail in man or elsewhere, the internal pressure which the blood is exercising on the walls of the capillaries and minute arteries and veins, may be approximately determined. In the frog's web this has been found to be equal to about 7 or 11 mm. mercury.

2. *The Flow in the Arteries.*

When an artery is severed, the flow from the proximal section is not equable, but comes in jets, which correspond to the heart-beats, though the flow does not cease between the jets. The blood is ejected with considerable force; thus, in Dr. Stephen Hales's experiments, when the crural artery of a mare was severed, the jet, even after much loss of blood, rose to the height of two feet. The larger the artery and the nearer to the heart, the greater the force with which the blood issues, and the more marked the .intermittence of the flow. The flow from the distal section may be very slight, or may take place with considerable force and marked intermittence, according to the amount of collateral communication.

Arterial Pressure.—If a mercury (or other) manometer (Fig. 40, m, m') be connected with a large artery—*e. g.*, the carotid, in such a way that while the blood is allowed to flow uninterruptedly along the artery, there is free communication between the interior of the artery and the proximal (descending) limb of the man-ometer, the following facts are observed :

Immediately that communication is established between the interior of the artery and the manometer, blood rushes from the former into the latter, driving some of the mercury from the descending limb into the ascending limb, and thus causing the level of the mercury in the ascending limb to rise rapidly. This rise is marked by jerks corresponding with the heart-beats. Having reached a certain level, the mercury ceases to rise any more. It does not, however, remain absolutely at rest, but undergoes oscillations; it keeps rising and falling. Each rise, which is very slight compared with the total height to which the mercury has risen, has the same rhythm as the systole of the ventricle. Similarly, each fall corresponds with the diastole.

If a float, swimming on the top of the mercury in the ascending limb of the manometer, and bearing a brush or other marker, be brought to bear on a travelling surface, some such tracing as that represented in Fig. 41 will be described. Each of the smaller curves (p, p) corresponds to a heart-beat, the rise corresponding to the systole and the fall to the diastole of the ventricle. The larger undulations (r, r) in the tracing, which are respiratory in origin, will be discussed hereafter. This observation teaches us that the blood, as it is passing along the carotid artery, is capable of supporting a column of mercury of a certain height (measured

by the difference of level between the mercury in the descending
limb, and that in the ascending limb, of the manometer), when
the mercury is placed in direct communication with the side of
the stream of blood.   In other words, the blood, as it passes
through the artery, exerts a lateral pressure on the sides of the
artery, equal to so many millimetres of mercury.   In this lateral
pressure we have further to distinguish between the slighter oscil-
lations corresponding with the heart-beats, and a *mean pressure*
above and below which the oscillations range.   A similar mean
pressure with similar oscillations is found, when any artery of

<div align="center">FIG. 41.</div>
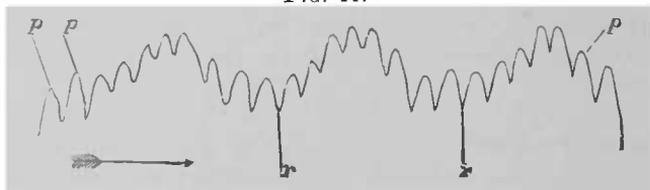
<div align="center">TRACING OF ARTERIAL PRESSURE WITH A MERCURY MANOMETER.</div>

The smaller curves $p\,p$ are the pulse-curves.   The space from r to r embraces a respiratory
undulation.   The tracing is taken from a dog, and the irregularities visible in it are those
frequently met with in this animal.

the body is examined in the same way.   In all arteries the blood
exerts a certain pressure on the walls of the vessels which contain
it.   This is generally spoken of as arterial pressure or arterial
tension, and the pressure in the aorta of any animal is usually
spoken of as its blood-pressure.

Description of Experiment.—The carotid, or other vessel, is laid
bare, clamped in two places, and divided between the clamps.   Into the
cut ends is inserted a hollow ⊢ piece of the same bore as the artery, the
cross portion forming the continuation of the artery.   The other portion
is connected by means of a non-elastic flexible tube with the descending
limb of the manometer.   In order to avoid loss of blood, fluid is injected
into the flexible tube until the mercury in the manometer stands a very
little below what may be beforehand guessed at as the probable mean
pressure.   The fluid chosen is a saturated solution of sodium carbonate,
or a solution of sodium bicarbonate of sp. gr. 1083, with a view to hinder
the coagulation of the blood in the tube.   When the clamps are removed
from the artery, the blood rushes through the cross of the ⊢ piece.   Some
passes into the side limb of the ⊢ piece, and continues to do so until the
mean pressure is quite reached.   Thenceforward there is no more escape;
but the pressure continues in the interior of the ⊢ piece, is transmitted
along the connecting tube to the manometer, and the mercury continues
to stand at a height indicative of the mean pressure, with oscillations
corresponding to the heart's beats.   Practically, the use of the ⊢ piece is

found inconvenient. Accordingly, the general custom is to ligature the artery, to place a clamp on the vessel on the proximal side of the ligature, and to introduce a straight canula (Fig. 40, *c*), connected with the manometer, into the artery between the ligature and the clamp, and to secure it in that position. In this case, on loosing the clamp, the whole column of blood in the artery is brought to bear on the manometer, and the tracings taken illustrate the lateral pressure not of the artery in which the canula has been placed, but of the vessel (aorta, etc., as the case may be) of which it is itself a branch.

Tracings of the movements of the column of mercury in the manometer may be taken either on a smoked surface of a revolving cylinder (Fig. 11), or by means of a brush and ink on a continuous roll of paper, as in the more complex kymograph (Fig. 42).

Fig. 42.
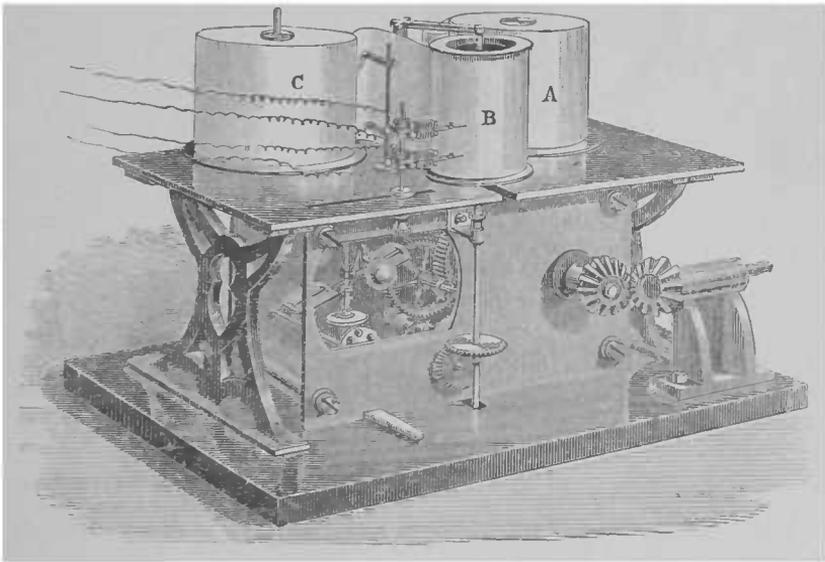
LARGE KYMOGRAPH WITH CONTINUOUS ROLL OF PAPER.

The **clock-work machinery**, some of the details of which are seen, unrolls the paper from the roll C, carries it smoothly over the cylinder B, and then winds it up into the roll A.

Two electromagnetic **markers** are seen in the position in which they record their movements on the paper as it travels over B. The manometer, or any other recording instrument used, can be fixed either in the notch immediately in front of B, or in any other position that may be desired.

In such a mercury manometer, the inertia of the mercury obscures many of the features of the minor curves caused by the heart-beats. When, therefore, these, rather than variations in the mean pressure, are being studied, [it is advisable to have recourse to the spring manometer (Fig. 43), introduced by Fick. In using this instrument, the tube *t*,

14*

FIG. 43.
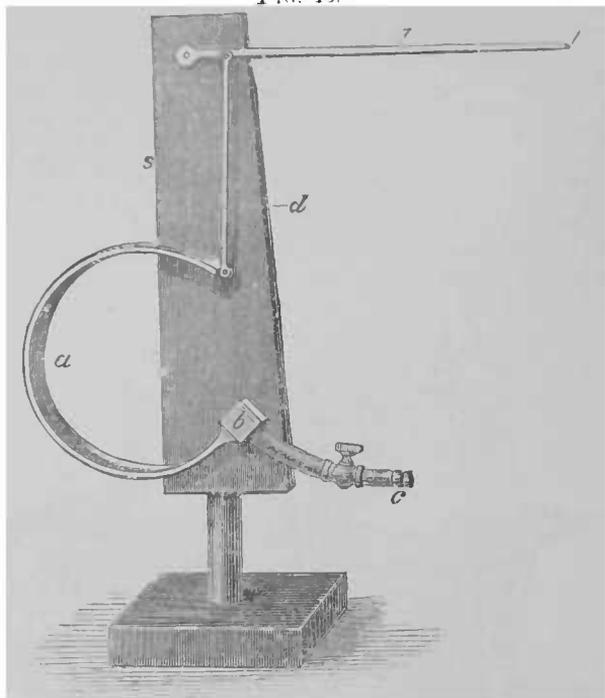
DIAGRAM ILLUSTRATING FICK'S SPRING MANOMETER.

This consists essentially of a hollow, flattened, German-silver tube (*a*), curved in the form of an incomplete circle. The lower open end *b*, firmly fastened to the stand *s*, is connected with a tube (*c*), bearing a stopcock To the upper closed end is attached a light upright rod (*d*), connected with the writing-lever *l*.

Through the tube *c* the hollow curved spring is filled with alcohol, and the stopcock closed. The tube *c* is then connected with the artery by means of a non-elastic flexible (leaden) tube filled with sodium carbonate solution On opening the stopcock, the variations of pressure of the blood in the artery are communicated to the fluid in the hollow curved spring; at each increase of pressure, the spring expands, and the movements of the free end are transferred by *d* to the writing-lever *l*. The instrument as generally sent out also bears an arrangement (not shown in the diagram) by which the point of the lever describes a straight instead of a curved line. The spring manometer is exceedingly useful where it is desirable to investigate closely the variations in the form of the pressure-curve. In order to measure the amount of variation, the instrument must be experimentally graduated.

Fig. 41, is connected with the tube *c*, Fig. 43. A tracing obtained by Fick's manometer is shown in Fig. 44.]

[FIG. 44.
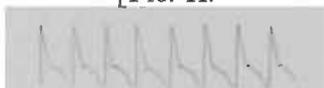
Normal arterial tracing obtained with the Spring Manometer ; dog under curara]

The average pressure of the blood in the same body is greatest in the largest arteries, and diminishes as the arteries get less ; but the fall is a very gradual one until the smallest arteries are reached, in which it becomes very rapid. In the carotid of the horse, the mean arterial pressure varies from 150 to 200 mm. of mercury ; of the dog, from 100 to 175 ; of the rabbit, from 50 to 90. In the carotid of man, it probably amounts to 150 or 200.

Since in all arteries the blood is pressing on the arterial walls with some considerable force, all the arteries must be in a state of permanent distention, so long as blood is flowing through them from the heart. When the blood-current is cut off, as by a ligature, this expansion or distention disappears.

Not only is there a permanent expansion corresponding to the mean pressure, but just as the mercury in the manometer rises above the level of mean pressure at each systole of the heart, and falls below it at each diastole, so at any spot in the artery there is for each heart-beat a temporary expansion succeeded by temporary contraction, the diameter of the artery in its temporary expansions and contractions oscillating, in correspondence with the oscillations of the manometer, beyond and within the diameter of permanent expansion. These temporary expansions constitute what is called the pulse, and will be discussed more fully hereafter.

The Velocity of the Flow.—When even a small artery is severed, a considerable quantity of blood escapes from the proximal cut end in a very short space of time. That is to say, the blood moves in the arteries from the heart to the capillaries with a very considerable velocity. By various methods, this velocity of the blood current has been measured at different parts of the arterial system ; the results, owing to imperfections in the methods employed, cannot be regarded as satisfactorily exact, but may be accepted as approximately true. The velocity of the arterial stream is greatest in the largest arteries, and diminishes from the heart to the capillaries, *pari passu* with the increase of the width of the bed—*i. e.*, with the increase of the united sectional area.

Methods.—The Hæmadromometer of Volkmann. (Fig. 45.) An artery—*e. g.*, a carotid, is clamped in two places, and divided between the clamps. Two canulæ, of a bore as nearly equal as possible to that of the artery, or of a known bore, are inserted in the two ends. The two canulæ are connected by means of two stop-cocks, which work together, with the two ends of a long glass tube, bent in the shape of a U, and filled with normal saline solution, or with a colored innocuous fluid. The clamps on the artery being released, a turn of the stop-cocks permits the blood to enter the proximal end of the long U tube, along which it

courses, driving the fluid out into the artery through the distal end. Attached to the tube is a graduated scale, by means of which the velocity with which the blood flows *along the tube* may be read off. Even supposing the canula to be of the same bore as the artery, it is evident that the conditions of the flow through the tube are such as will only admit of the result thus gained being considered as an approximative estimation of the real velocity in the artery itself.

[Fig. 45.
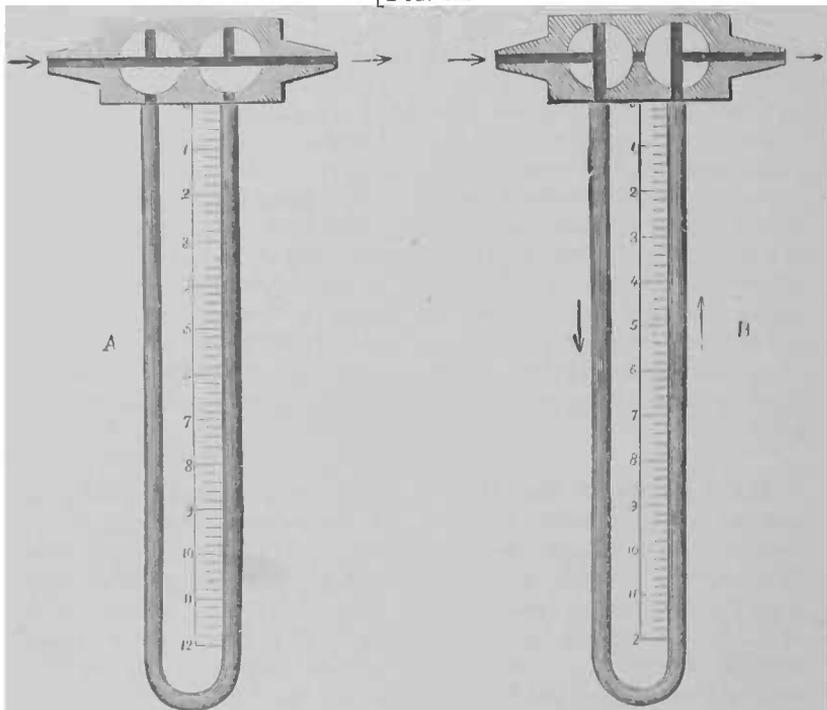
VOLKMANN'S HÆMADROMOMETER.

The conical portions of the instrument are inserted in the cut ends of a vein or artery. By a simple arrangement of a double stopcock, the blood-current can be made to pass immediately through the transverse arm, as in A, or to pass through the graduated U-shaped tube, as in B.]

The Rheometer (Stromuhr) of Ludwig. This consists of two glass bulbs (A and B, Fig. 46), communicating above with each other and with the common tube C, by which they can be filled. Their lower ends are fixed in the metal disk D, which can be made to rotate, through two right angles, round the lower disk E. In the upper disk are two holes, a and b, continuous with A and B, respectively, and in the lower disk are two similar holes, a' and b', similarly continuous with the tubes H and G. Hence, in the position of the disks shown in the figure, the tube G is continuous through the two disks with the bulb A, and the tube H with the bulb B. On turning the disk D through two right angles, the tube G

becomes continuous with B instead of A, and the tube H with A instead of B. There is a further arrangement, omitted from the figure for the sake of simplicity, by which, when the disk D is turned through one instead of two right angles from either of the above positions, G becomes directly continuous with H, both being completely shut off from the bulbs.

FIG. 46.
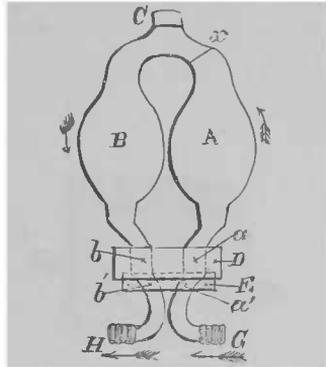
DIAGRAMMATIC REPRESENTATION OF LUDWIG'S STROMUHR

The ends of the tubes H and G are made to fit exactly into two canulæ inserted into two cut ends of the artery about to be experimented upon, and having a bore as nearly equal as possible to that of the artery.

The method of experimenting is as follows: The disk D being placed in the intermediate position, so that a and b are both cut off from a' and b', the bulb A is filled with pure olive oil up to the mark x, and the bulb B, the rest of A, and the junction C, with defibrinated blood; and C is then clamped. The tubes H and G are also filled with defibrinated blood, and G is inserted into the canula of the central, H into that of the peripheral end of the artery. On removing the clamps from the artery the blood flows through G to H, and so back into the artery. The observation now begins by turning the disk D into the position shown in the figure; the blood then flows into A, driving the oil there contained out before it into the bulb B, in the direction of the arrow, the defibrinated blood previously present in B passing by H into the artery, and so into the system. At the moment that the blood is seen to rise to the mark x, the disk D is, with all possible rapidity, turned through two right angles, and thus the bulb B, now largely filled with oil, placed in communication with G. The blood-stream now drives the oil back into A, and the new blood in A through H into the artery. As soon as the oil has wholly returned to its original position, the disk is again turned round, and A once more placed in communication with G, and the oil once more driven from A to B. And this is repeated several times, indeed generally, until the clotting of the blood or the admixture of the oil with the blood puts an end to the experiment. Thus the flow of blood is used to fill alternately with blood or oil the space of the bulb A, whose cavity as far as the mark x has been exactly measured; hence, if the number of times in any given time the disk D has to be turned round be known, the number of times A has been filled is also known, and thus the quantity of blood which has passed in that time through the canula connected with the tube G is directly measured. For instance, supposing that the

quantity held by the bulb *A* when filled up to the mark *a* is 5 c.c., and supposing that from the moment of allowing the first 5 c.c. of blood to begin to enter the tube to the moment when the escape of the last 5 c.c. from the artery into the tube was complete, 100 seconds had elapsed, during which time 5 c.c. had been received 10 times into the tube from the artery (all but the last 5 c.c. being returned into the distal portion of the artery), obviously 0.5 c.c. of blood had flowed from the proximal section of the artery in one second. Hence, supposing that the diameter of the canula (and of the artery, they being the same) were 2 mm., with a sectional area therefore of 3.14 square mm., an outflow through the section of 0.5 c.c. or 500 c.mm. in a second would give $\left(\frac{500}{3.14}\right)$, a velocity of about 159 mm. in a second.

[FIG. 47.
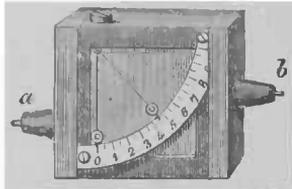
HÆMATOCHOMETER OF VIERORDT. *a* and *b* mouthpiece.]

The Hæmatachometer of Vierordt is constructed on the principle of measuring the velocity of the current by observing the amount of deviation undergone by a pendulum, the free end of which hangs loosely in the stream. A square or rectangular chamber, one side of which is of glass and marked with a graduated scale in the form of an arc of a circle, is connected by means of two short tubes with the two cut ends of an artery ; the blood consequently flows from the proximal (central) portion

[FIG. 48.
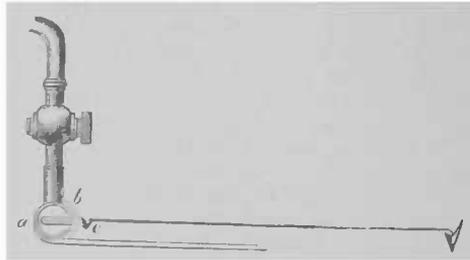
M. LORTET'S INSTRUMENT

a, tube open at both ends: *b*, square opening closed by India-rubber membrane, which is pierced by the lever, the thick end of which projects into the vessel]

of the artery through the chamber into the distal portion of the artery. Within the chamber, and suspended from its roof, is a short pendulum, which, when the blood-stream is cut off from the chamber, hangs motionless in a vertical position, but when the blood is allowed to flow through the chamber, is driven by the force of the current out of its position of rest. The pendulum is so placed that a marker attached to its free end travels close to the inner surface of the glass side along the arc of the

graduated side. Hence the amount of deviation from a vertical position may easily be read off on the scale from the outside. The graduation of the scale having been carried out by experimenting with streams of known velocity, the velocity can at once be calculated from the amount of deviation.

An instrument based on the same principle has been invented by Chauveau and improved by Lortet. In this the part which corresponds to the pendulum in Vierordt's instrument is prolonged outside the chamber, and thus the portion within the chamber is made to form the short arm of a lever, the fulcrum of which is at the point where the wall of the chamber is traversed, and the long arm of which projects outside. A somewhat wide tube, the wall of which is at one point composed of an India-rubber membrane, is introduced between the two cut ends of an artery. A long light lever pierces the India-rubber membrane. The short expanded arm of this lever projecting within the tube is moved on its fulcrum in the India-rubber ring by the current of blood passing through the tube, the greater the velocity of the current, the larger being the excursion of the lever. The movements of the short arm give rise to corresponding movements in the opposite direction of the long arm outside the tube, and these, by means of a marker attached to the end of the long arm, may be directly inscribed on a recording surface. This instrument is very well adapted to observing changes in the velocity of the flow. In determining actual velocities, for which purpose it has to be experimentally graduated, it is not so useful.

In the horse, Volkmann found the velocity of the stream to be in the carotid artery about 300 mm., in the maxillary artery 165 mm., and in the metatarsal artery 56 mm. in the second. Chauveau determined the velocity in the carotid of the horse to vary from 520 to 150 mm. per second at each beat of the heart, flowing at the former rate during the height of each pulse-expansion, and at the latter in the interval between each two beats. Ludwig and Dogiel found the velocity in the dog and in the rabbit to vary within very wide limits, not only in different arteries, but in the same artery under different circumstances. Thus while in the carotid of the rabbit it may be said to vary from 100 to 200 mm. per second, and in the carotid of the dog from 200 to 500 mm. per second, both these limits are frequently passed.

3. *The Flow in the Veins.*

When a vein is severed, the flow from the distal cut end (*i. e.*, the end nearest the capillaries) is continuous, the blood is ejected with comparatively little force, and with no great velocity.

When a vein is connected with a manometer, the lateral pressure is found to be very small ; it is greater in the veins further from the heart than in those nearer the heart. In the former it is much less than that of the small arteries, and in the latter amounts only to a few millimetres of mercury. Indeed, in the immediate neighborhood of the heart the pressure may (during

the inspiratory movement) become negative—*i. e.*, when the manometer is brought into connection with the interior of the vein, the mercury in the distal limb falls, instead of, as in the case of an artery, rising.

In the case of most veins, under ordinary circumstances the mercury of a manometer connected with a vein does not show any of those pulse-oscillations which are so striking in the arteries. As a general rule, the pulse is seen on the arterial side only of the capillaries, though in special cases, under conditions which we shall study presently, it may make its way through the capillaries from the arteries to the small veins; and it is probable that in general a slight impulse does make its way right through the capillaries, but so feeble that it cannot be recognized by ordinary instruments save in special cases. Moreover, in the great veins near the heart, under certain circumstances at all events, the movements of that organ may make themselves felt as a so-called "venous pulse" transmitted in a backward direction along the veins from the heart. But these exceptional instances and these recurrent oscillations do not invalidate the truth of the general statement that the pulse is absent from the veins. The exact determination of venous pressure is attended with great experimental difficulties, and our knowledge in this direction is very incomplete; but in all probability the pressure in a vein varies within much wider limits than does the pressure in the corresponding artery.

In the small veins the velocity of the current, measured in the same way as in the case of the arteries, is very slight. It increases in the larger veins, corresponding to the diminution of the area of "the bed;" it is about 200 mm. per second in the jugular vein of the dog.

Thus the flow in the veins presents strong contrasts with that in the arteries. In the arteries, even in the smallest branches, there is a considerable mean pressure. In the veins, even in the small veins where it is largest, the mean pressure is very slight. In other words, there is always a difference of pressure tending to make the blood flow continuously from the arteries into the veins. A pulse is present in the arteries, but, with certain exceptions, absent in the veins. The velocity of the stream of blood in the arteries is considerable; in the small veins it is much less, but it increases in the larger trunks; for in both arteries and veins it corresponds with the area of the bed, diminishing in the former from the heart to the capillaries, and increasing in the latter from the capillaries to the heart.

Hydraulic Principles of the Circulation.

All the above phenomena are the simple results of an intermittent force (like that of the systole of the ventricle) working in a closed circuit of branching elastic tubes, so arranged that while the individual tubes first diminish (from the heart to the capillaries) and then increase (from the capillaries to the heart), the area of the bed first increases and then diminishes, the tubes together thus forming two cones placed base to base at the capillaries, with their apices converging to the heart. To this it must be added that the friction in the small arteries and capillaries, at the junction of the bases of the cones, offers a very great resistance to the flow of the blood through them. It is this peripheral resistance (in the minute arteries and capillaries, for the resistance offered by the friction in the larger vessels may, when compared with this, be practically neglected), reacting through the elastic walls of the arteries upon the intermittent force of the heart, which gives the circulation of the blood its peculiar features.

Circumstances Determining the Character of the Flow.—When fluid is driven by an intermittent force, as by a pump, through a perfectly rigid tube (or system of tubes), there escapes at each stroke of the pump from the distal end of the system just as much fluid as enters it at the proximal end. The escape, moreover, takes place at the same time as the entrance, since the time taken up by the transmission of the *shock* is so small, that it may be neglected. This result remains the same when any resistance to the flow is introduced into the system. The force of the pump remaining the same, the introduction of the resistance undoubtedly lessens the quantity issuing at the distal end at each stroke, but it does so simply by lessening the quantity entering at the proximal end; the income and outgo remain equal to each other, and occur at almost the same time. And what is true of the two ends, is also true of any part of the course of the system, so far, at all events, as the following proposition is concerned, that in a system of rigid tubes, either with or without an intercalated resistance, the flow caused by an intermittent force is, in every part of the tubes, intermittent synchronously with that force.

In a system of elastic tubes in which there is little resistance to the progress of the fluid, the flow caused by an intermittent force is also intermittent. The outgo being nearly as easy as the income, the elasticity of the walls of the tubes is scarcely at all called into play. These behave practically like rigid tubes.

When, however, sufficient resistance is introduced into any part
of the course, the fluid, being unable to pass by the resistance as
rapidly as it enters the system from the pump, tends to accumu-
late on the proximal side of the resistance. This it is able to do
by expanding the elastic walls of the tubes. At each stroke of
the pump a certain quantity of fluid enters the system at the
proximal end. Of this only a fraction can pass through the
resistance during the stroke. At the moment when the stroke
ceases, the rest still remains on the proximal side of the resist-
ance, the elastic tubes having expanded to receive it. During
the interval between this and the next stroke, the distended
elastic tubes, striving to return to their natural undistended con-
dition, press on this extra quantity of fluid which they contain
and tend to drive it past the resistance. Thus, in the rigid sys-
tem (and in the elastic system without resistance) there issues,
from the distal end of the system, at each stroke, just as much
fluid as enters it at the proximal end, while between the strokes
there is perfect quiet. In the elastic system with resistance, on
the contrary, the quantity which passes the resistance is only a
fraction of that which enters the system from the pump, the re-
mainder or a portion of the remainder continuing to pass during
the interval between the strokes. In the former case, the system
is no fuller at the end of the stroke than at the beginning; in
the latter case there is an accumulation of fluid between the
pump and the resistance, and a corresponding distention of that
part of the system, at the close of each stroke—an accumulation
and distention, however, which go on diminishing until the next
stroke comes. The amount of fluid thus remaining after the
stroke will depend on the amount of resistance in relation to the
force of the stroke, and on the distensibility of the tubes; and
the amount which passes the resistance before the next stroke
will depend on the degree of elastic reaction of which the tubes
are capable. Thus, if the resistance be very considerable in
relation to the force of the stroke, and the tubes very distensible,
only a small portion of the fluid will pass the resistance, the
greater part remaining lodged between the pump and the re-
sistance. If the elastic reaction be great, a large portion of this
will be passed on through the resistance before the next stroke
comes. In other words, the greater the resistance (in relation to
the force of the stroke), and the more the elastic force is brought
into play, the less intermittent, the more nearly continuous, will
be the flow on the far side of the resistance.

If the first stroke be succeeded by a second stroke before its
quantity of fluid has all passed by the resistance, there will be
an additional accumulation of fluid on the near side of the re-
sistance, an additional distention of the tubes, an additional strain

on their elastic powers, and, in consequence, the flow between this
second stroke and the third will be even more marked than that
between the first and the second, though all three strokes were
of the same force, the addition being due to the extra amount of
elastic force called into play. In fact, it is evident that, if there
be a sufficient store of elastic power to fall back upon, by con-
tinually repeating the strokes a state of things will be at last
arrived at, in which the elastic force, called into play by the con-
tinually increasing distention of the tubes on the near side of
the resistance, will be sufficient to drive through the resistance,
between each two strokes, just as much fluid as enters the near
end of the system at each stroke. In other words, the elastic
reaction of the walls of the tubes will have converted the inter-
mittent into a continuous flow. The flow on the far side of the
resistance is in this case not the direct result of the strokes of the
pump. All the force of the pump is spent, first in getting up,
and afterwards in keeping up, the overdistention of the tubes on
the near side of the resistance ; the cause of the continuous flow
lies in the overdistention of the tubes which leads them to empty
of themselves into the far side of the resistance, at such a rate,
that they discharge through the resistance during a stroke and
in the succeeding interval just as much as they receive from the
pump by the stroke itself.

This is exactly what takes place in the vascular system. The
friction in the minute arteries and capillaries presents a consider-
able resistance to the flow of blood through them into the small
veins. In consequence of this resistance, the force of the heart's
beat is spent in maintaining the whole of the arterial system in
a state of overdistention, as indicated by the arterial pressure.
The overdistended arterial system is, by the agency of its elastic
walls, continually emptying itself by overflowing through the
capillaries into the venous system, overflowing at such a rate,
that just as much blood passes from the arteries to the veins
during each systole, and its succeeding diastole, as enters the
aorta at each systole.

It cannot be too much insisted upon that the whole arterial
system is overdistended. This is what is meant by the high
arterial pressure. On the other hand, the veins are much less
distended. This is shown by the low venous pressure. The dis-
tended arteries are continually striving to pass their surplus in
a continuous stream through the capillaries into the veins, so as
to bring both venous and arterial pressure to the same level. As
continually the heart by its beat is keeping the arteries distended,
and thus maintaining the difference between the arterial and
venous pressure, and thus preserving the steady capillary stream.
When the heart ceases to beat, the arteries do succeed in empty-

ing their surplus into the veins, and when the pressure on both sides of the capillaries is thus equalized, the flow through the capillaries ceases.

In the facts just discussed, it makes no essential difference whether the outflow on the far side of the resistance be an open one, or whether, as is the case in the vascular system, the fluid be returned to the pump, provided only that the resistance offered to that return be sufficiently small. We shall see, in speaking of the heart, that, so far from there being any resistance to the flow of blood from the great veins into the auricle, the flow is favored by a variety of circumstances. We have seen, moreover, that, besides the very sudden decrease in the immediate neighborhood of the capillaries, there is in passing along the whole vascular system from the aorta to the venæ cavæ a gradual fall of pressure. A little consideration shows that this must be the case. After what has been said it is obvious that the movement of the blood may be compared to that of a body of fluid, driven by pressure from the ventricle through the vessels to its outflow in the auricle. Were the pressure a continuous one, and were there no peripheral resistance, there would be a gradual fall of pressure, from the part furthest from the outfall, viz., the aorta, to the part nearest the outfall, viz., the venæ cavæ. The introduction of the peripheral resistance and its attendant phenomena gives rise to the feature of a very sudden and marked fall in the capillary region, but leaves untouched the gradual character of the fall in the rest of the course, from the aorta to the minute arteries, and from the minute veins to the venæ cavæ.

To recapitulate: there are three chief factors in the mechanics of the circulation, (1) the force and frequency of the heart-beat, (2) the peripheral resistance, (3) the elasticity of the arterial walls. These three factors, in order to produce a normal circulation, must be in a certain relation to each other. A disturbance of these relations brings about abnormal conditions. Thus, if the peripheral resistance be reduced beyond certain limits, while the force and frequency of the heart remain the same, so much blood passes through the capillaries at each stroke of the heart that there is not sufficient left behind to distend the arteries, and bring their elasticity into play. In this case, the intermittence of the arterial flow is continued on into the veins. An instance of this is seen in the experiments on the submaxillary gland, where sometimes the resistance offered by the minute arteries of the gland is so much lowered, that the pulse is carried right through the capillaries, and the blood in the veins of the gland pulsates.[1] A like result occurs when the peripheral resist-

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[1] See Book I. cap. i. sec. 2, on the Secretion of the Digestive Juices.

ance remaining the same, the frequency of the heart's beat is lowered. Thus, the beats may be so infrequent that the whole quantity sent on by a stroke has time to escape before the next stroke comes. Lastly, if, while the heart's beat and the peripheral resistance remain the same, the arterial walls become more rigid, the arteries will be unable to expand sufficiently to retain the surplus of each stroke or to exert sufficient elastic reaction to carry forward the stream between the strokes; and in consequence more or less intermittence will become manifest.

Circumstances Determining the Velocity of the Flow.—We have seen that the velocity of the blood-stream diminishes from the aorta to the capillaries, and increases from the capillaries to the great veins. Thus, in the dog the velocity in the great arteries may be stated at from 300 to 500 mm., in the capillaries at less than 1 mm. (0.5 to 0.75 mm.), and in the large veins at about 200 mm. in a second. In fact, the greater part of the time of the circuit is taken up in the capillary region. An iron salt, injected into the jugular vein of one side of the neck of a horse, makes its appearance in the blood of the jugular vein of the other side in about 30 seconds.

Hering's mean result in the horse was 27.6 seconds. In the dog Vierordt found it to be 15.2 seconds; in the rabbit 7 seconds.

Without laying too much stress on this experiment, it may be taken as a fair indication of the time in which the whole circuit may be completed. It takes about the same time to pass through about 20 mm. of capillaries. Hence, if any corpuscle had in its circuit to pass through 10 mm. of capillaries, half the whole time of its journey would be spent in the narrow channels of the capillaries. Since, however, the average length of a capillary is about 0.5 mm., about one second is spent in the capillaries. Inasmuch as the purposes served by the blood are chiefly carried out in the capillaries, it is obviously of advantage that its stay in them should be prolonged.

The *local* differences in the velocity of the stream are directly dependent on the area of the "bed." When a fluid is driven by a uniform pressure through a narrow tube with an enlargement in the middle, the velocity of the stream diminishes in the enlargement, but increases again when the tube once more narrows. So a river slackens speed in a "broad," but rushes on rapidly again when the banks close in. Exactly in the same way the velocity of the blood-stream slackens from the aorta to the capillaries corresponding with the increased total bed, but hurries on again as the numerous veins are gathered into the smaller bed of the venæ cavæ. The loss of velocity in the capillaries, as com-

pared with the arteries, is not due to there being so much more friction in the narrow channels of the former than in the wide canals of the latter.   For the peripheral resistance caused by the friction in the capillaries and small arteries is an obstacle not only to the flow of blood through these small vessels where the resistance is actually generated, but also to the escape of the blood from the large into the small arteries, and indeed from the heart into the large arteries.   It exerts its influence along the whole arterial tract.   And it is obvious that if it were this peripheral resistance which checked the flow in the capillaries, there could be no recovery of velocity along the venous tract. The rapidity of the flow in arteries, capillaries, and veins, is in each case determined by the total sectional area of the channels. There is, however, a loss of velocity on the whole course.   At each stroke as much blood enters the right auricle as issues from the left ventricle; but the sectional area of the venæ cavæ is greater than that of the aorta, so that even if the auricle were filled in exactly the same time as the ventricle is emptied, the blood must pass more rapidly through the narrow aorta than through the broad venæ cavæ, in order that the same quantity of blood should pass each in the same time.   The diastole of the auricle, however, is distinctly longer than the systole of the ventricle; the time during which the auricle is being filled is greater than that during which the ventricle is being emptied, and hence the velocity of the venous flow into the auricle must be still less than that of the arterial blood in the commencing aorta.

The *temporary* variations of the velocity of the stream in any given channel, and these we have already (p. 167) seen to be very considerable in the case of the arteries at least, are dependent on a variety of circumstances.   In a tube of constant calibre, the velocity with which fluid flows from one point to another, for instance from the point a to the point b, will be in main dependent on the difference between the pressures existing at a and b.   The lower the pressure at b as compared with a the greater the rapidity with which the fluid flows from a to b.   And temporary variations of pressures form undoubtedly the main cause of the temporary variations observable in the velocity of the arterial flow.   Thus with each systole of the ventricle there is an increase of velocity in the whole arterial flow, followed by a diminution during the diastole.   So, also, if the peripheral resistance in the minute arteries into which a larger artery divides be suddenly lowered (by the action of vaso-motor nerves, in a manner which we shall presently discuss), *without the calibre of the larger artery itself being changed*, the pressure on the distal (peripheral) side of the artery may be much diminished, while the pressure on the proximal (cardiac) side remains at first unaltered; and this would

necessarily cause an increase in the rapidity of the stream through that artery. But, as we shall see later on, from the complications of the vascular machinery such problems as these become very intricate; and the results of observations on variations in arterial velocity are not altogether intelligible. It has been suggested that varying conditions of the blood, by affecting the amount of adhesion between the blood and the walls of the vessels, may be an important factor in determining the variations in the velocity of the stream.[1]

Sec. 2.—The Heart.

[*The Physiological Anatomy of the Heart.*

The heart is a hollow, muscular organ, having a shape similar to that of a flattened cone. It is situated obliquely within the chest, immediately posterior to the sternum, resting upon the diaphragm, supported in position by the bloodvessels, and covered by the pericardium. Roughly sketched, the position of the base of the cone corresponds to a line drawn a little to the right of the sternum, from the second intercostal space to the sternal articulation of the sixth and seventh cartilages of the right side. The apex corresponds to a point in the left fifth intercostal space, a little interior to a vertical line drawn across the nipple.

The muscular fibres composing the heart are peculiar in character to the organ itself. They are striated, but differ from the ordinary skeletal muscles. In the skeletal muscles the fibres are entirely distinct and separable, possessing distinct longitudinal and transverse lines of cleavage. But in the fibres of the heart, as seen in Fig. 49, the lines of cleavage are partially lost and apparent anastomoses formed. The fibres of the heart rarely have a sarcolemmatous covering. These fibres may conveniently be divided into two layers, the superficial and deep. The superficial layer of the fibres of the ventricles consists of several laminæ, which have a peculiar spiral arrangement running from right to left, simulating a figure 8. This peculiar arrangement is of physiological importance in explaining several of the phenomena observed in the cardiac beat, as will be pointed out hereafter. The deep layer is circular.

The heart can with great propriety be considered as a double organ—a right, or pulmonary; a left, or systemic heart; each containing two cavities, called respectively an auricle and ventricle. The right and left cavities of the heart are separated by

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[1] Ludwig and Dogiel, Ludwig's Arbeiten, 1867. Cf. also Ewald, Archiv f. Anat. u. Phys., 1877, p. 208.

a muscular partition called the inter-auriculo-ventricular septum. The position of this septum is marked on the external surface of the heart by two grooves.

The walls of the left heart are much thicker than those of the right. This is due to the fact of the greater repulsive force necessary to overcome the resistance of the systemic, than is necessary to overcome that of the pulmonic vessels.

The auricles are separated from the ventricles by peculiar valve-like pendulous curtains, so arranged as freely to allow of

FIG. 49.
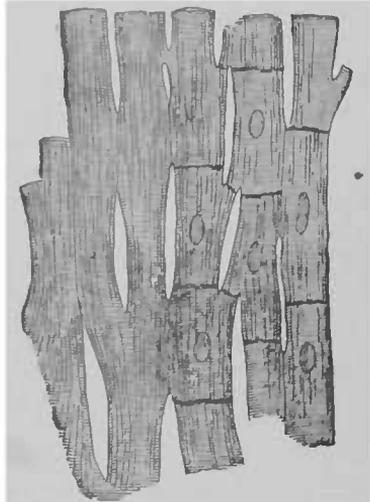
Anastomosing muscular fibres of the heart seen in longitudinal section. On the right the limits of the separate cells with their nuclei are exhibited somewhat diagrammatically.

the passage of blood from the auricles into the ventricles, and, by a peculiar valve-like mechanism, as is commonly supposed, prevent a reflux current by becoming closed.

There are two distinct sets of valves in the heart, the auriculo-ventricular and the semilunar.   The auriculo-ventricular valves are two in number, the right and left (Figs. 50, 51, 52).   The right is called the tricuspid, and consists of three cusps or leaflets (Figs. 50, 52).   The left or mitral valve consists of two leaflets only (Figs. 51, 52), and is physiologically the stronger of the two.   The auriculo-ventricular valves are formed by reduplications of the endocardium, and strengthened by fibrous tissue. They are attached by their bases to the auriculo-ventricular orifices; the portions of their sides nearest the bases are attached to each other, thus forming a continuous circular membrane. To the free margin and ventricular surfaces of these valves are

attached numerous tendinous cords, which connect the valves with the *musculi papillares*. They are called the *chordæ tendineæ*. On the intraventricular surface of the heart, numerous muscular bands are seen, which are called the *columnæ carneæ*. These

FIG 50.
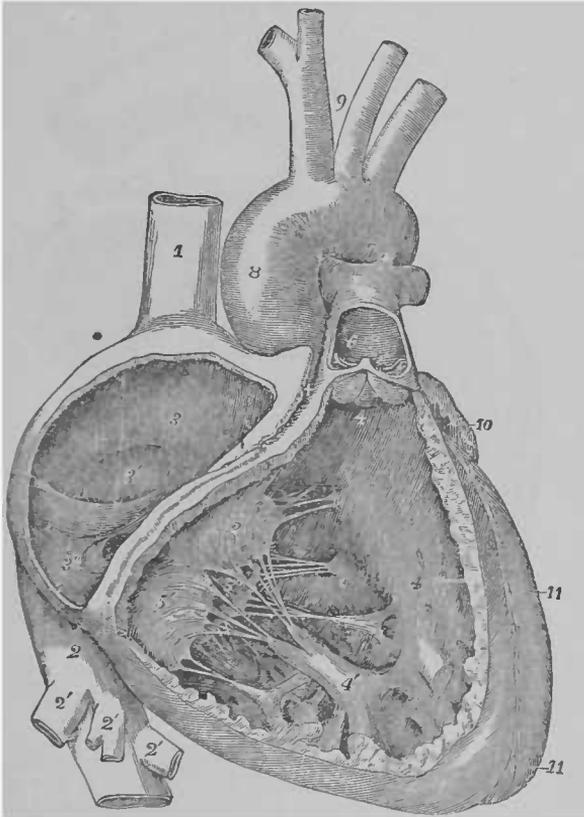
The right auricle and ventricle opened, and a part of their right and anterior walls removed, so as to show their interior—½. 1, superior vena cava; 2, inferior vena cava; 2′, hepatic veins cut short; 3, right auricle; 3′, placed in the fossa ovalis, below which is the Eustachian valve; 3″, is placed close to the aperture of the coronary vein; + +, placed in the auriculo-ventricular groove, where a narrow portion of the adjacent walls of the auricle and ventricle has been preserved; 4, 4, cavity of the right ventricle, also showing interventricular septum; the upper figure is immediately below the semilunar valves; 4′, large columna carnea or musculus papillaris; 5, 5′, 5″, tricuspid valve; 6, placed in the interior of the pulmonary artery, a part of the anterior wall of that vessel having been removed, and a narrow portion of it preserved at its commencement where the semilunar valves are attached; 7, concavity of the aortic arch close to the cord of the ductus arteriosus; 8, ascending part or sinus of the arch covered at its commencement by the auricular appendix and pulmonary artery; 9, placed between the innominate and left carotid arteries; 10, appendix of the left auricle; 11, 11, the outside of the left ventricle, the lower figure near the apex.—From *Quain's Anatomy*.

Fig. 51.
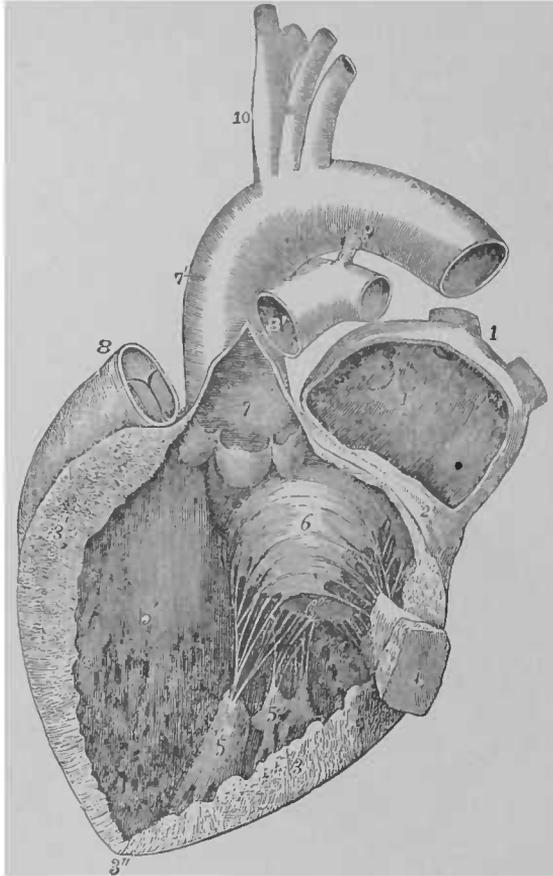
The left auricle and ventricle opened, and a part of their anterior and left walls removed, so as to show their anterior—½. The pulmonary artery has been divided at its commencement so as to show the aorta; the opening into the left ventricle has been carried a short distance into the aorta, between two of the segments of the semilunar valves; the left part of the auricle, with its appendix, has been removed. The right auricle has been thrown out of view. 1, the two right pulmonary veins cut short; their openings are seen within the auricle; 1′, placed within the cavity of the auricle on the left side of the septum and on the part which forms the remains of the valve of the foramen ovale, of which the crescentic fold is seen towards the left hand of 1′; 2, a narrow portion of the wall of the auricle and ventricle preserved round the auriculo-ventricular orifice; 3, 3′, the cut surface of the walls of the ventricle seen to become very much thinner towards 3″ at the apex; 4, a small part of the anterior wall of the left ventricle, which has been preserved with the principal anterior columna carnea or musculus papillaris attached to it; 5, 5, musculi papillares; 5′, the left side of the septum, between the two ventricles, within the cavity of the left ventricle; 6, 6′, the mitral valve; 7, placed in the interior of the aorta, near its commencement and above the three segments of its semilunar valve, which are hanging loosely together; 7′, the exterior of the great aortic sinus; 8, the root of the pulmonary artery and its semilunar valves; 8′, the separated portion of the pulmonary artery remaining attached to the aorta by 9, the cord of the ductus arteriosus; 10, the arteries rising from the summit of the aortic arch.— From *Quain's Anatomy.*

bands are of three kinds: those attached by one of their sides and by both extremities to the ventricles; those attached by both extremities; and those attached by one extremity alone, the other extremity connecting with the auriculo-ventricular valves by means of the intervening chordæ tendineæ. These latter *columnæ carneæ* are distinguished by the name of *musculi papillares* (Figs. 50, 51).

There are also two sets of semilunar valves, the aortic and pulmonary (Figs. 50, 51, 52). Each of these sets of valves consists of three semilunar segments. The pulmonary is situated

Fig. 52.
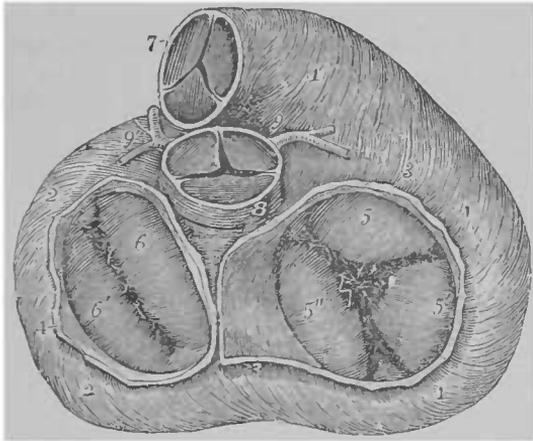
View of the base of the ventricular part of the heart, showing the relative position of the arterial and auriculo-ventricular orifice—⅔. The muscular fibres of the ventricles are exposed by the removal of the pericardium, fat, bloodvessels, etc.: the pulmonary artery and aorta have been removed by a section made immediately beyond the attachment of the semilunar valves, and the auricles have been removed immediately above the auriculo-ventricular orifices. The semilunar and auriculo-ventricular valves are in the nearly closed condition. 1, 1, the base of the right ventricle: 1′, the conus arteriosus, which is a conical expansion of the right ventricle, immediately at the point where the pulmonary artery arises; 2, 2, the base of the left ventricle; 3, 3, the divided wall of the right auricle; 4, that of the left; 5, 5′, 5″, the tricuspid valve; 6, 6′, the mitral valve. In the angles between these segments are seen the smaller fringes frequently observed; 7, the anterior part of the pulmonary artery; 8, placed upon the posterior part of the root of the aorta; 9, the right, 9′, the left coronary artery.— From *Quain's Anatomy*.

at the junction of the pulmonary artery with the right ventricle. The aortic is situated at the junction of the aorta with the left ventricle. On the middle of each of the free edges of these valves is a small nodule, called the *corpus Arantii*, which, when the valves become closed, come together, and are disposed in a

spiral form.   They thus close up an opening which would obviously be present were they absent.

Behind each of the semilunar valves is a pouch-like expansion; these are termed the *sinuses of Valsalva.*   In the aortic walls, at about the free margin of the right and left semilunar valves, the orifices of the coronary arteries, which supply the heart with blood, are seen.

The semilunar valves are formed by reduplications of the lining membrane, and strengthened by fibrous tissue.

The passage of blood through the heart can thus be briefly stated : Coming from the system through the venæ cavæ, it enters the right auricle ; from the right auricle it passes to the right ventricle ; thence to the lungs through the pulmonary artery. After passing through the lungs, it again enters the heart through the pulmonary veins, into the left auricle ; from the left auricle it passes into the left ventricle, and thence through the aorta into the general system (Fig. 53).

[FIG. 53.
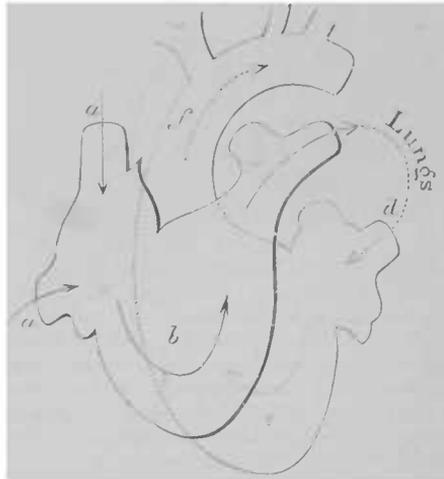
DIAGRAM OF THE CIRCULATION THROUGH THE HEART.

a, a, Vena cava, superior and inferior. *b,* Right ventricle. *c,* Pulmonary artery. *d,* Pulmonary vein. *e,* Left ventricle. *f,* Aorta.   After DALTON.]

The heart is a pump, the motive power of which is supplied by the contraction of its muscular fibres.   Its action consequently presents problems which are partly mechanical, and partly vital. Regarded as a pump, its effects are determined by the frequency of the beats, by the force of each beat, by the character of each beat—whether, for instance, slow and lingering, or sudden and

sharp—and by the quantity of fluid ejected at each beat. Hence, with a given frequency, force, and character of beat, and a given quantity ejected at each beat, the problems which have to be dealt with are, for the most part, mechanical. The vital problems are chiefly connected with the causes which determine the frequency, force, and character of the beat. The quantity ejected at each beat is governed more by the state of the rest of the body, than by that of the heart itself.

The Phenomena of the Normal Beat.

The Visible Movements.—When the chest of a mammal is opened and artificial respiration kept up, a complete beat of the whole heart, or cardiac cycle, may be observed to take place as follows:

The great veins, inferior and superior venæ cavæ, and pulmonary veins, are seen, while full of blood, to contract in the neighborhood of the heart; the contraction runs in a peristaltic wave towards the auricles, increasing in intensity as it goes. Arrived at the auricles, which are then full of blood, the wave suddenly spreads, at a rate too rapid to be fairly judged by the eye, over the whole of those organs, which accordingly contract with a sudden sharp systole. In the systole, the walls of the auricles press towards the auriculo-ventricular orifices, and the auricular appendages are drawn inwards, becoming smaller and paler. During the auricular systole, the ventricles may be seen to become more and more turgid. Then follows, as it were, immediately the ventricular systole, during which the ventricles become more conical. Held between the fingers, they are felt to become tense and hard. As the systole progresses, the aorta and pulmonary arteries expand and elongate, and the heart twists slightly on its long axis, moving from the left and behind towards the front and right, so that more of the left ventricle becomes displayed. As the systole gives way to the succeeding pause or diastole, the ventricles resume their previous form, the aorta and pulmonary artery contract and shorten, the heart turns back towards the left, and thus the cycle is completed.

A more exact determination of the changes in the form and position of the heart during a beat is attended with considerable difficulties. The following experiment has been made with the view of studying these changes without opening the chest, and thus without depriving the heart of its natural supports. If, in the unopened chest of a rabbit or dog, three needles be inserted through the chest-wall so that their points are plunged into the substance of the ventricle, one (B) at the base, close to the auricles, another (A) through the apex, and a third (M) at about

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the middle of the ventricle, all three needles will be observed to move at each beat of the heart. The head of B will move suddenly upwards, showing that the point of the needle plunged in the ventricle moves downwards, whereas A will only quiver, and move neither distinctly upwards nor downwards. M will move upwards (and therefore its point downwards), but not to the same extent as B. The nearer to B, M is, the more it moves; the nearer to A, the less. After the death of the animal, the needles, if properly inserted at first, perpendicular to the chest, will be found with all their heads directed downwards, indicating that the whole ventricle has been drawn up by the contraction of the empty aorta and pulmonary artery.

The behavior of the needles during the beat has been interpreted as follows. At the systole the whole heart is thrust downward by the elongation of the aorta and pulmonary artery. The needle A at the apex, however, does not move its place, because this downward movement is compensated by an upward movement due to a shortening, during systole, of the longitudinal diameter of the ventricle. The base in which the needle B is plunged, moves downwards and draws closer to A—*i. e.*, to the apex, partly by the downward thrust from the elongation of the great arteries, and partly from the shortening of the ventricle itself. Naturally, the behavior of the needle M is intermediate in character, its downward movement being the more conspicuous the nearer it is to B. The experiment then is taken to prove that during the systole the ventricle shortens in its longitudinal diameter, but that the apex remains stationary on account of the compensating downward thrust of the whole ventricle. It has been urged, however, that this method is untrustworthy, and that similar movements of needles thus placed might be produced by the twisting of the heart on its long axis, combined with an approximation of the heart to the chest-wall. And different conclusions have been arrived at by taking plaster-of-Paris models, on the one hand, of a dog's heart, which, while having ceased beating but not yet become rigid, has been filled with blood at a moderate pressure, and, on the other hand, of a heart of the same size in which a condition simulating systolic contraction has been brought about by immersing the empty heart in a saturated solution of potassium bichromate at 50° C. The former is taken to represent the diastolic and the latter the systolic form of the heart; and the results are checked by measurements taken between marks placed on various points of the surface of the heart, as well as by sections of a heart filled with blood and hardened in a cold solution of potassium bichromate, and of one emptied and hardened in the same solution warmed to 50°. A comparison of the two hearts in these different conditions tends

to show that while both the right-to-left and antero-posterior diameters are diminished during systole, especially in the plane of the ostia venosa (whereby the auriculo-ventricular orifices become narrowed), the longitudinal diameter, at all events of the left ventricle, is not lessened, the distance between the apex and the auriculo-ventricular groove remaining unchanged. The right ventricle, the change of form of which is complicated, does shorten to a certain extent, and there is during systole a downward movement of the conus arteriosus upon the plane of the ventricular base (which possibly may explain the movement of the needle B in the above-mentioned experiment), so that the distance between the apex and the upper border of the conus is less during systole than during diastole. This method also confirms the view that the left ventricle in systole turns on its long axis towards the right, the movement increasing from the base downwards, so that the groove between the two ventricles forms a closer spiral than during diastole.

Objections may be brought against this method also, and it seems impossible to explain the movements of a lever placed upon the heart, unless we admit that during systole the antero-posterior diameter of the middle portion of the ventricle at least is increased, instead of lessened. We may, however, probably go so far as to conclude that as far as the ventricles are concerned the chief change during systole is one from a roughly hemispherical to a more conical form, effected without any marked diminution of the distance between the apex and the ventricular base.

Cardiac Impulse.—If the hand be placed on the chest, a shock or impulse will be felt at each beat, and on examination this impulse—"cardiac impulse"—will be found to be synchronous with the systole of the ventricle. In man, the cardiac impulse may be most distinctly felt in the fifth costal interspace, about an inch below and a little to the median side of the left nipple. The same impulse may be felt in an animal by making an incision through the diaphragm from the abdomen, and placing the finger between the chest-wall and the apex. It then can be distinctly recognized as the result of the hardening of the ventricle during the systole. And the impulse which is felt on the outside of the chest is the same hardening of the stationary portion of the ventricle in contact with the chest-wall, transmitted through the chest-wall to the finger. In its flaccid state, during diastole, the apex is (in a standing position at least) at this point in contact with the chest-wall, lying between it and the tolerably resistant diaphragm. During the systole, while being brought even closer to the chest-wall, by the movement to the front and to the right

of which we have already spoken, it suddenly grows tense and hard. The ventricles, in executing their systole, have to contract against resistance. They have to produce within their cavities tensions greater than those in the aorta and pulmonary arteries respectively. This is, in fact, the object of the systole. Hence, during the swift systole, the ventricular portion of the heart becomes suddenly tense, just as a bladder full of fluid would become tense and hard when forcibly squeezed. The sudden onset of this hardness gives an impulse or shock both to the chest-wall and to the diaphragm, which may be felt readily both on the chest-wall and also through the diaphragm when the abdomen is opened, and the finger inserted. If the modification of the sphygmograph (see section on Pulse), called the cardiograph, be placed on the spot where the impulse is felt most strongly, the lever is seen to be raised during the systole of the ventricles, and to fall again as the systole passes away, very much as if it were placed on the heart directly. A tracing may thus be obtained, of which we shall have to speak more fully immediately. If the button of the lever be placed, not on the exact spot of the impulse, but at a little distance from it, the lever will be *depressed* during the systole. While at the spot of impulse itself, the contact of the ventricle is increased during systole, away from the spot the ventricle retires from the chest-wall (by the diminution of its right-to-left diameter), and hence, by the mediastinal attachments of the pericardium, draws the chest-wall after it.

Endo-cardiac Events.—In order to study more fully the changes going on in the heart during the cardiac cycle, it becomes necessary to know something of what is taking place in the interior of the cavities of the heart. Chauveau and Marey, by introducing into the right auricle and ventricle respectively of the horse, through the jugular vein, small elastic bags, each communicating with a recording tambour, were enabled to take simultaneous tracings of changes occurring in the two cavities. These results are embodied in Fig. 54, of which the upper curve is a tracing taken from the auricle, the middle curve a similar tracing taken from the ventricle, while the lower curve is a cardiographic tracing of the cardiac impulse. All these curves were taken simultaneously on the same recording surface.

Method.—A tube of appropriate curvature is furnished with two small elastic bags, one at the extreme end and the other at such a distance that when the former is within the cavity of the ventricle the latter is in the cavity of the auricle; such an instrument is spoken of as a "cardiac sound." Each bag (Fig. 55, A), or "ampulla," communicates by a separate air-tight tube with an air-tight tambour (Fig. 55, B) on which a lever rests so that any pressure on either bag is communicated to the cavity of its respective tambour, the lever of which is raised in proportion.

The writing-points of all three levers are brought to bear on the same recording surface exactly underneath each other. The tube is carefully introduced through the right jugular vein into the right side of the heart until the lower (ventricular) bag is fairly in the cavity of the right ventricle, and consequently the upper (auricular) bag in the cavity of the right auricle. Changes of pressure on either ampulla then cause movements of the corresponding lever. When the pressure, for instance, on the ampulla in the auricle is increased, the auricular lever is raised and

FIG. 54.
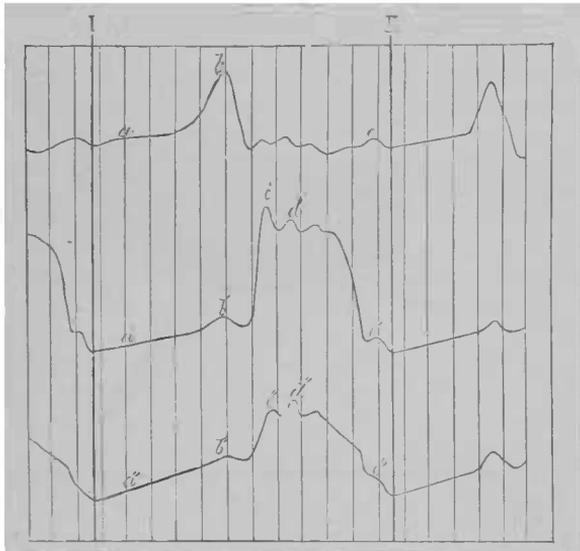
SIMULTANEOUS TRACINGS FROM THE INTERIOR OF THE RIGHT AURICLE, FROM THE INTERIOR OF THE RIGHT VENTRICLE, AND OF THE CARDIAC IMPULSE, IN THE HORSE. After CHAUVEAU AND MAREY. To be read from left to right.]

The upper curve represents changes taking place within the auricle, the middle curve changes within the ventricle. The lower curve represents the variations of pressure transmitted to a lever outside the chest and constituting the cardiac impulse. A complete cardiac cycle, beginning at the close of the ventricular systole, is comprised between the thick vertical lines I and II. The thin vertical lines represent tenths of a second. The explanation of the letters is given in the text.

describes on the recording surface an ascending curve; when the pressure is taken off, the curve descends; and so, also, with the ventricle.

The "sound" may in a similar manner be readily introduced through the carotid artery into the *left* ventricle, and the changes taking place in that chamber also explored; these are found to be very similar to those of the right ventricle.

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[1] It must be remembered that the curves in the diagram are intended merely to illustrate the changes occurring at different times in the same chamber, or to show what changes in the one chamber are coincident in point of time with changes in the other. They in no way indicate the *amount of pressure* exerted in the auricle as compared with that in the ventricle.

We may employ these curves as giving a general and useful view of the sequence of events in the interior of the heart; but we must bear in mind exactly what they mean. The tracings given by the auricular and ventricular levers really represent variations in the pressure exerted on the respective ampullæ, and so far are instructive; but they must not be taken as representing variations in the pressure exerted on the blood in the several

Fig 55.
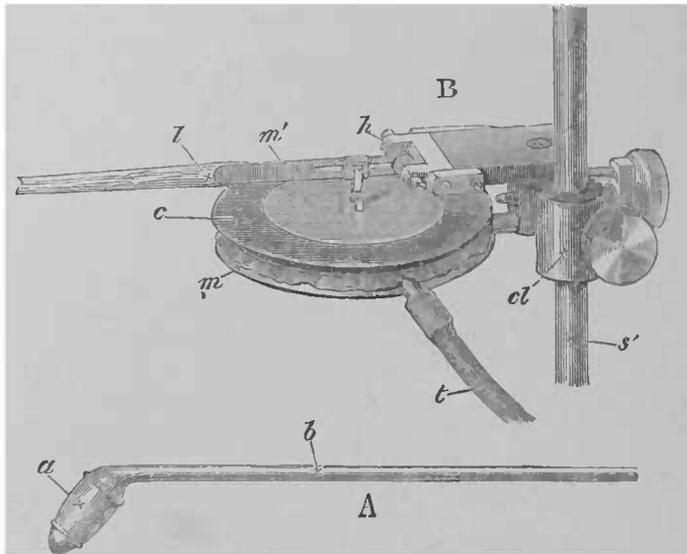
MAREY'S TAMBOUR, WITH CARDIAC SOUND.

A A simple cardiac sound, such as may be used for exploration of the left ventricle. The portion (*a*) of the ampulla at the end is of thin India-rubber, stretched over an open framework with metallic supports above and below. The long tube *b* serves to introduce it into the cavity which it is desired to explore.

B. The tambour. The metal chamber *m* is covered in an air-tight manner with the India-rubber *c*, bearing a thin metal plate, *m'*, to which is attached the lever *l* moving on the hinge *h*. The whole tambour can be placed by means of the clamp *cl* at any height on the upright *s'*. The India-rubber tube *t* serves to connect the interior of the tambour either with the cavity of the ampulla of A or with any other cavity. Supposing that the tube *t* were connected with *b*, any pressure exerted on *a* would cause the roof of the tambour to rise and the point of the lever would be proportionately raised.

cavities.　For we can easily conceive that, in the systole of the ventricle, for instance, the contraction of the muscular walls might continue after all the blood contained in the ventricle had been driven out.　In such a case, the ventricle would continue to press upon the ampulla, and this continued pressure would be transmitted to the lever, and indicated on the curve; but we should be in error in interpreting this part of the curve as mean-

ing that the ventricle was still continuing to exert pressure on the blood as yet remaining in its cavity. With this caution, and with the remark that the tracing of the cardiac impulse is very unlike the usual cardiographic tracings taken from man, we may use the curves to deduce the following conclusions:

A complete cardiac cycle is comprised between the vertical lines I and II. The recording surface was travelling at such a rate that the intervals between any two of the thin vertical lines corresponds to one-tenth of a second. Hence, in this case (the heart being that of a horse), the whole cardiac cycle occupied about $\frac{12}{10}$ths of a second. Any point in the cycle might, of course, be taken as its commencement. In the figure, the cycle is supposed to begin shortly after the end of the ventricular systole, and the beginning of the diastole.

On examining the three curves, we see, at a, a steady rise of the auricular, accompanied by similar gradual ascents of the ventricular and also of the cardiograph lever. These may be interpreted as indicating that the blood is pouring from the great veins into the auricle, increasing the pressure there, and at the same time passing on into the ventricle, increasing the internal pressure there as well, a', and also, by distending the ventricle, causing it to press somewhat on the chest-wall, and thus to raise the cardiograph lever, a''. This continues for about $\frac{4}{10}$ths of a second, and is then followed by the sudden rise of auricular pressure, b, due to the auricular systole, followed by a sudden fall as the blood escapes into the ventricle and the systole ceases. The sudden entrance of blood into the ventricle causes a sudden increase of the pressure in the ventricle, as indicated by the ventricular lever b', and a sudden increase in the pressure on the chest-wall b''. The auricular systole is followed immediately by the sudden, strong, ventricular systole c', the lever rising very abruptly. Owing to the presence of the tricuspid valves, the pressure exerted by the ventricular systole is kept off the auricle almost altogether; but the chest-wall, as shown by the tracing at c'', feels the sudden increase of the pressure of the ventricle against it. The most important points concerning this rise of ventricular pressure are that it is sudden in its onset and also rapid in its decline, and that it lasts for a comparatively long time; in the figure this part of the curve embraces more than four-tenths of a second. These features—the sudden rise, the long duration, and the rapid fall of the pressure exerted by the ventricle—are seen in all tracings of the ventricles engaged in a cardiac beat, whatever be the method employed. They mean, of course, that the muscular contractions which constitute the ventricular systole come on suddenly, that they last altogether a considerable time, and that relaxation is also rapid. With the

end of the ventricular systole, the cycle represented in the figure ends, and a new cycle begins, repeating the same changes. The meaning of the features on the curves marked s and d, etc., as well as a more complete discussion of the changes thus briefly described, we must defer till we have spoken of

The Mechanism of the Valves.

The auriculo-ventricular valves present no difficulty. As the blood is being driven by the auricular systole into the ventricle, a reflux current is probably set up, by which the blood, passing along the sides of the ventricle, gets between them and the flaps of the valve (whether tricuspid or mitral). As the pressure of the auricular systole diminishes, the same reflux current floats the flaps up, until at or immediately after the close of the systole they meet, and thus the orifice is at once and firmly closed, at the very beginning of the ventricular beat. (Figs. 56, 57.) The

[Fig. 56.
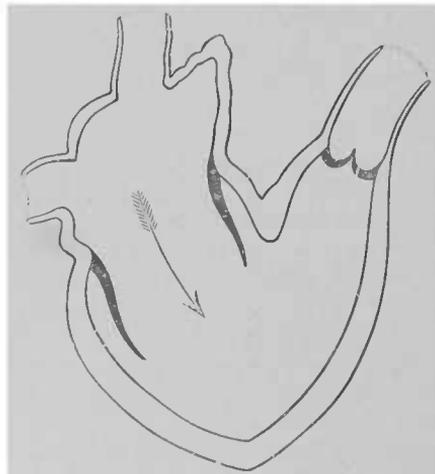
DIAGRAM OF VALVES OF THE HEART. After Dalton.]

increasing intraventricular pressure serves only to render the valve more and more tense, and, in consequence, more secure, the chordæ tendineæ (the slackening of which, through the change of form of the ventricle, is probably obviated by a regulative contraction of the papillary muscles) at the same time preventing the valve from being inverted or even bulging into the auricle, and, indeed, according to some observers, keeping the valvular sheet actually convex to the ventricular cavity, by which means the complete emptying of the ventricle is more fully effected.

Since the same papillary muscle is in many cases connected by chordæ with the adjacent edges of two flaps, its contraction also serves to keep these flaps in more complete apposition. Moreover, the extreme borders of the valves, outside the attachments of the chordæ, are excessively thin, so that when the valve is closed, these thin portions are pressed flat together, back to back ;

[FIG. 57.
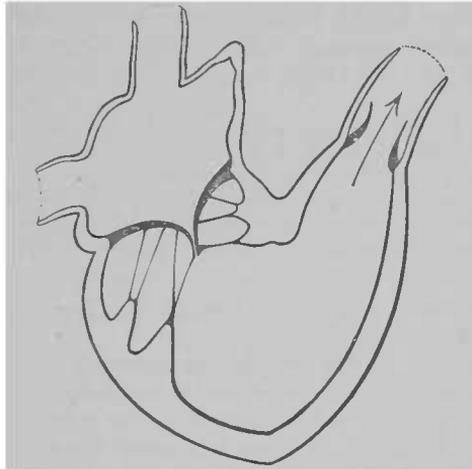
DIAGRAM OF VALVES OF THE HEART   After DALTON.]

hence, while the tougher central parts of the valves bear the force of the ventricular systole, the opposed thin membranous edges, pressed together by the blood, more completely secure the closure of the orifice.

The semilunar valves are, during the ventricular systole, pressed outwards towards but not close to the arterial walls, reflex currents probably keeping them in an intermediate position, their orifice forming an equilateral triangle with curved sides; they thus offer little obstacle to the escape of blood from the cavities of the ventricles. The ventricle propels the blood with great force and rapidity into the aorta and the whole contents are speedily ejected. Now, when in a closed channel a rapid current suddenly ceases, a negative pressure makes its appearance in the rear of the fluid, and sets up a reflux current. So when the last portions of blood leave the ventricle a negative pressure makes its appearance behind them in the ventricle, and leads to a reflux current from the aorta towards the ventricle. This alone would tend to bring the valves together, but in all probability it is not till a short (variable) time afterwards, that upon the com-

mencing diastolic relaxation of the ventricle, the elastic rebound of the arterial walls completely fills and renders tense the pockets, causing their free margins to come into close and firm contact, and thus entirely blocking the way. The corpora Arantii meet in the centre, and the thin membranous festoons or lunulæ are brought into exact apposition. As in the tricuspid valves, so here, while the pressure of the blood is borne by the tougher bodies of the several valves, each two thin adjacent lunulæ, pressed together by the blood acting on both sides of them are kept in complete contact, without any strain being put upon them ; in this way the orifice is closed in a most efficient manner.

The ingenious view put forward by Brücke that during the ventricular systole the flaps are pressed back flat against the arterial walls, and in the case of the aorta completely cover up the orifices of the coronary arteries, so that the flow of blood from the aorta into the coronary arteries can take place only during the ventricular diastole, or at the very beginning of the systole, and not at all during the systole itself, has been disproved.

The Sounds of the Heart.

When the ear is applied to the chest, either directly or by means of a stethoscope, two sounds are heard, the first a comparatively long dull booming sound, the second a short sharp sudden one. Between the first and second sounds, the interval of time is very short, too short to be measurable, but between the second and the succeeding first sound there is a distinct pause. The sounds have been likened to the pronunciation of the syllables, lūbb, dŭp, so that the cardiac cycle, as far as the sounds are concerned, might be represented by lūbb, dŭp, pause.

The second short sharp sound presents no difficulties. It is coincident in point of time with the closure of the semilunar valves, and is heard to the best advantage over the second right costal cartilage close to its junction with the sternum—i. e., at the point where the aortic arch comes nearest to the surface. Its characters are such as would belong to a sound generated by the sudden tension of valves like the semilunar valves. It is obscured and altered, replaced by "murmurs" when the semilunar valves are affected by disease, the alteration being most manifest to the ear at the above-mentioned spot when the aortic valves are affected. When the aortic valves are hooked up by means of a wire introduced down the arteries, the second sound is obliterated and replaced by a murmur. These facts prove that the second sound is due to the sudden tension of the aortic (and pulmonary) semilunar valves.

The first sound, longer, duller, and of a more "booming" character than the second, heard with greatest distinctness at the spot where the cardiac impulse is felt, presents many difficulties in the way of a complete explanation. It is heard distinctly when the chest-walls are removed. The cardiac impulse, therefore, can have little or nothing to do with it. In point of time, and in the position in which it may be heard to the greatest advantage (at the spot of the cardiac impulse where the ventricles come nearest to the surface), it corresponds to the closure of the auriculo-ventricular valves. In point of character it is not such a sound as one would expect from the vibration of membranous structures, but has, on the contrary, many of the characters of a muscular sound. In favor of its being a valvular sound, may be urged the fact that it is obscured, altered, replaced by murmurs, when the tricuspid or mitral valves are diseased, and according to some authors clamping the great veins so as to shut off the blood supply stops the sound though the beat continues. The first argument may be met by the consideration that a murmur, though itself undoubtedly of valvular origin, might largely or completely hide a sound occurring at the same time as the closure of the valves but due to other causes, and the second is directly contradicted by an experiment of Ludwig and Dogiel. These observers tied in succession, in the order of the flow of blood, the great veins and arteries of the heart of a dog so as completely to deprive the heart of blood, and listened to the heart both within the body and after removal. For the short time that the heart continued to beat, the first sound was heard, feeble but with its main characters recognizable. From this they inferred that the sound was of muscular origin. But there is a great difficulty in regarding the sound as a muscular one, for a muscular sound is the result of a tetanic contraction, the height of the note produced varying with the rate of repetition of the simple contractions which go to make up the tetanus. A simple contraction or spasm cannot possibly produce a sound having the characters of the first cardiac sound. And the evidence, though perhaps not conclusive, goes to show that the beat of the heart is a slow long-continued single spasm, intermediate between the contraction of an ordinary striated and that of an unstriated muscle, and not a tetanic contraction. We cannot, it is true, now rely in support of this view on the fact that when the nerve of a rheoscopic muscle-nerve preparation is placed on the beating ventricle, each beat is followed by a single spasm of the muscle, and not by a tetanus, for we now know that many forms of tetanus (*e. g.*, those caused by the constant current, by strychnia, and probably all natural voluntary contractions) give rise, in a rheoscopic muscle-nerve

preparation, to a single initial spasm and not to a tetanus. But the general features of the beat, its long latent period and the gradation of the ventricular systole through the auricular systole into the rhythmic contractions of the unstriated fibres of the walls of the great veins, render it difficult to suppose that the beat is really a tetanus. Moreover, the long duration of the ventricular systole is readily explained by the wave of contraction passing in a complicated peristaltic manner over the different fibres in succession. But if the beat be a simple contraction, it cannot give rise to a muscular sound, unless we suppose that this sequence of simple contractions over various parts of the ventricle in succession is adequate to produce such a sound. This, however, does not seem very satisfactory.

On the other hand, if we reject the distinctly muscular origin of the sound, we are almost driven to suppose that the abrupt systole is able even in the absence of blood to produce such a sudden tension of the valves, and of the ventricular walls, as to give rise to a note. On such a view, the sound ought to vary in character according as the ventricle is more or less filled, being low and booming when it is full, and high and sharp when the contents are scanty. And such is said to be the case. But the matter does not at present seem ripe for any dogmatic statement.

In the normal state of things, the beats of the two ventricles are so far synchronous with each other that practically only one first sound and one second sound is heard. It sometimes happens, however, that the synchronism fails to such an extent, and the closure of the pulmonary and aortic valves respectively are separated by such an interval as to give the second sound a double character.

On the Relative Duration and Special Characters of the Cardiac Events.

We may now return to a more detailed study of what is taking place in the heart during a beat. We have already spoken of the conclusions which may be drawn from Chauveau and Marey's curves, and have incidentally (p. 184) referred to the cardiograph.

Various forms of cardiograph have been used to record the cardiac impulse. In some the pressure of the impulse as in the sphygmograph is transmitted directly to a lever which writes upon a travelling surface. In others the impulse is, by means of an ivory button, brought to bear on an air-chamber, connected by a tube with a tambour as in Fig. 58; the pressure of the cardiac impulse compresses the air in the air-chamber, and through this the air in the chamber of the tambour by which the lever is

raised. In such delicate and complicated movements as those of the heart, however, the use of long tubes filled with air is liable to introduce various errors. A cardiographic tracing of ordinary characters is given in Fig. 58.

Curves of the variations in internal pressure may be obtained by passing a tube connected with a mercurial manometer (as in

FIG. 58.
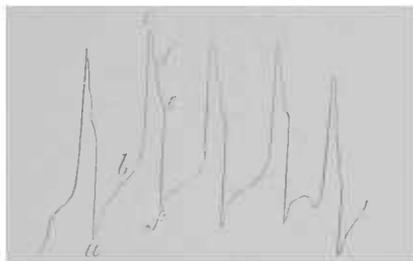
CARDIOGRAPHIC TRACING OF CARDIAC IMPULSE IN MAN. From LANDOIS.

An entire beat occurs between *a* and *f*. The auricular systole is marked by *b*, the end of the ventricular relaxation by *f*. At *c*, the highest point of the curve, the blood begins to be propelled from the ventricle. *d* and *e* are considered by some to indicate the closure of the aortic and semilunar valves respectively (see text). Five cardiac beats are represented; the convex curve which their base-line forms is due to the respiratory movements.

the investigation of arterial pressure, p. 160) into the right ventricle through the jugular vein or into the left ventricle through the carotid artery. But this method, though useful for the purpose of investigating generally the pressure exerted by the cardiac walls, is, by reason of the inertia of the mercury, unsuitable for detecting rapid and small changes.

Tracings of the movements of the ventricles themselves, corresponding to the cardiac impulse and so to a certain extent to the variations of internal pressure, may also be taken directly by bringing a light lever to bear on the outside of the ventricles, the chest having been previously opened and artificial respiration kept up. A curve[1] taken by this method is shown in Fig. 59.

[1] The majority of cardiographic, sphygmographic, and other tracings, show certain points which can be understood at a glance, but many characteristics can only be learned by "measuring out the curve," as it is termed. This is done as follows:

Every tracing ought to bear on it an abscissa line, marked by a point which remains motionless while the recording surface is travelling. Moreover, either before or after taking a curve, while the paper or recording surface is at rest, the point of the lever should be always moved up and down, so as to describe a segment of a circle of which the axis of the lever is the centre.

The tracing thus prepared, when it has to be measured, is pinned out on a board, and, by means of a pair of compasses, the distance between whose points has previously been made equal to the distance between the axis and the point of the lever used in making the experiment, the centre of the circle of which the

The chief interest and the chief difficulties are attached to the systole of the ventricles. In order to understand this, the most

FIG. 59.
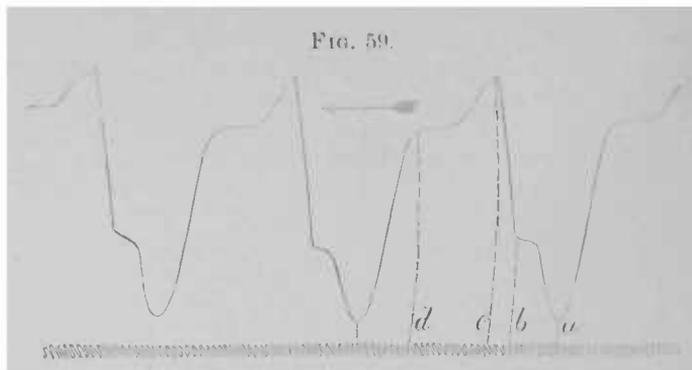
Normal heart-curve, showing changes in the antero-posterior diameter of the ventricle, obtained from the cat by a light recording lever moved by a button which pressed gently on the anterior surface of the ventricle. The time curve gives 50 double vibrations per second, and lines have been drawn to show the duration of the different phases of the ventricular movement. *a* to *b* corresponds to the distention of the ventricle, including the auricular systole, the wave-like rise during this period being due to the increase in the diameter of the ventricle resulting from the entrance into it of the contents of the auricle. The period from *b* to *c* corresponds to the time from the commencement of the ventricular contraction to the moment when the organ has completed its change in shape from a flattened to a more rounded form. The highest part of the curve corresponds also in time with the opening of the semilunar valves as well as the firm closure of the auriculo-ventricular valves. The duration of this period in this case is only about 3-50ths of a second. The period from *c* to *d* is that during which the ventricle having grasped its contents is emptying its cavity and remaining contracted. It can be seen that only during the first half of this period is there any marked descent of the lever point; in other words, the antero-posterior diameter does not continue to diminish during the whole period of the systole, indicating that little or no blood was thrown out during the second half of this period, the ventricle remaining simply contracted after having emptied its cavity. The period from *d* to *a* is that during which the ventricular muscle is relaxing. Here, as is frequently the case, there is no period of pause between the close of the relaxation of the ventricle and the commencement of the succeeding distention. The tracing gives no evidence as to the time of closure of the semilunar valves.

important of the cardiac events, it must be borne in mind that, as we have already seen, the pressure of the blood in the aorta

curved lines previously made as directed are segments is found and marked on the paper. Through this centre, which, of course, corresponds to the position of the axis of the lever, a horizontal line is drawn parallel to the abscissa line.

Keeping one of the compass points on this line, segments of circles are drawn in succession through various points of the curve, the distance between the points of the compass being fixed, but the centre of the circle described being shifted backwards and forwards along the horizontal line. The points where these segments cut the horizontal line are marked upon it, and the distances between them measured as, for example, in Fig. 66, p. 213. If the curve of a tuning-fork, the point of whose recording style was carefully placed on the same vertical line as the point of the lever, be also present, the segments of circles may be continued until they cut this, and the time corresponding to distances between them (as, for instance, in Fig. 59, the intervals between *a, b, c, d*) thus directly measured off.

is always considerable. This pressure closes and keeps closed the semilunar valves; and it is not till the pressure in the ventricle becomes greater than the pressure in the aorta that these valves open to allow of the escape of the ventricular contents. The blood, therefore, does not begin to pass from the left ventricle into the aorta until some time, and that a variable time, after the commencement of the systole of the ventricle; and the same may be said of the right ventricle and pulmonary artery, it being understood that the arterial pressure on the right side is less than on the left. In Fig. 59 the ventricular lever reaches its maximum c at once, gradually declining afterwards till the more sudden fall begins, and we may suppose that the escape of blood from the ventricle begins at the moment when the maximum is attained ; and this view is confirmed by carefully comparing a tracing of the expansion of an artery with the cardiac tracing. It is quite possible, however, to conceive that owing to circumstances, such as an increasing contraction of the ventricular fibres or deficient expansion of the arteries, the pressure might continue to increase even after blood was escaping from the cavity of the ventricle. And, indeed, in some curves, the ventricular lever, after the first sudden leap, continues to rise gradually, and does not reach the maximum point until afterwards. In such cases, the summit of the first rise must be taken as marking the beginning of the flow from the ventricle.

By the sudden systole the blood is ejected with considerable force and rapidity from the ventricle, and as the ventricle becomes empty a negative pressure, as we have seen, makes its appearance behind the column of blood which leaves the cavity and leads to the closure of the semilunar valves. Much dispute has taken place as to the exact condition of the ventricle at the moment of closure of the semilunar valves. The slight rise e' in Chauveau and Marey's curves (Fig. 54) in the ventricular curve, seen also in the auricle at e and in the cardiac impulse at e'', and which has been taken to indicate the shutting of the semilunar valves, appears quite at the close of the descent of the ventricular lever. This would mean that at the moment of the closure of the valves, the ventricle had not only completed its contraction, but was far advanced in relaxation. Such a view is not only *à priori* improbable, but is directly contradicted by the fact that when we compare a tracing obtained by placing a lever directly on the heart, or, indeed, a tracing of the cardiac impulse with a pulse-tracing of an artery, we find that the ventricle continues contracted after the artery has ceased to be expanded by the blood ejected from the ventricle. That is to say, the actual flow of blood takes place only during the middle portion of the time during which the muscular fibres of the ventricle are contracting

and engaged in carrying on the systole. During the first part, pressure is being got up, during the second the blood is being propelled, during the third the ventricle continues to remain empty and contracted. By this means the complete emptying of the ventricle is effectually secured. And others have urged that the closure of the semilunar valves, being entirely due to the reflux spoken of above, follows close upon the emptying of the ventricle; in other words, that it takes place while the ventricle is still contracted. It is very difficult to point out indications on the ventricular curve which indubitably correspond to this event. In tracings (of the cardiac impulse, and in tracings taken by a lever placed directly on the heart, a notch, followed by a rise, is sometimes observed in that part of the curve which intervenes between the first large rise and the final sudden fall; and this secondary rise has been taken to indicate the closure of the semilunar valves; but, if this be the case, the time during which the ventricle remains contracted after the closure of the valves forms a very considerable fraction of the whole period of the systole; and this presents difficulties. Sometimes two such notches and peaks are seen, and the occurrence of the two has been attributed to a want of synchronism in the closure of the pulmonary and aortic semilunar valves, the latter closing some little time before the former. But it is by no means clear that these notches and peaks are thus due to the closure of the valves; they may possibly have another origin, they are not always present, and the attempt to fix the time of the closure of the semilunar valves by them cannot be regarded as satisfactory. On the other hand, the second sound of the heart is undoubtedly due to the complete closure and sudden tension of the semilunar valves; and not only is this second sound separated from the first sound by a distinctly appreciable interval (from which we may infer either that the systole of the ventricle ceases before the complete closure and sudden tension of the semilunar valves, or that the first sound does not last so long as the systole itself, and is, therefore, not a muscular sound), but the time elapsing between the beginning of the first sound and the second sound is, as we shall see, remarkably constant. Now, we have reason to believe that the quantity of blood expelled at any one beat, and hence the time taken up in its escape, does vary very considerably; whereas, the duration of the actual systole is probably much more constant. Hence we may infer, and the conclusion may be supported by other arguments, that at the actual closure of the semilunar valves, giving rise to the second sound, the ventricle has just finished its systole and is beginning to relax. If this view be correct, the time of the closure of the valves is not indicated on the cardiographic tracing by any special mark, but coincides with the

commencement of the more sudden and final fall of the lever, as at *d*, in Fig. 59.

Marey thought that the oscillations seen at *d'* in his curves, and obvious in the auricle and cardiac impulse as well, were due to oscillations of the auriculo-ventricular valve, but in that case they would be inverted in the auricular curve; whereas they are not. It is difficult to say what gives rise to them. We may repeat that many of the details of these curves vary considerably, even with the same method of investigation and when the same apparatus is employed. In all probability the character and sequence of the events are modified by various circumstances, such as the rate and rapidity of the beat, the quantity of blood flowing into the heart, and the pressure obtaining in the arteries.

Amount of Pressure.—Although the instrument of Chauveau and Marey may be experimentally graduated and has been used to measure the amount of pressure in the several cavities of the heart, it is, as we have said, open to objections. Better results may be gained by passing through the jugular vein into the right auricle, and thence into the right ventricle, or through the carotid artery into the left ventricle, a tube open at the end introduced into the heart and connected at the other end with a manometer. Variations of pressure in the cardiac cavities are thus transmitted directly to the mercury column of the manometer in the same way as those of an artery when arterial pressure is measured. The inertia of the mercury column, however, prevents an exact response to the rapid movements of the heart, and obscures the results; though by using maximum and minimum manometers, the maximum and minimum pressures of the several cavities may be determined.

The principle of the maximum manometer (Fig. 60) consists in the introduction into the tube leading from the heart to the mercury column of a (modified cup-and-ball) valve, opening, like the aortic semilunar valves, easily from the heart, but closing firmly when fluid attempts to return to the heart. By reversing the direction of the valve, the manometer is converted from a maximum into a minimum instrument. When an ordinary manometer is connected with a ventricular cavity, the movements of the mercury do not follow exactly the rapid variations of pressure of the cavity, and the height of the column fails to indicate both the highest and the lowest pressures.

In this way, in the dog, a maximum pressure has been observed in the left ventricle of about 140 mm. (mercury), in the right ventricle of about 60 mm., and in the right auricle of about 20 mm. Marey had previously, by means of his own instrument, determined the pressure in the horse to be in the left ventricle about

150 mm., in the right ventricle only about 30 mm., while that of
the right auricle he estimated at not more than a few mm.

It is interesting to observe that the minimum pressure may
fall below that of the atmosphere; thus in the left ventricle (of
the dog) a minimum pressure varying from —52 to —20 mm. may
be reached, the minimum of the right ventricle being from —17
to —16 mm., and of the right auricle from —12 to —7 mm.[1]
Part of this diminution of pressure in the cardiac cavities may

Fig. 60

THE MAXIMUM MANOMETER OF GOLTZ AND GAULE.

At *e* a connection is made with the tube leading to the heart. When the screw clamp *k* is
closed, the valve *v* comes into action, and the instrument, in the position of the valve shown
in the figure, is a maximum manometer. By reversing the direction of *v* it is converted into
a minimum manometer. When *k* is opened, the variations of pressure are conveyed along *a*,
and the instrument then acts like an ordinary manometer.

be due, as will be explained in a later part of this work, to the
aspiration of the thorax in the respiratory movements. But
even when the thorax is opened, and artificial respiration kept
up, under which circumstances no such aspiration takes place,
the pressure in the left ventricle may still sink as low as
—24 mm. The minimum manometer, which shows most dis-
tinctly the existence of this negative pressure, obviously gives
no information as to the exact phase of the beat in which it
occurs; and there is some difference of opinion as to the exact

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[1] These numbers are to be considered merely as instances which have been
observed, and not as averages drawn from a large number of cases.

time at which it takes place. Goltz and Gaule, to whom we are indebted for the maximum and minimum manometer, believed that the negative pressure appeared at the beginning of the diastole and indeed that it was caused by the expansion of the ventricle. Were this the case, the ventricle might be regarded not only as a force pump driving blood into the arteries, but also as a suction pump drawing blood from the auricles and great veins.

Others, however, find great difficulties in supposing that the ventricular walls can, either by virtue of the elasticity of their fibres, or by the contraction of special dilating fibres, or by becoming suddenly injected with blood through the coronary arteries, actually expand so as to exert any such suction power. And they maintain that the negative pressure seen in the ventricle is merely that same negative pressure due to the sudden emptying of the ventricle which we have already described as serving to close the semilunar valves. When the minimum manometer is used, the lowest limit of negative pressure is not reached until after several beats, indicating that its duration in any single beat must be very brief. The negative pressure due simply to the cessation of the flow is in fact almost immediately made away with by the ventricular walls, in their continued contraction coming into complete contact; it passes off therefore before any blood can enter into the ventricle from the auricle, and hence can exert no suction power.

Admitting this, however, it is still open for us to suppose that after this negative pressure has passed away, a second negative pressure is caused by the expansion of the ventricle in diastole ; and that this, though also brief, does exert a suction power. And indeed the view that the ventricle in expanding can produce such a negative pressure is one which cannot as yet be regarded as definitely disproved.

The Duration of the Several Phases.—The time measurements given in Fig. 54 afford a general idea of the relative duration of the several events in the slowly beating heart of the horse. Thus it is obvious that the longest phase (viz., about $\frac{6}{10}$ of a second) is that occurring between the end of the ventricular systole at e' to the beginning of the auricular systole at b; this is often spoken of as the diastole, or as the "passive interval," since during this time both auricles and ventricles are in diastole. The next longest phase is the systole of the ventricles (viz., rather more than $\frac{4}{10}$ of a second), and the shortest (viz., rather less than $\frac{2}{10}$ of a second) is the systole of the auricles.

When we desire to arrive at more complete measurements, we are obliged to make use of calculations based on various data ; and these give only approximate results. Naturally the most interest is attached to the duration of events in the human heart.

The datum which perhaps has been most largely used is the interval between the beginning of the first and the occurrence of the second sound. This may be determined with approximative correctness, and according to Donders varies from 0.301 to 0.327 of a second, occupying from 40 to 46 per cent. of the whole period; and being fairly constant for different rates of heart-beat.

The observer, listening to the sounds of the heart, made a signal at each event on a recording surface, the difference in time between the marks being measured by means of the vibrations of a tuning-fork recorded on the same surface. By practice it was found possible to reduce the errors of observation within very small limits.

Now, whatever be the exact causation of the first sound, it is undoubtedly coincident with the systole of the ventricles, though possibly the actual commencement of its becoming audible may be slightly behind the actual beginning of the muscular contractions. Similarly the occurrence of the second sound due to the closure of the semilunar valves may, as we have seen, be taken to mark the close of the ventricular systole. And thus the interval between the beginning of the first and the occurrence of the second sound has been regarded as indicating approximatively the duration of the ventricular systole—*i. e.*, the period during which the ventricular fibres are contracting. If, however, we accept the view that the ventricle still remains contracted for a brief period after the valves are shut, then the second sound does not mark the end of the systole, and the duration of the systole is rather longer than the 0.3 second given above.

The propulsion of the blood into the aorta leads to an expansion of the aorta walls, known as the pulse, which we shall study more fully immediately. This pulse travels, as we shall see, along the arteries at a certain rate; it is later at arterial points more distant from the heart than at points nearer the heart. We can calculate with approximative correctness the time it takes for the expansion to travel from the aortic valves to the radial artery at the wrist, for example. Now, when we record, as we may do on the same recording surface, the exact moment at which the first sound begins, or at which the lever of the cardiograph begins to rise in the ventricular systole, and also the exact moment at which the expansion of the corresponding pulse at the wrist begins, and measure the interval of time between them, we find that the interval is greater than is required for the expansion of the pulse-wave to travel from the heart to the wrist. The difference gives the measure of the time during which the ventricle by its contraction is getting up an adequate pressure upon its contents, and during which, as yet, blood has not escaped from the ventricular cavity and begun to expand the aorta—the measure, in fact, of what we called, a little while ago, the first period of

the ventricular systole. This may also be estimated by directly measuring the time taken up by the upstroke of the cardiographic tracing, and has been said to be on an average about 0.085 second. These measurements, however, are approximative only, and there can be no doubt that the time varies very largely, being dependent on the quantity of blood in the ventricle. on the blood-pressure in the aorta, and on the condition of the heart.

During the expansion of the artery, and probably for some little time beyond—viz., up to the occurrence of what, in speaking of the pulse-wave, we shall call the dicrotic notch, blood is being propelled from the ventricle. By measuring this time, or by deductions from the curve of the cardiac impulse, it has been concluded that the time during which blood is escaping from the ventricle, or the duration of the second phase of the ventricular systole, amounts to about 0.1 second.

Deducting these two periods from the total period of 0.3 second, there would be left a period of 0.115 second, marking the third phase of the systole, during which the ventricle, though empty, is continuing its contractions. Upon the view, however, that the closure of the valves does not mark the end of the systole, this phase must be taken as still longer.

In a heart beating 72 times a minute, which may be taken as the normal rate, each entire cardiac cycle would last about 0.8 second ; and taking 0.3 second as the duration of the systole, the deduction of this would leave 0.5 second for the whole diastole of the ventricle, including its relaxation.

At the close of this period, there occurs the systole of the auricles, the exact duration of which it is difficult to determine, it being hard to say when it really begins, but which, perhaps, may be taken as lasting on an average 0.1 second. The systole of the ventricle follows so immediately upon that of the auricles, that practically no interval exists between the two events.

We may sum up, therefore, the details of the duration of the more important phases of the cardiac cycle in the following tabular form :

	Second.	Second.
Systole of ventricular previous to opening of semilunar valves	0.085	
Escape of blood into aorta	0.100	
Continued contraction of the emptied ventricle	0 115	
Total systole of the ventricle		0.3
Diastole of both auricle and ventricle, or " passive interval"	0.400	
Systole of auricle .	0.100	
Sum of above two, making the diastole of ventricle, or "pause" between second and first sound		0 5
Total cardiac cycle		0.8

Or, selecting only the important facts out of the $\frac{8}{10}$ second occupying the whole cardiac cycle, $\frac{3}{10}$ second, or possibly rather more, are taken up by the systole, and $\frac{5}{10}$ second, or possibly rather less, by the diastole of the ventricle.

The following diagram may be useful as giving in a graphic form a general idea of the sequence and duration of the several cardiac events. It will be understood, of course, that the diagram is intended to show merely the general relations of the several events, and not to represent exact measurements.

FIG. 61.

DIAGRAMMATIC REPRESENTATION OF THE MOVEMENTS AND SOUNDS OF THE HEART DURING CARDIAC PERIOD. After DR. SHARPEY.
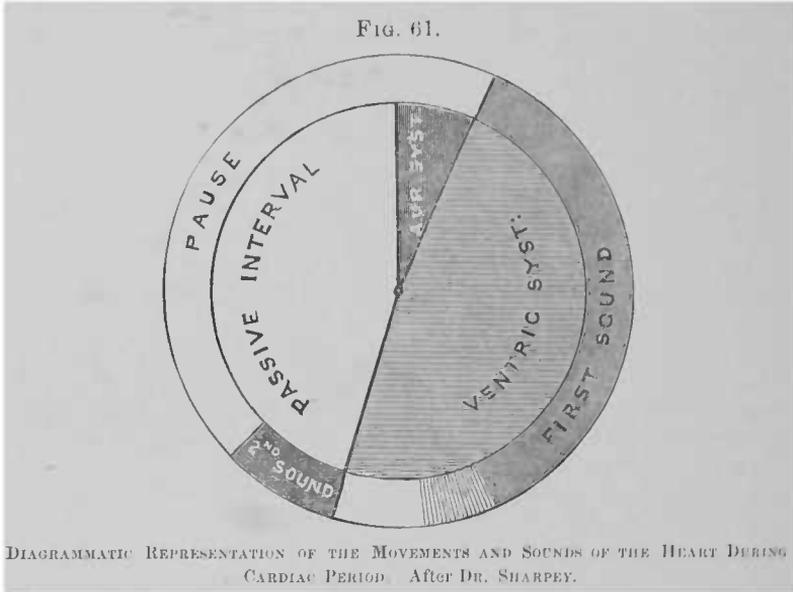
We may repeat that the details given above are at the best approximative only, and, we may add, to a certain extent hypothetical. We have given them at such length not on account of their intrinsic importance, or because they are trustworthy data for further calculations, but because the study of them may help the reader in forming a more vivid image in his mind of what is taking place in the heart during a beat. Moreover, it must be remembered that the figures quoted are those belonging to what may be considered a normal rate of heart-beat. The rate however at which the heart beats varies, as we shall see, under the influence of circumstances, within very wide limits. With regard to the duration of the several phases at different rates of heart-beat, the most important fact is perhaps that the pause varies much more than does the systole of the ventricles. A quickly beating heart differs from a slowly beating heart by

reason of the pause being shortened, much more than by each systole being of less duration.

We may briefly recapitulate the main facts connected with the passage of blood through the heart as follows: The right auricle during its diastole, by the relaxation of its muscular fibres, and by the fact that all pressure from the ventricle is removed by the tension of the tricuspid valves, offers but little resistance to the ingress of blood from the veins. On the other hand, the blood in the trunks, of both the superior and inferior vena cava, is under a pressure, which diminishing towards the heart and becoming within the thorax actually negative (as we shall see in speaking of respirations), remains higher than the pressure obtaining in the interior of the auricle ; the blood in consequence flows into the empty auricle, its progress in the case of the superior vena cava being assisted by gravity. At each inspiration, this flow is favored by the increased negative pressure in the heart and great vessels caused by the respiratory movements. Before this flow has gone on very long, the diastole of the ventricle begins, its cavity dilates, the flaps of the tricuspid valve fall back, and blood for some little time flows in an unbroken stream from the venæ cavæ into the ventricle. In a short time, however, probably before much blood has had time to enter the ventricle, the auricle is full, and forthwith its sharp sudden systole takes place. Partly by reason of the onward pressure in the veins, which increases rapidly from the heart towards the capillaries, partly from the presence of valves in the venous trunks and at the mouth of the inferior vena cava, but still more from the fact that the systole begins at the great veins themselves and spreads thence over the auricle, the force of the auricular contraction is spent in driving the blood, not back into the veins, but into the ventricle, where the pressure is still exceedingly low. Whether there is any backward flow at all into the great veins or whether by the progressive character of the systole the flow of blood continues, so to speak, to follow up the systole without break so that the stream from the veins into the auricle is really continuous, is at present doubtful, though a slight positive wave of pressure synchronous with the auricular systole, travelling backward along the great veins has been observed at least in cases where the heart is beating vigorously.

The ventricle thus being filled by the auricular systole, the play of the tricuspid valves described above comes into action, the auricular systole is followed by that of the ventricle and the pressure within the ventricle, cut off from the auricle by the tricuspid valves, is brought to bear entirely on the *conus arteriosus* and the pulmonary semilunar valves. As soon as by the rapidly increasing shortening of the ventricular fibres the pressure

within the ventricle becomes greater than that in the pulmonary artery, the semilunar valves open and the still continuing systole discharges the contents of the ventricle into that vessel.

As the ventricle thus rapidly and forcibly empties itself, a transient negative pressure makes its appearance in the rear of the ejected column of blood. This in return leads to a reflux of blood towards the ventricle. The first act of this reflux, however, is, as we have seen, to close the semilunar valves, and even if it be urged that the exit of the ventricular contents does not always end with sufficient abruptness to cause a negative pressure adequate to produce this result, the elastic rebound of the arteries, upon their receiving no fresh blood, has the same effect of closing the semilunar valves, and thus of shutting off the blood in the over-distended arteries from the emptied ventricle. Coincidently with this closure, the systole, as we have seen, probably ends and relaxation begins; then once more the cavity of the ventricle becomes unfolded and finally distended by the influx of blood from the auricle.

During the whole of this time the left side has with still greater energy been executing the same manœuvre. At the same time that the venæ cavæ are filling the right auricle, the pulmonary veins are filling the left auricle. At the same time that the right auricle is contracting, the left auricle is contracting, too. The systole of the left ventricle is synchronous with that of the right ventricle, but executed with greater force; and the flow of blood is guided on the left side by the mitral and aortic valves in the same way that it is on the right by the tricuspid valves and those of the pulmonary artery.

The Work Done.

We can measure with approximative exactness the intraventricular pressure, the length of each systole, and the number of times the systole is repeated in a given period, but the quantity ejected from the ventricle into the aorta at each systole, which is, perhaps, the most important factor of all in the determination of the work of the vascular mechanism, cannot accurately be determined. We are obliged, therefore, to fall back on calculations having many sources of error. The mean result of these calculations gives about 180 grms. (6 oz.) as the quantity of blood which is driven from each ventricle at each systole in a full-grown man of average size and weight. It is evident that exactly the same quantity must issue at a beat from each ventricle; for, if the right ventricle at each beat gave out rather less than the left, after a certain number of beats the whole of the blood would be gathered in the systemic circulation. Similarly, if the left ven-

tricle gave out less than the right, all the blood would soon be crowded into the lungs. The fact that the pressure in the right ventricle is so much less than that in the left (probably 30 or 40 mm. as compared with 200 mm. of mercury), is due, not to differences in the quantity of blood in the cavities, but to the fact that the peripheral resistance which has to be overcome in the lungs is so much less than that in the rest of the body.

Various methods have been adopted for calculating the average amount of blood ejected at each ventricular systole. It has been calculated from the capacity of the recently removed and as yet not rigid ventricle, filled with blood under a pressure equal to the calculated average pressure in the ventricle. This method, of course, presupposes that the whole contents of the ventricle are ejected at each systole. Volkmann measured the sectional area of the aorta, and, taking an average velocity of the blood in the aorta (a very uncertain datum), calculated the quantity of blood which must pass through the sectional area in a given time. The number of beats in that time then gave him the quantity flowing through the area, and consequently ejected from the heart, at each beat. The mean of many experiments on different animals came out 0.0025 per cent. the body-weight, which in a man of 75 kilos would be 187.5 grms. Vierordt measured the mean velocity and the sectional area in the carotid, and thence, from a measurement of the sectional area of the aorta, and from a calculation of the blood's mean velocity in it, based on the supposition that the mean velocity in an artery was inversely as its sectional area, arrived at the quantity flowing through the aortic sectional area in a given time, and thus at the quantity passing at each beat. Both these calculations are vitiated by the fact that the variations of velocity in the aorta are so great that any mean has really but little positive value.

Fick, by means of calculations based partly on the data gained by observing the increase of the volume of the whole arm at each cardiac systole, arrived at results much less than either of the above. In one case he estimated the quantity ejected from the heart at each beat at 53 grms., and in a second case at 77 grms.

It must be remembered that, though it is of advantage to speak of an average quantity ejected at each stroke, it is more than probable that that quantity may vary within very wide limits. Taking, however, 180 grms. as the quantity in man ejected at each stroke at a pressure of 250 mm.[1] of mercury, which is equivalent to 3.21 metres of blood, this means that the left ventricle is capable at its systole of lifting 180 grms. 3.21 m. high— *i. e.*, it does 578 gram-metres of work at each beat. Supposing the heart to beat 72 times a minute, this would give for the day's work of the left ventricle nearly 60,000 kilogram-metres; calculating the work of the right ventricle at one-fourth that of the left, the work of the whole heart would amount to 75,000 kilogram-metres, which is just about the amount of work done in the

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[1] A high estimate is purposely taken here.

ascent of Snowdon by a tolerably heavy man. A calculation of more practical value is the following: Taking the quantity of blood as ₁₃ of the body-weight, the blood of a man weighing 75 kilos would be about 5780 grms. If 180 grms. left the ventricle at each beat, a quantity equivalent to the whole blood would pass through the heart in 32 beats—*i. e.*, in less than half a minute.

Variations in the Heart's Beat.

These are, for the most part, in reality vital phenomena—*i. e.*, brought about by events depending on changes in the vital properties of the different tissues of the body. It will be convenient, however, briefly to review them here, though the discussion of their causation must be deferred to its appropriate place.

The *frequency* of the heart—*i. e.*, the number of beats in any given time, may vary. The average rate of the human pulse or heart-beat is 72 a minute. It is quicker in children than in adults, but quickens again a little in advanced age. It is quicker in the adult female than in the adult male, in persons of short stature than in tall people. It is increased by exertion, and thus is quicker in a standing than in a sitting, and in a sitting than in a lying posture. It is quickened by meals, and while varying thus from time to time during the day, is, on the whole, quicker in the evening than in early morning. It is said to be, on the whole, quicker in summer than in winter. Even independently of muscular exertion, it seems to be quickened by great altitudes. It is profoundly influenced by mental conditions.

The *length of the systole* may vary—indeed, we have reason to think that it does vary considerably, though as a general and broad rule it may be stated that a frequent differs from an infrequent pulse chiefly by the length of the diastole. Donders found the length of the systole as measured by the interval between the first and second sounds to be for ordinary pulses remarkably constant in different persons, varying not more than from 0.327 to 0.301 second, and being, therefore, relatively to the whole cardiac period less in slow than in quick pulses.

The *force of the beat* may vary; the ventricular systole may be weak or strong. When the rate of beat is suddenly increased there is a tendency for the individual beats to be diminished in force, and on the other hand to be increased in force when the rate is diminished. But there is no necessary connection between rate and strength; both a frequent and an infrequent pulse may be either weak or strong.

The *character of the beat* may vary; the systole may be sudden and sharp, rapidly reaching a maximum and rapidly declining, or slow and lengthened, reaching its maximum only after some

time and declining very gradually; the latter being the slow pulse (*pulsus tardus*) as distinguished from the infrequent pulse (*pulsus rarus*). The pulse is also sometimes spoken of as being slapping, and sometimes as heaving. But, as we shall see immediately, the features of the pulse are dependent not only on the heart-beat, but also on the condition of the arteries.

The *rhythm* may be intermittent or irregular. Thus, in an intermittent pulse, a beat may be, so to speak, dropped; the hiatus occurring either regularly or irregularly. In an irregular rhythm, succeeding beats may differ in length, force, or character.

Sec. 3.—The Pulse.

When the finger is placed on an artery, such as the radial, an intermittent pressure on the finger, coming and going with the beat of the heart, is felt. When a light lever, such as that of the sphygmograph (Fig. 62), is placed on the artery, the lever is

[Fig. 62.

Marey's Sphygmograph

B, B, is where the sphygmograph is applied to the arm; R, spring which rests upon radial artery; V, screw for adjusting marking lever L; H, clock-work; P, smoked paper upon which tracing is made; r, small spring for causing descent of lever after raising.]
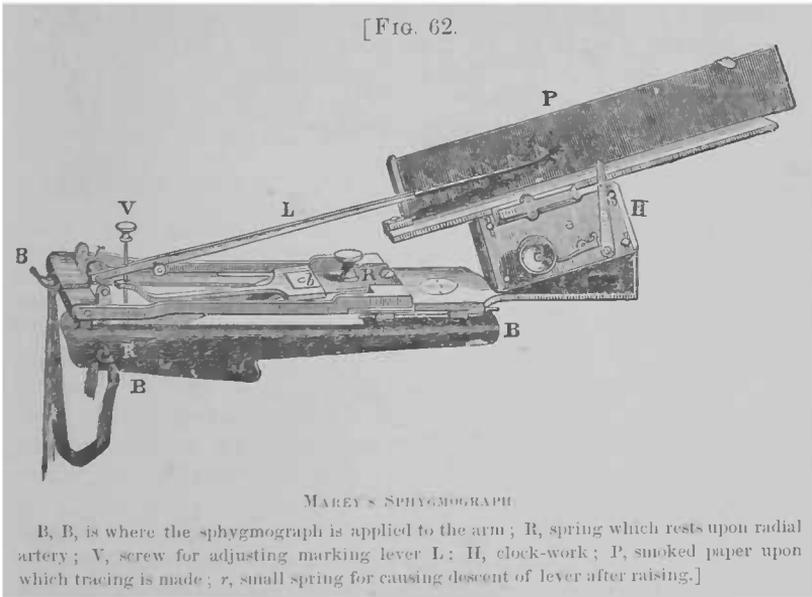
raised at each beat, falling between. The pressure on the finger, and the raising of the lever, are expressions of the expansion of the elastic artery, of the temporary additional distention which the artery undergoes at each systole of the ventricle. This intermittent expansion is called the pulse; it corresponds to the

intermittent outflow of blood from a severed artery, being present in the arteries only, and, except under particular circumstances, absent from the veins and capillaries. The expansion is frequently visible to the eye; and, in some cases, as where an artery has a bend, may cause a certain amount of locomotion of the vessel.

All the more important phenomena of the pulse may be witnessed on an artificial scheme (Fig. 63).

[FIG. 63.

APPARATUS OF MAREY FOR SHOWING MODE IN WHICH PULSE IS PROPAGATED IN THE ARTERIES.

B is a rubber pump, with valve attachment, to prevent a regurgitant current; l, l', l", are levers resting on a gum tube, at intervals of 20 cm. of tubing; C, drum upon which tracing is made; H, clock-work to revolve drum.]
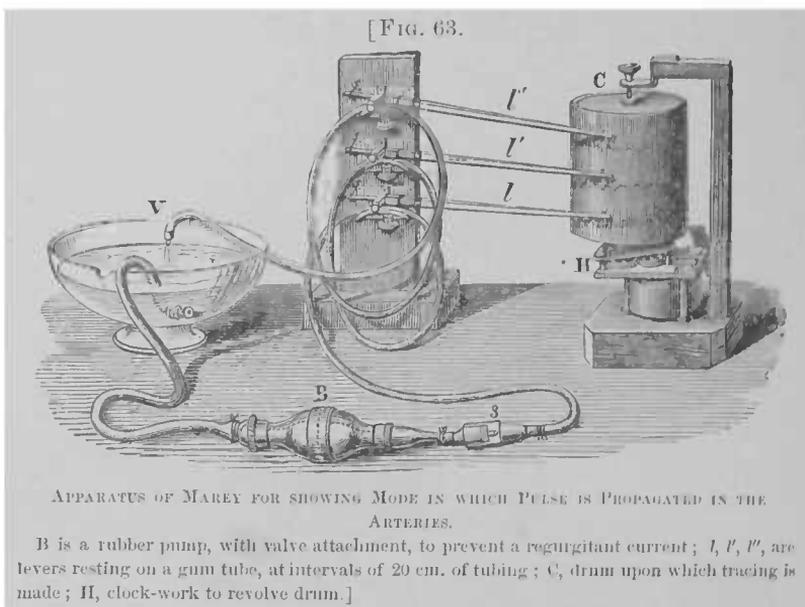
If two levers be placed on the arterial tubes of an artificial[1] scheme, one near to the pump, and the other near to the peripheral resistance, with a considerable length of tubing between them, and both levers be made to write on a recording surface, one immediately below the other, so that their curves can be more easily compared, the following facts may be observed, when the pump is set to work regularly:

1. With each stroke of the pump, each lever (Fig. 64, I. and II.) rises to a maximum (1a, 2a), and then falls again, thus describing a curve—the pulse-curve. This shows that the expansion of the tubing passes the point on which the lever rests in the

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[1] By this is simply meant a system of tubes, along which fluid can be driven by a pump worked at regular intervals. In the course of the tubes a (variable) resistance is introduced in imitation of the peripheral resistance. The tubes on the proximal side of the resistance consequently represent arteries; those on the distal side. veins.

form of a wave. At one moment the lever is quiet; the tube
beneath it is simply distended to the normal permanent amount

[FIG. 64.
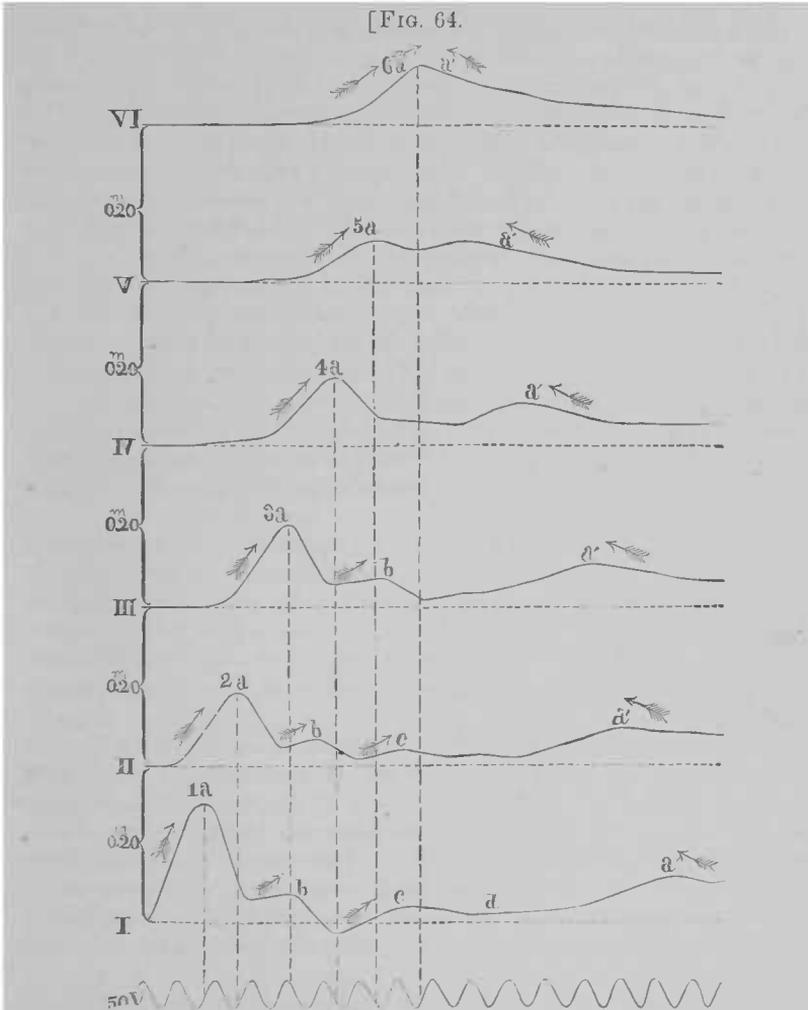
Pulse-curves described by a series of sphygmographic levers placed at intervals of 20 cm.
from each other along an elastic tube into which fluid is forced by the sudden stroke of a
pump. The pulse-wave is travelling from left to right, as indicated by the arrows over the
primary (*a*) and secondary (*b*, *c*) pulse-waves. The dotted vertical lines drawn from the
summit of the several primary waves to the tuning-fork curve below, each complete vibration
of which occupies one-fiftieth second, 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 MAREY.

indicative of the mean arterial pressure; at the next moment the pulse expansion reaches the lever, and the lever begins to rise, and continues to do so until the top of the wave reaches it, after which it falls again until it is once more at rest, the wave having completely passed by.

The rise of each lever is somewhat sudden, but the fall is more gradual, and is generally marked by some irregularities. The suddenness of the rise is due to the suddenness with which the sharp stroke of the pump expands the tube; the fall is more gradual because the elastic reaction of the walls, whereby the tube returns to its former condition after the expanding power of the pump has ceased, is gradual in its action.

2. The size and form of each curve depend in part on the amount of pressure exerted by the levers on the tube. If the levers only just touch the tube in its expanded state, the rise in each will be insignificant. If on the other. hand they be pressed down too firmly, the tube beneath will not be able to expand as it otherwise would, and the rise of the levers will be proportionately diminished. There is a certain pressure, depending on the expansive power of the tubing, at which the tracings are best marked.

3. If the points of the two levers be placed exactly one under the other on the recording surface, it is obvious that the levers being alike except for their position on the tube, any difference in time between the movements of the two levers will be shown by an interval between the beginnings of the curves they describe, if the recording surface be made to travel sufficiently rapidly.

If the movements of the two levers be thus compared, it will be seen that the far lever (Fig. 64, II.) commences later than the near one (Fig. 64, I.), the further apart the two levers are, the greater is the interval in time between their curves. Compare the series I. to VI. (Fig. 64). This means that the wave of expansion, the pulse-wave, takes some time to travel along the tube. By exact measurement it would similarly be found that the rise of the near lever began some fraction of a second after the stroke of the pump.

The velocity with which the pulse-wave travels depends chiefly on the amount of rigidity possessed by the tubing. The more extensible (with corresponding elastic reaction) the tube, the slower is the wave; the more rigid the tube becomes, the faster the wave travels. The width of the tube is of much less influence, though according to some observers the wave travels more slowly in the wider tubes.

The rate at which the normal pulse-wave travels in the human body has been variously estimated at from 10 to 5 metres per

second. In all probability the lower estimate is the more correct one; but it must be remembered that in all probability the rate varies very considerably under different conditions. According to all observers the velocity of the wave in passing from the groin to the foot is greater than that in passing from the axilla to the wrist (6 m. against 5 m.). This is probably due to the fact that the femoral artery with its branches is more rigid than the axillary. So also in the arteries of children, the wave travels more slowly than in the more rigid arteries of the adult; and the velocity appears to be increased by circumstances which heighten, and decreased by those which lessen the mean arterial pressure, since with increasing or diminishing pressure the arterial walls become more or less rigid.

4. When two curves taken at different distances from the pump are compared with each other, the far curve will be found to be shallower, with a less sudden rise, and with a more rounded summit than the near curve; compare 5a with 1a, Fig. 64. In other words, the pulse-wave as it travels onward becomes diminished and flattened out. If a series of levers, otherwise alike, were placed at intervals on a piece of tubing sufficiently long to convert the intermittent stream into a continuous flow, the pulse-wave might be observed to flatten out gradually and grow less until it ceased to be visible.

Care must be taken not to confound the progression of the pulse-wave with the progression of the fluid itself. The pulse-wave travels over the moving blood somewhat as a rapidly moving natural wave travels along a sluggishly flowing river, the velocity of the pulse-wave being 9 metres per second, while that of the current of blood is not more than half a metre per second, even in the large arteries, and diminishes rapidly in the smaller ones.

Taking the duration of the pulse-wave—that is, the time taken by any point in the arterial tract in expanding and returning to its former calibre, so low as $\frac{4}{10}$ of a second, it is evident that the pulse-wave started by any one systole, even if it travels so slowly as 5 m. per second, will before it is completed have reached a point $\frac{4}{10}$ of 5m. = 2m. distant from the ventricle. But even in the tallest man the tips of the toes are not 2m. distant from the heart. In other words, the length of the pulse-wave is much greater than the whole length of the arterial system, so that the beginning of each wave has become lost in the small arteries and capillaries some time before the end of it has finally passed away from the beginning of the aorta.

The general causation of the pulse may then be summed up somewhat as follows: The systole of the ventricle drives a quantity of blood into the already full aorta. The sudden

injection of this quantity of blood expands the portion of the aorta next to the heart, and thus gives rise to the sudden up-stroke of the pulse-curve. The rapidity of the flow from the ventricle being greatest at its beginning, the maximum of expansion is soon reached, and the aortic walls, even while for a short time blood is still, with diminishing rapidity, issuing from the ventricle, tend by virtue of their elasticity to return to their former calibre. This return continues after the flow has ceased, and the aortic valves soon becoming closed, the elastic force thus brought into play serves to drive the blood onward. The elastic recoil being slower than the initial expansion, the down-stroke of the pulse-curve is more gradual than the up-stroke. Of this portion of the aorta, which actually receives the blood ejected from the heart, the part immediately adjacent to the semilunar valves begins to expand first, and the expansion travels thence on to the end of this portion. In the same way it travels on from this portion through all the succeeding portions of the arterial system. For the total expansion required to make room for the new quantity of blood cannot be provided by that portion alone of the aorta into which the blood is actually received; it is supplied by the whole arterial system; the old quantity of blood which is replaced by the new in this first portion has to find room for itself in the rest of the arterial space. As the expansion travels onward, however, the *increase* of pressure which each portion transmits to the succeeding portion will be less than than which it received from the preceding portion. For the whole increase of pressure due to the systole of the ventricle has to be distributed over the whole of the arterial system, and a fraction of it must therefore be left behind at each stage of its progress; that is to say, the expansion is continually growing less, as the pulse travels from the heart to the capillaries; hence the diminished height of the pulse-curve in the more distant arteries, and its disappearance in the capillaries.

Secondary Waves and Dicrotism.—In nearly all pulse-tracings, the curve of the expansion and contraction of the artery is broken by two, three, or several smaller elevations and depressions; secondary waves are imposed upon the fundamental wave. In the sphygmographic tracing from the carotid and radial reproduced in Figs. 65 and 66 and in many of the other tracings given, these secondary elevations are marked as B, C, D. When one such secondary elevation only is conspicuous, so that the pulse-curve presents two notable crests only, the primary crest and the secondary one, the pulse is said to be "dicrotic;" when two secondary crests are prominent, the pulse is often called "tricrotic;" where several, "polycrotic." As a general rule, the secondary eleva-

tions appear only on the descending limb of the whole wave, as in most of the curves given, and the curve is then spoken of as "katacrotic." Sometimes, however, the first elevation or crest is
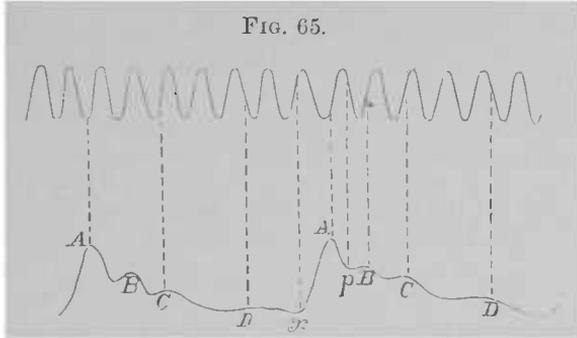
Fig. 65.

PULSE-TRACING FROM CAROTID ARTERY OF HEALTHY MAN.[1] From Moens.

☀, commencement of expansion of the artery. A, summit of the first rise. C, dicrotic secondary wave. B, predicrotic secondary wave ; p, notch preceding this. D, succeeding secondary wave. The curve above is that of a tuning-fork with ten double vibrations in a second.
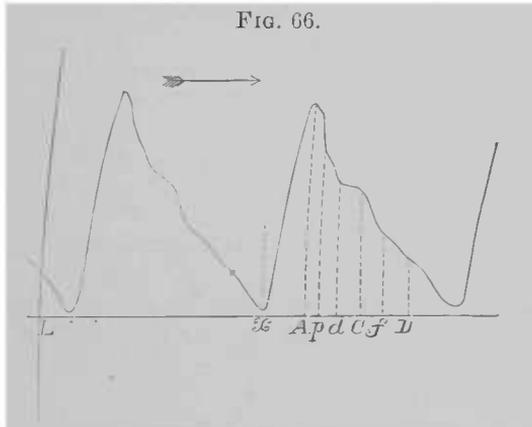
Fig. 66.

[1]PULSE-CURVE FROM RADIAL OF MAN.

Taken with extra vascular pressure of 70 mm. mercury. The vertical curved line L gives the tracing which the recording lever made when the blackened paper was motionless. The horizontal line forms the abscissa of the tracing. The curved interrupted lines show the distance from one another in time of the chief phases of the pulse wave. x = commencement and A close of expansion of artery. p, predicrotic notch. d, dicrotic notch. C, dicrotic crest. D, post-dicrotic crest. f, the post-dicrotic notch.

[1] It will be understood that in the case of this and the succeeding sphygmographic tracings (for the latter I am indebted to Dr. Galabin and Dr. Roy) comparisons between the several curves can only be made in a limited manner and with precautions, since the tracings are taken with different amplifications, pressures, etc.—and are some from man, others from animals. They are introduced simply to illustrate points treated of successively in the text.

not the highest, but appears on the ascending portion of the main curve as in Fig. 67 and Fig. 70; such a curve is spoken of as "anacrotic."

Of these secondary elevations, the most frequent, conspicuous, and important is the one which appears some way down on the descending limb and is marked C on most of the curves. It is

FIG. 67.

ANACROTIC PULSE-TRACING FROM THE CAROTID OF RABBIT.
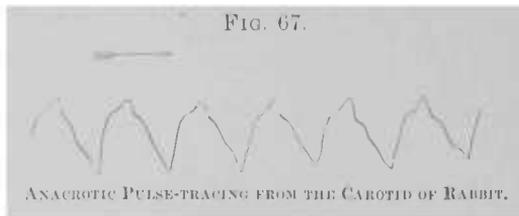
more or less distinctly visible on all sphygmographic tracings and may be seen in sphygmograms of the aorta as well as of other arteries. Sometimes it is so slight as to be hardly discernible; at other times it may be so marked as to give rise to a really double pulse (Fig. 68)—*i. e.*, a pulse which can be felt as double

FIG. 68.
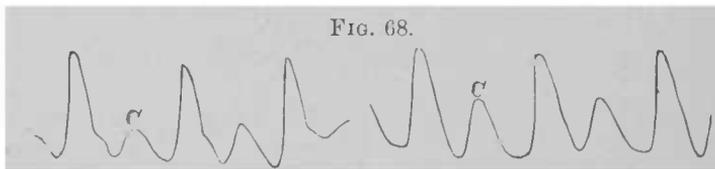
TWO GRADES OF MARKED DICROTISM IN RADIAL PULSE OF MAN.   (Typhoid Fever.)

by the finger, hence it has been called the *dicrotic* elevation or the dicrotic wave, the notch preceding the elevation being spoken of as the "dicrotic notch." Neither it nor any other secon dary elevations can be recognized in the tracings of blood-

FIG. 69.
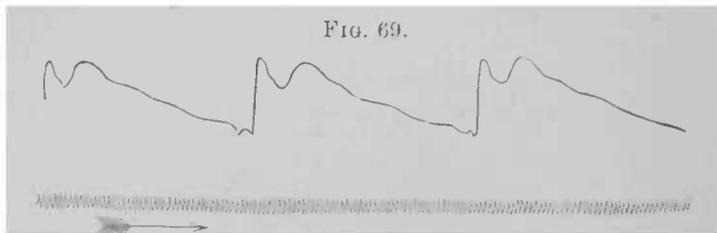
NORMAL PULSE-CURVE IN THE AORTA FROM THE DOG.

pressure taken with a manometer. This may be explained by the fact that the movements of the mercury column are too sluggish to reproduce these finer variations, but dicrotism is also conspicuous by its absence in the tracings given by more deli-

cately responsive instruments. Moreover, when the normal pulse is felt by the finger, most persons find themselves unable to detect any dicrotism. Hence some have been led to maintain that this and the other secondary elevations do not really exist in the normal pulse. But it seems difficult to maintain this view in face of the experiment of Landois, in which the tracing obtained by allowing the blood to spirt directly from an opened small artery, such as the dorsalis pedis, upon a recording surface, showed in an unmistakable manner the existence of the dicrotic wave.

Less constant and conspicuous than the dicrotic wave, but yet appearing in most sphygmograms, is an elevation which appears

FIG. 70.
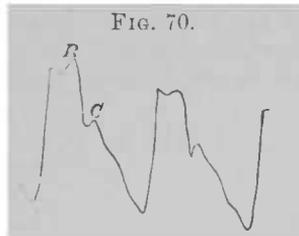
ANACROTIC SPHYGMOGRAPH TRACING FROM THE ASCENDING AORTA (Aneurism).

higher on the descending limb of the main wave; it is marked B on some of the curves and is frequently called the *predicrotic* wave; it may become very prominent. Sometimes other secondary waves are seen following the dicrotic wave at D in Fig. 65, but these are very inconstant and usually even when present inconspicuous.

When tracings are taken from several arteries or from the same artery under different conditions of the body, these secondary waves are found to vary very considerably, giving rise to

FIG. 71.
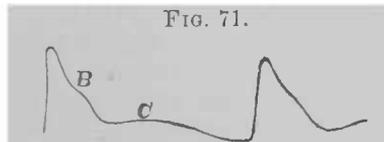
PULSE-TRACING FROM THE DORSALIS PEDIS.

many characteristic forms of pulse-curve. Moreover, in the same artery, and with the same instrument, the form and even the special features of the curve vary according to the amount of pressure (expressed either in ounces or in mm. of mercury) with which the lever is pressed upon the artery. Figs. 72, 73 show a series of changes thus brought about by varying the

pressure of the lever, and Fig. 74 shows the effect of this extra-vascular pressure on the form of a fully dicrotic pulse. This effect of pressure in fact varies according to the condition of the vascular system.

Were we able with certainty to trace back the several features of the curves to their respective causes, an adequate examination of sphygmographic tracings would undoubtedly disclose much valuable information concerning the condition of the body presenting them. Unfortunately the problem of the origin of these secondary waves is a most difficult and complex one, so much so that the detailed interpretation of a sphygmographic tracing is still in most cases extremely uncertain.

Various causes have been suggested as bringing about the secondary waves, and much discussion has arisen especially concerning the dicrotic wave. When the tube of the artificial scheme bearing two levers is blocked just beyond the far lever,

FIG. 72.
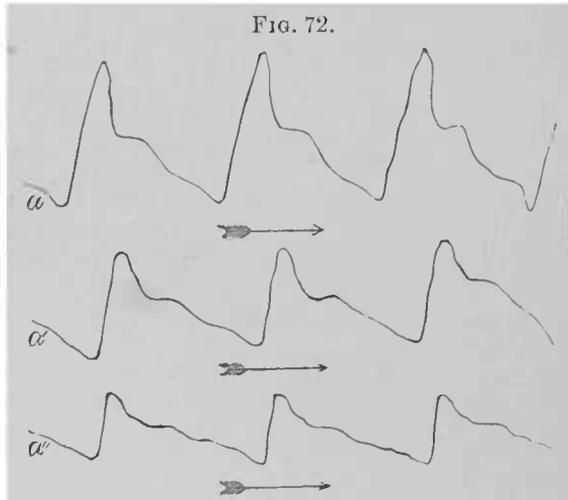
INFLUENCE OF CHANGES IN THE PRESSURE APPLIED TO THE EXTERIOR OF THE VESSEL ON THE FORM OF THE CURVE.

a, From the art. radialis of healthy man of 27 years of age, with an extra arterial pressure equal in *a* to 70 mm., in *a'* to 50 mm., in *a''* to 30 mm. mercury.

the primary wave is seen to be accompanied by a second wave, which at the far lever is seen close to, and often fused into, the primary wave (Fig. 68, VI. *a'*), but at the near lever is at some distance from it (Fig. 68, I. *a'*), being the further from it, the longer the interval between the lever and the block in the tube. The second wave is evidently the primary wave reflected at the block and travelling backwards towards the pump. It thus, of

course, passes the far lever before the near one. And it has been argued that the dicrotic wave of the pulse is really such a reflected wave, started either at the minute arteries and capillaries, or at the points of bifurcation of the larger arteries, and travelling backwards to the aorta. But if this were the case, the distance between the primary crest and the dicrotic crest ought to be less in arteries more distant from the heart than in those nearer, just as in the artificial scheme the reflected wave is fused with a primary wave near the block, but becomes more and more separated from it the further back we trace it. Now, this is not the case with the dicrotic wave. Careful measurements show that the distance between the primary and dicrotic crests is either greater or certainly not less in the smaller or more distant arteries

Fig. 73.

NORMAL PULSE-CURVE FROM CAROTID OF RABBIT;
showing influence on height and form of curve of changes in the extra vascular pressure, which was in *a* 20 mm., in *b* 30 mm., in *c* 40 mm, and in *d* 50 mm. of mercury.
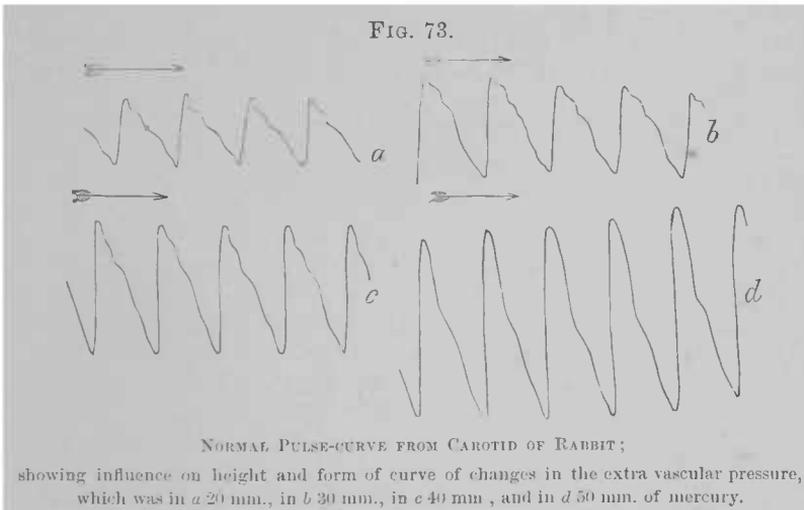
than in the larger or nearer ones. This feature, indeed, proves that the dicrotic wave cannot be in any way a retrograde wave. Again, the more rapidly the primary wave is obliterated, or at least diminished on its way to the periphery, the less conspicuous should be the dicrotic wave. Hence, increased extensibility and increased elastic reaction of the arterial walls which tend to use up rapidly the primary wave, should also lessen the dicrotic wave. But, as a matter of fact, these conditions are favorable to the prominence of the dicrotic wave. Besides, the multitudinous peripheral division would render one large peripherically reflected wave impossible.

But in addition to reflected waves, other waves which may be called "waves of oscillation," make their appearance when a fluid is driven through a system of tubes, by means of an intermittent

force.   And different origins have been assigned to secondary
waves of this description.

Thus when the rapid flow of a fluid along a tube is suddenly
checked at a point of its course, the inertia of the fluid will carry
the column of fluid still forwards so as to leave behind it a dim-
uution of pressure.   This diminution will appear on a graphic
record of the pressure as a depression or notch; and will be fol-
lowed by a secondary rise as a reflux of fluid takes place towards
the point where the pressure has become diminished.   Both the

FIG. 74.

DICROTIC PULSE-CURVE DUE TO LOSS OF BLOOD.

From carotid of rabbit with extra vascular pressures in *a* of 50 mm., *b* of 40 mm., *c* of 20 mm.,
and *d* of 10 mm. of mercury.
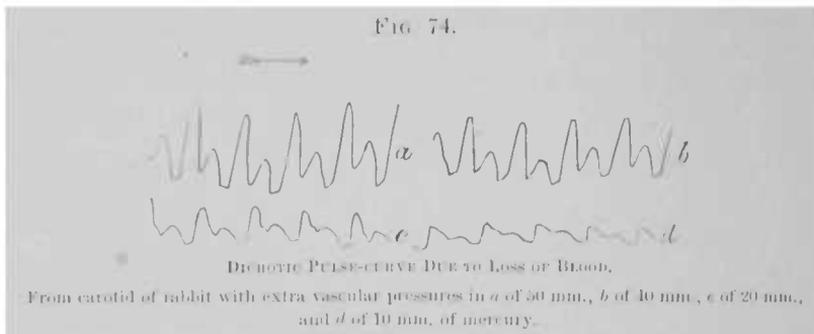
depression and the secondary rise will travel as a wave along the
tube, being frequently followed by other smaller waves of similar
character and similar origin.   Waves thus originating have been
appealed to as explaining the secondary waves of the pulse-curve.
Thus at the moment when the ventricle, having emptied itself,
ceases to throw any more blood into the aorta, the blood which
was last ejected being carried forward by its inertia gives rise to
a diminution of pressure in the ventricle and at the root of the
aorta.   The aortic walls forthwith contract upon this diminished
pressure, and a reflux of blood towards the semilunar valves
takes place, leading to the appearance of a depression or notch
in the pulse-curve, which is propagated forwards along the aorta.
This reflux closes the semilunar valves and at the same time leads
to a recovery of pressure which similarly appears on the pulse-
curve as an elevation succeeding the notch.

Then, again, it has been argued that in any section of the
arterial tract, the inertia of the walls and of the contained blood,
in each expansion of the section, carries them on in their move-
ment of expansion some little time after the actual expanding
force has ceased to act.   This leads to a falling back or contrac-
tion, which again by reason of the same inertia overshoots its
mark, and thus through a series of oscillations, of which the first
is the most conspicuous, the artery settles down to its normal
calibre before the next expansion reaches it.   The extent of such

oscillatious is determined not only by the character of the walls, but by the specific gravity of the contained fluid. In the artificial scheme with the same elastic tubing, the secondary waves thus caused are much greater with mercury thau with water, and disappear almost wholly· when air is employed. Such waves of oscillation may be supposed to be generated in differeut degrees, in each aud every section of the arterial tract; the waves due to a cessation of the flow are, on the contrary, generated at the point where the intermittence is effected, and may be seen in rigid as well as iu elastic tubes; but these latter waves also are profoundly modified by the nature of the walls of the tubes along which they are transmitted.

Lastly, it has been maintained that these secondary waves are of active, not passive, origin; that is, that they are caused by a rapid muscular contractiou of the arterial walls following up, so to speak, the arterial beat.

We have dwelt at so great a length on these secoudary waves of the pulse-curve because of the importance attached to them in clinical medicine; but it would be hardly profitable to enter more fully into the discussion of these several contending views. As an instance of the difficulty of the subject, and the insufficiency of our knowledge, we may point out that observers are not yet agreed as to which part of the curve corresponds to the closure of the semilunar valves. Thus some maintain that this event corresponds to and indeed is indicated by the dicrotic wave, the dicrotic notch representing the reflux towards the ventricle, and the dicrotic elevation a new forward movement reflected from the closed valves. But under this view, though it seems the more probable, the predicrotic wave presents a difficulty; and, indeed, others maintain that the moment of closure of the semilunar valves is indicated by this, the predicrotic, and not by the dicrotic wave. Until this and other points are fiually settled, all interpretatious of modifications of the pulse-curve must remain uncertain and unsatisfactory.

The following facts, however, may be borne in mind as not only of practical importance, but as necessary data for any judgments concerning the pulse-curve.

1. Whatever the origiu of the dicrotic wave, its features may be modified by changes taking place in the peripheral (arterial) districts without any alteration in the central (cardiac) events. Thus, dicrotism may become conspicuous in one artery, while remaining indistinct in others.

2. The prominence of the dicrotic wave, though favored by a sudden, strong, ventricular systole, is especially assisted by a diminution of blood-pressure. Thus. it is a marked characteristic of the pulse in many cases of fever (Fig. 69) where blood-pressure

is low. So, also, it may be brought on at once in an artery in
which it was previously insignificant by sudden lowering of the
blood-pressure, as is shown in Fig. 75.   It may similarly be
induced by section of the vaso-motor nerves belonging to the
branches of the artery : this, as we shall presently see, diminishes
the peripheral resistance, through an expansion of the minute
arteries, and so leads to a lowering of the blood-pressure in the
main arteries.   The prominence of the dicrotic wave is further
dependent on the amount of extensibility and elastic reaction of
the arterial walls.   Hence, the dicrotic wave is not well marked
in arteries which have become rigid by disease or old age.

FIG. 75.

TRACING FROM RADIAL IN MAN ;

showing change in form of pulse-curve accompanying a sudden fall in the blood-pressure.
The pulse, at first not markedly dicrotic, rapidly becomes so, and then passes on into the con-
dition known as hyperdicrotism, where the dicrotic notch reaches a level lower than that from
which the primary rise started.
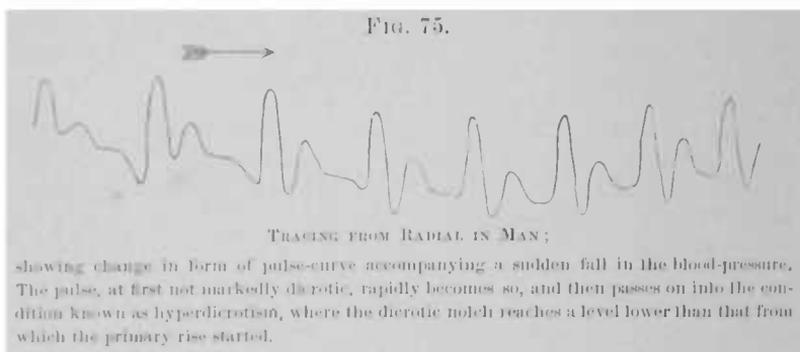
We may add that an anacrotic pulse, in which a crest followed
by a notch is visible on the ascending portion of the curve, before
the maximum of expansion is reached, though it may sometimes
be produced temporarily in healthy persons, is generally asso-
ciated with diseased conditions, usually such in which the arteries
are abnormally rigid.   It has been interpreted as due to the
pressure in the aorta rising even after the first rapid rush from
the ventricle.   Under normal conditions, as we have already
seen, the maximum expansion is soon reached, but in cases where
the arterial walls are unusually rigid and the heart at the same
time not abnormally weak, the ventricle may continue to empty
itself against a resistance which increases rapidly with the amount
of blood passing into the aorta, so that in spite of the diminishing
rapidity with which the blood is leaving the ventricle the insuffi-
cient distensibility of the vessels causes the pressure in their
interior to continue to rise until nearly the end of the outflow
from the heart.   An anacrotic pulse also frequently accompanies
hypertrophy and dilation of the left ventricle.

The pulse, then, is the expression of two sets of conditions :
one pertaining to the heart, and the other to the arterial system.
The arterial conditions remaining the same, the characters of the

pulse may be modified by changes taking place in the beat of the heart; and, again, the beat of the heart remaining the same, the pulse may be modified by changes taking place in the arterial walls. Hence, the diagnostic use of the pulse-characters. It must, however, be remembered that arterial changes may be accompanied by compensating cardiac changes, to such an extent, that the same features of the pulse may obtain under totally diverse conditions, provided that these conditions affect both factors in compensating directions.

Venous Pulse.—Under certain circumstances, the pulse may be carried on from the arteries through the capillaries into the veins. Thus, when the salivary gland is actively secreting, the blood may issue from the gland through the veins in a rapid pulsating stream. The nervous events which give rise to the secretion of saliva, lead, at the same time, by the agency of vasomotor nerves, of which we shall presently speak, to a dilation of the small arteries of the gland. This dilatation of the small arteries diminishes the peripheral resistance by allowing more blood to pass through them with less friction; in consequence, the elasticity of the arterial walls is brought into play to a less extent than before, and this may, in certain cases, go so far that, as in the case of the artificial apparatus, where the elastic tubing has an open end (see p. 170), not enough elasticity is brought into action to convert the intermittent arterial flow into a continuous one. A similar venous pulse is also sometimes seen in other organs.

Careful tracings of the great veins in the neighborhood of the heart show elevations and depressions, which appear due to the variations of intracardiac pressure, and which may, perhaps, be spoken of as constituting a "venous pulse;" but at present they need further elucidation. In cases of insufficiency of the tricuspid valves, the systole of the ventricle makes itself felt in the great veins; and a distention travelling backwards from the heart becomes very visible in the veins of the neck. This is sometimes spoken of as a venous pulse.

Variations of pressure in the great veins due to the respiratory movements are also sometimes spoken of as a venous pulse; the nature of these variations will be explained in treating of respiration.

II. THE VITAL PHENOMENA OF THE CIRCULATION.

So far the facts with which we have had to deal, with the exception of the heart's beat itself, have been simply physical facts. All the essential phenomena which we have studied may be

reproduced on a dead model. Such an unvarying mechanical vascular system would, however, be useless to a living body whose actions were at all complicated. The prominent feature of a living mechanism is the power of adapting itself to changes in its internal and external circumstances. In such a system as we have sketched above there would be but scanty power of adaptation. The well-constructed machine might work with beautiful regularity; but its regularity would be its destruction. The same quantity of blood would always flow in the same steady stream through each and every tissue and organ, irrespective of local and general wants. The brain and the stomach, whether at work and needing much, or at rest and needing little, would receive their ration of blood, allotted with a pernicious monotony. Just the same amount of blood would pass through the skin on the hottest as on the coldest day. The canon of the life of every part for the whole period of its existence would be furnished by the inborn diameter of its bloodvessels, and by the unvarying motive power of the heart.

Such a rigid system, however, does not exist in actual living beings. The vascular mechanism in all animals which possess one is capable of local and general modifications, adapting it to local and general changes of circumstances. These modifications fall into two great classes:

1. Changes in the heart's beat. These, being central, have of course a general effect.

2. Changes in the peripheral resistance, due to variations in the calibre of the minute arteries, brought about by the agency of their contractile muscular coats. These changes may be either local or general.

To these may be added as subsidiary modifying events:

3. Changes in the peripheral resistance of the capillaries due to alterations in the adhesiveness of the capillary walls or to other influences arising out of the as yet obscure relations existing between the blood within and the tissue without the thin permeable capillary walls, and depending on the vital conditions of the one or of the other. Such changes causing an increase of peripheral resistance are seen to a marked degree in the pathological condition known as stasis.

4. Changes in the quantity of blood in circulation.

The first two and chief classes of events (and probably the third) are directly under the dominion of the nervous system. It is by means of the nervous system that the heart's beat and the calibre of the minute arteries are brought into relation with each other, and with almost every part of the body. It is by means of the nervous system acting either on the heart, or on the small arteries, or on both, that a change of circumstances affect-

ing either the whole or a part of the body is met by compensating or regulative changes in the flow of blood. It is by means of the nervous system that an organ has a more full supply of blood when at work than when at rest, that the stream of blood through the skin rises and ebbs with the rise and fall of the temperature of the air, that the work of the heart is tempered to meet the strain of overfull arteries, and that the arterial gates open and shut as the force of the central pump waxes and wanes. Each of these vital factors of the circulation must therefore be considered in connection with those parts of the nervous system which are concerned in its action.

Sec. 4.—Changes in the Beat of the Heart.

We have already discussed the more purely mechanical phenomena of the heart. We have therefore in the present section only to inquire into the nature and working of the mechanism (chiefly at least nervous) by which the beat of the heart is maintained, varied, and regulated.

In studying closely the phenomena of the beat of the heart, it becomes necessary to obtain a graphic record of various movements.

1. In the frog or other cold-blooded animal, a light lever may be placed directly on the ventricle (or on an auricle, etc.) and changes of form, due either to distention by the influx of blood, or to the systole, will cause movements of the lever, which may be recorded on a travelling surface. The same method may be applied to the mammalian heart, but difficulties are introduced by the locomotion of the heart caused by the movements of the lungs.

2. Or, as in Gaskell's method, the heart may be fixed by a clamp carefully adjusted round the auriculo-ventricular groove, while the apex of the ventricle and some portion of one auricle are attached by threads to horizontal levers placed respectively above and below the heart. The auricle and the ventricle each in its systole pulls at the lever attached to it; and the times and extent of the contractions may thus be recorded.

3. A record of intracardiac pressure may be taken in the frog or tortoise, as in the mammal, by means of an appropriate manometer. And in these animals, at all events, it is easy to keep up an artificial circulation. A canula is introduced into the sinus venosus and another into the ventricle through the aorta. Serum or dilute blood (or any other fluid which it may be desired to employ) is driven by moderate pressure through the former; to the latter is attached a tube connected by means of a side piece with a small mercury manometer. So long as the exit tube is open at the end, fluid flows freely through the heart and apparatus. Upon closing the exit tube at its far end, the force of the ventricular systole is brought to bear on the manometer, the index of which registers in the usual way the movements of the mercury column. Newell Martin has succeeded in applying a modification of this method to the mammalian heart.

4. The movements of the ventricle may be registered by introducing into it through the auriculo-ventricular orifice a so-called "perfusion" canula, Fig. 76 I, with a double tube, one inside the other, and tying the ventricle on to the canula at the auriculo-ventricular groove, or at any level below that which may be desired. The blood or other fluid is driven at an adequate pressure through the tube *a*, enters the ventricle, and returns by the tube *b*. If *b* be connected with a manometer, as in method 3, the movements of the ventricle may be registered.

5. In the apparatus of Roy, Fig. 76 II, the exit tube is free, but the ventricle (the same method may be adopted for the whole heart) is placed in an air-tight chamber filled with oil or partly with normal saline solution and partly with oil. By means of the tube *b* the interior of the

FIG. 76.
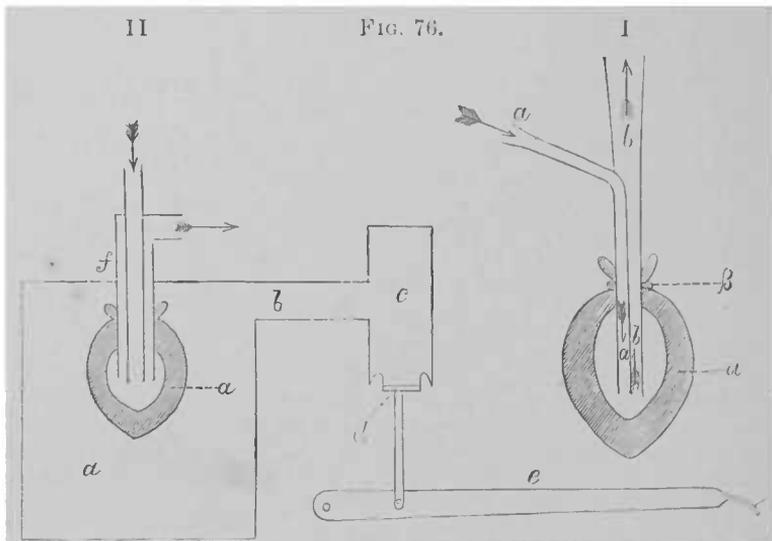
PURELY DIAGRAMMATIC FIGURES OF

I. Perfusion canula tied into frog's ventricle. *a*, entrance, *b*, exit, tube; *a*, wall of ventricle; *β*, ligature.

II. Roy's apparatus modified by Gaskell. *a*, chamber filled with saline solution and oil, containing the ventricle *a* tied on to perfusion canula *f*. *b*, tube leading to cylinder *c*, in which moves piston *d*, working the lever *e*.

chamber *a* is continuous with that of a small cylinder *c* in which a piston *d* secured by thin flexible animal membrane works up and down. The piston again bears on a lever *e* by means of which its movements may be registered. When the ventricle contracts and, by contracting, diminishes in volume, there is a lessening of pressure in the interior of the chamber, this is transmitted to the cylinder, and the piston correspondingly rises, carrying with it the lever. As the ventricle subsequently becomes distended, the pressure in the chamber is increased, and the piston and lever sink. In this way variations in the volume of the ventricle may be recorded without any interference with the flow of blood or fluid through it.

The Mechanism of the Normal Beat.

The Cardiac Muscles.—When a frog's heart which has ceased to beat spontaneously is stimulated by touching it with a blunt needle, a beat is frequently called forth; this artificial beat differs in no obvious characters from a natural beat. The latent period of such an artificial beat is remarkably long, the length varying within very wide limits. Thus the cardiac contraction is more like that of an unstriated than of a striated muscle. The beat is in fact a modified or peculiar form of peristaltic contraction. In the hearts of some animals, the ventricle forms a straight tube; and in these the peristaltic character of the beat is obvious; but in a twisted tube like that of the vertebrate ventricle ordinary peristaltic action would be impotent to drive the blood onward, and is accordingly so far modified that the peristaltic character of the beat is recognized only when the action of the heart becomes slow and feeble.

The cardiac, like the skeletal muscular fibre, after a contraction returns by relaxation to its previous shape, and the whole ventricle (or whole heart) regains after a beat the form natural to its quiescent state. This diastolic expansion, though increased by, is not dependent on, the influx of fluid into the cavities of the heart. Thus the cavity of the empty quiescent mammalian left ventricle, though smaller than when it is distended with blood, as in its normal action, is larger than when it is in systole or when rigor mortis has set in; moreover, if its dimensions be artificially lessened, as when it is squeezed with the hand, it returns by an elastic reaction to its former volume when the pressure is removed.

The cardiac muscles in a healthy condition are, like the skeletal muscles, very elastic. Their elasticity is, however, soon interfered with by imperfect nutrition; and a "contraction remainder" (p. 86), under certain circumstances, is readily developed.

Under the influences of certain poisons, veratrin, digitalin, etc., the length of the beat is enormously prolonged, and the ventricle is eventually thrown into a remarkable contracted condition, the exact nature of which is perhaps not thoroughly understood, though it is believed by many to be due to a deficiency of elastic reaction.

One great feature of the cardiac beat produced by artificial stimulation is the absence of that relationship between the strength of the stimulus employed and the amount of contraction evoked which is so striking in a skeletal muscle (p. 116). The beat with which a heart responds to a stimulus—e. g., a single induction-shock—is, if there be any response at all, equally large

when a feeble as when a strong stimulus is used, though the strength of the beat evoked either by a strong or a weak stimulus may vary considerably within even a very short period of time.

When a second induction-shock is sent in at a certain interval after a first, the beat due to the second shock is often larger than the first, the beneficial effects of a contraction (see p. 127) being even still more manifest in the heart than in an ordinary skeletal muscle. Frequently by successive shocks of equal intensity a "staircase" of beats of successively increasing amplitude may be produced.

When a second induction-shock follows upon the first too rapidly, it is apparently without effect; no second beat is produced. So also when a series of rapidly repeated induction-shocks are sent in, a certain number of them are thus "ineffectual;" the application of the ordinary interrupted current gives rise not to a tetanus but to a rhythmic series of beats. The "refractory period," which is so brief in the skeletal muscle is very prolonged in the cardiac muscle. So also in a spontaneously beating heart, induction-shocks sent in at a certain phase of a cardiac cycle—e. g., the commencement of the systole, are ineffectual, though they produce forced beats when sent in at the other phases of the cycle.

As we shall immediately see, the beat of the heart, and even of a part of the heart such as the ventricle, is not a mere muscular contraction but a complex act, in which both nervous and muscular elements intervene; and it is difficult in all cases to distinguish the action of the one from that of the other. It is probable, however, that many of the features which we have just described are due to peculiarities of the cardiac muscle.

Nervous Mechanism of the Beat.—The heart of a mammal or of a warm-blooded animal ceases to beat almost immediately after being removed from the body in the ordinary way; and though by special precautions and by means of an artificial circulation of blood, an isolated mammalian heart may be preserved in a pulsating condition for a considerable time, our knowledge of the exact nature and of the causes of the cardiac beat is as yet almost entirely based on the study of the hearts of cold-blooded animals, which will continue to beat for hours, or under favorable circumstances even for days, after they have been removed from the body with only ordinary care. We have reason to think that the mechanism by which the beat is carried on, varies in some of its secondary features in even cold-blooded animals : that the hearts, for instance, of the snake, the tortoise and the frog, differ as to the exact manner of carrying out the beat, both from each other and from the bird and the mammal ; but we may, at first

at all events, take the heart of the frog as illustrating the main
and important truths concerning the causes and mechanism of
the beat.

The heart of the frog, as we have just said, will continue to
beat for hours after removal from the body ; and the beats are in

[FIG. 77.

DIAGRAM TO AID IN UNDERSTANDING THE ACTION OF THE NERVES UPON THE HEART.

The right half represents the course of the inhibitory, and the left the course of the accel-
erating nerves of the heart ; the arrows showing the direction in which impressions are
conveyed. The ellipse at the upper extremity of the vagus looking like the section of the
nerve is intended to represent the vagal nucleus or centre. After CARPENTER.]

all important respects identical with the beats executed by the
heart in its normal condition within the living body. Hence we
may infer that the beat of the heart is an automatic action : the

muscular contractions which constitute the beat are caused by impulses which arise spontaneously in the heart itself.

The beat goes on even after the cavities have been cleared of blood, and, indeed, when they are almost empty of all fluid. A beat cannot therefore be, as was once thought, a reflex act excited by the entrance of blood into the cavities of the heart.

In the frog's heart, as in that of the mammal, there is a distinct sequence of events. First comes the beat of the sinus venosus, preceded by a more or less peristaltic contraction of the large veins leading into it, next follows the sharp beat of the two auricles together, then comes the longer beat of the ventricle, and lastly the beat of the bulbus arteriosus completes the cycle. If the incisions, by which the heart is removed, be made carefully, so as not to injure at all the sinus venosus, the beats will continue after a very short pause, or sometimes without any real interruption, with great vigor for a very considerable time. In order that the frog's heart may beat after removal from the body with the nearest approach in rapidity, regularity, and endurance to the normal condition, the removal must be carried out so as to leave the sinus venosus intact.

When the incision is carried through the auricles so as to leave the sinus venosus behind in the body, the result is different. The sinus venosus beats forcibly and regularly, having suffered hardly any interruption from the operation. The excised heart, however, remains, in the majority of cases, for some time motionless. Stimulated by a prick or an induction-shock, it will give one, two, or several beats, and then come to rest. But it will in the majority of cases, the animal having previously been in a vigorous condition, recommence after a while its spontaneous beating, the systole of the ventricle following that of the auricles; but the rhythm of beat will not necessarily be the same as that of the sinus venosus left in the body, and the beats will not continue to go on for so long a time as will those of a heart still retaining the sinus venosus.

When the incision is carried through the auriculo-ventricular groove, so as to leave the auricles and sinus venosus within the body, and to isolate the ventricle only, the results are similar but more marked. The sinus and auricles beat regularly and vigorously, with their proper sequence, but the ventricle generally remains for a long time quiescent. When stimulated, however, the ventricle will give one, two, or several beats, and after a while, in many cases at least, will eventually set up a spontaneous pulsation with an independent rhythm; and this may last for some considerable time, but the beats are not so regular and will not go on for so long a time as will those of a ventricle to which the auricles are still attached.

If a transverse incision be carried through the ventricle at about its upper third, leaving the base of the ventricle still attached to the auricles, the portion of the heart left in the body will go on pulsating regularly, with the ordinary sequence of sinus, auricles, ventricle, but the isolated lower two-thirds of the ventricle will not beat spontaneously at all, however long it be watched. Moreover, in response to a single stimulus such as an induction-shock or a gentle prick it gives, not as in the case of the entire ventricle or of the ventricle to which the auricles are attached, a series of beats, but a single beat.

Lastly, to complete the story we may add, that when the heart is bisected longitudinally, each half continues to beat spontaneously, with an independent rhythm, so that the beats of the two halves are not necessarily synchronous, and this continuance of spontaneous pulsations after longitudinal bisection may be seen in the conjoined auricles and ventricle, or in the isolated auricles, or in the isolated but entire ventricle. Moreover, the auricles may be divided in many ways and yet many of the segments will continue beating; small pieces even may be seen under the microscope pulsating, feebly it is true, but distinctly and rhythmically.

The various parts of the frog's heart thus form, as regards the power of spontaneous pulsation, a descending series—sinus venosus, auricles, entire ventricle, lower portions of ventricle, the last exhibiting under ordinary circumstances no spontaneous pulsations at all.

Now, ganglia, containing nerve-cells, are found in great abundance in the sinus venosus, are seen in various parts of the auricles, and occur as the so-called Bidder's ganglia at the junction of the auricles and ventricle, whence they also spread into the upper part of the ventricle; in the lower two-thirds of the ventricle they are entirely wanting. It is natural to infer from this that the ganglia are in some way the agents of the spontaneous pulsation.

The uncertainty, and in most cases temporary character of the pulsations, occurring with seeming spontaneity, in the auricles or ventricle separated from the sinus venosus, have led many to the opinion that these are not really spontaneous, but of the nature of reflex acts, induced by some obscurely acting stimuli, and that really spontaneous pulsations proceed only from the sinus venosus. And a view has been generally adopted which teaches that the spontaneous beats of the frog's heart are due to rhythmic nervous impulses started in the ganglia of the sinus venosus and spreading thence to other parts, the ganglia of the auricles and of the auriculo-ventricular groove acting in subordination to those of the sinus, or behaving under certain circumstances in-

dependently as reflex centres, or performing other functions which we shall have to speak of immediately as of a restraining or inhibitory character. And the same view with possibly some slight modifications has been supposed to hold good for the hearts of all vertebrate animals.

Facts, however, are met with which appear to oppose this conception. If the "perfusion" canula previously described be introduced into a frog's ventricle and secured by a ligature carried round the ventricle some little distance below the base, the lower part of the ventricle remains motionless and free from pulsations in the same way as when it has been removed by an incision. If, however, the cavity be regularly supplied with serum or diluted blood (that of the rabbit being practically the most useful), after a longer or shorter time, this portion of the ventricle begins to pulsate with a more or less regular rhythm and will continue these apparent spontaneous beats for an almost indefinite time. It is usual to explain these pulsations, which may be witnessed even when only the extreme tip of the ventricle is tied on to the canula, as not really spontaneous but as excited by the serum or dilute blood, supplied under pressure, acting as a stimulus; such an explanation is, however, hardly satisfactory. Then again, though it is quite true that the beats of an isolated frog's ventricle are uncertain and temporary, so much so as perhaps to justify the view that they are not really spontaneous, the isolated ventricle of the tortoise beats with such regularity and for so long a time, that it seems almost impossible to avoid the conclusion that in this animal, at all events, the ventricle by itself possesses a real power of spontaneous pulsation. Moreover, even in the frog, section at various points, of the nerves with which the ganglia are connected, may be effected and indeed Bidder's ganglia carefully extirpated, without the natural sequence of beat of the several parts being changed. And careful investigation has disclosed many other facts which we cannot discuss here, but which go far to show that the generation of the beat of the heart is a very complex matter indeed. While we must admit that the ganglia of the sinus venosus (in the frog, or what corresponds to these in other animals) are prepotent in the work of producing the beat, our knowledge will not at present allow us to make a definite and consistent statement as to what it is they exactly do, or as to the share in generating and carrying out the beat, which is taken by the other ganglia, and their respective nerves, or by the muscular fibres themselves.

Inhibition of the Beat.—The beat of the heart may be stopped or checked—*i. e.*, may be inhibited by efferent impulses descending the vagus nerve.

If while the beats of the heart of a frog are being carefully registered (Fig. 78) an interrupted current of moderate strength be sent through one of the vagi, the heart is seen to stop beating. It remains for a time in diastole, perfectly motionless and flaccid. If the duration of the current be short and the strength of the current great, the standstill may continue after the current has been shut off; the beats when they reappear are generally at first feeble and infrequent, but soon reach or even go beyond their previous vigor and frequency. A wholly similar inhibition may be seen in the mammal, and, indeed, in man. Czermak, by pressing his vagus against a small osseous tumor in his neck, and thus mechanically stimulating the nerve, was able to stop at will the beating of his own heart; it need hardly be added that such an experiment is a dangerous one.

The effect is not produced instantaneously; if on the curve the point be exactly marked as at a (Fig. 78), when the current

Fig. 78.
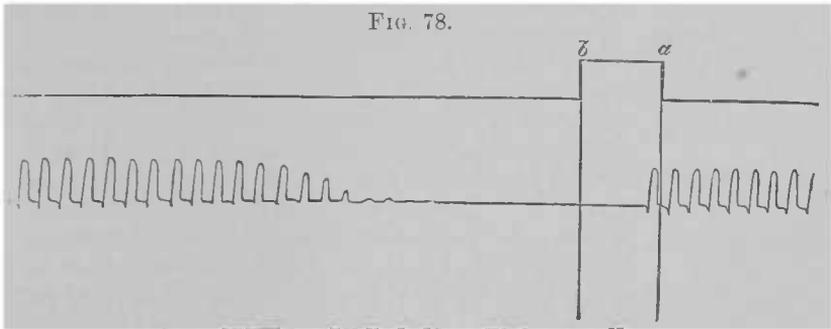
INHIBITION OF FROG'S HEART BY STIMULATION OF THE VAGUS.

The contractions of the ventricle are registered by means of a simple lever, so that each rise of the lever corresponds to a beat   The interrupted current was thrown in at a, and shut off at b. It will be seen that one beat occurred after a, and that the pause continued for some time after b. To be read from right to left.

is thrown in it will frequently be found that one beat at least occurs after the current has passed into the nerve. In other words, the inhibitory action of the vagus has a long latent period; this has been estimated by Donders to last in the rabbit 0.16 second.   The inhibitory effect is at a maximum soon after the moment of application of the current, and diminishes gradually onward; so much so in this case, that when the current is applied for more than a very short time, the heart recommences beating before the current is removed.

It is obvious that the normal beat of the heart may be interfered with in two distinct ways; on the one hand, the systole of the auricles and ventricle (or of either) may be diminished in vigor; on the other hand, the diastole or passive interval may be

prolonged. The vagus is able to act upon the heart in both these directions; and sometimes the one, sometimes the other effect, is most prominent. Thus at times, as in the instance shown in Fig. 78, the most conspicuous result is the total suppression for some time of all visible contractions of the ventricle; and the beats, when they appear again, are separated by diastolic intervals not much larger than the normal. At other times, stimulation of the vagus does not cause any disappearance of the beats, but the intervals between the beats are much prolonged, so that the rhythm is for a while very slow. It is possible that these two different effects are brought about by more or less distinct mechanisms.

We said just now that, after the stimulation of the vagus has ceased, the beats may go beyond their previous vigor and frequency. This is sometimes remarkably the case. We might be tempted to speak of it as a reaction, were it not that no necessary relation obtains between the amount of slowing or weakening and the amount of succeeding acceleration or augmentation. Indeed, the latter effect may make its appearance without any previous inhibition—that is to say, under certain circumstances, stimulation of the vagus may produce, not inhibition, but either augmentation of the beats, or quickening of the rhythm, or both.

During the standstill, direct stimulation of the heart, as by touching the auricle or ventricle, will produce a single beat; though spontaneous pulsations are absent, the mechanism for the production of a beat is capable of being put into action.

The stimulus need not be an interrupted current; mechanical and chemical stimulation of the vagus also produces inhibition, though less readily.

The stimulus may be applied at any part of the course of either vagus (though it frequently happens in some animals, as in the frog, that one vagus is more efficient than the other); but perhaps the most marked effects are produced when the electrodes are placed on the boundary-line between the sinus venosus and the auricles.

The effects of various poisons in reference to this inhibitory action are very interesting. After atropin, even in a minute dose, has been injected into the blood, stimulation of the vagus, even with the most powerful currents, produces no inhibition whatever. The heart continues to beat as if nothing were happening; atropin, in some way or other, does away with the normal inhibitory action of the vagus.

In slight urari poisoning, the inhibitory action of the vagus is still present; in the profounder stages it disappears; but even then inhibition may be obtained by applying the electrodes to the sinus. In order to explain this result, it has been supposed

that what we may call the inhibitory fibres of the vagus terminate in an inhibitory mechanism (probably ganglionic in nature), seated in the heart itself, and that the urari, while in large doses it may paralyze the terminal fibres of the vagus, leaves this inhibitory mechanism intact and capable of being thrown into activity by a stimulus applied directly to the sinus. After atropin has been given, inhibition cannot be brought about by stimulation either of the vagus fibres or of the sinus, or, indeed, of any part of the heart. Hence it is inferred that atropin, unlike urari, paralyzes this intrinsic inhibitory mechanism itself.

After the application of muscarin[1] or pilocarpin, the heart stops beating, and remains in diastole in perfect standstill. Its appearance is then exactly that of a heart inhibited by profound and lasting vagus stimulation. This effect is not hindered by urari. The application, however, of a small dose of atropin at once restores the beat. These facts are interpreted as meaning that muscarin (or pilocarpin) stimulates or excites the inhibitory apparatus spoken of above, which atropin paralyzes or places *hors de combat*.

There are many other effects of various poisons which have been appealed to as throwing light on the action of the heart; but we must not enter into the discussion of these here. We may, however, in this connection call attention to a remarkable experiment known as that of Stannius. If a ligature be drawn tightly round the junction of the sinus venosus with the auricles, or if the auricles be separated from the sinus by an incision carried along the boundary-line between them, a standstill is produced closely resembling a very prolonged vagus inhibition. Quiescence thus induced, may last a very considerable time. During the standstill, a pulsation may be induced by a stimulus applied directly to the heart, a whole series of beats being evoked when a mechanical stimulus, such as the prick of a needle, is applied over the seat of Bidder's ganglia at the junction of the auricles with the ventricles, or to the ganglia in the auricles, or to those in the bulbus; and when the ventricle is separated by an incision from the auricles, the former will recommence beating, while the latter remain as quiescent as before. The condition of the heart in this experiment so closely resembles the standstill produced by vagus stimulation, that the effect might be supposed to be caused by the ligature (or section) stimulating the vagus fibres or the inhibitory mechanism at the sinus; but this view is clearly disproved by the fact that the experiment succeeds perfectly well after atropin has been given. Another explanation attributes the standstill to the section depriving the heart of the prepotent

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[1] The poisonous effects of many mushrooms are probably in large measure due to a similar action on the heart.

ganglia in the sinus, and the recommencement of pulsation in the ventricle after separation by incision or ligature from the auricles to the incision or ligature acting as a stimulus to the ventricle but not to the auricle. The experiment, in fact, is brought forward in support of the views enunciated on p. 226. But these, as we have said, are not satisfactory, and an adequate interpretation of the experiment has yet to be supplied. Indeed, did it seem profitable, we might relate many other puzzling results which have been obtained in experimenting on the heart. We have already warned the reader that the problem of the causes of the normal spontaneous beat is as yet far from being solved, and until we get clearer views as to that main event we cannot expect to understand exactly how inhibition is brought about. The conception of an inhibitory mechanism, in which certain of the fibres of the vagus end, must be regarded as a temporary hypothesis, useful only until we gain further light; and we have ventured to dwell on so obscure a topic at so great a length only because inhibition of the heart through the vagus is not only a factor of immense importance in the general operations of the economy, and plays so prominent a part in the action of many drugs, but because it is a type of other inhibitory processes in the nervous system and elsewhere, which, perhaps even more than itself, contribute to render the working of the complicated machine of the animal body, at once both uniform when regularity is required, and delicately responsive when variety is needed.

Reflex Inhibition.—For it must not be thought that cardiac inhibition by means of the vagus nerve is a mere experiment of the laboratory; we have reason to think that it is an incident continually recurring in daily life. For we have evidence that the inhibitory action of the vagus may be brought about by reflex action. If the abdomen of a frog be laid bare, and the intestine be struck sharply, as with the handle of a scalpel, the heart will stand still in diastole with all the phenomena of vagus inhibition. If the *nervi mesenterici* or the connections of these nerves with the sympathetic chain be stimulated with the interrupted current, cardiac inhibition is similarly produced. If in these two experiments both vagi are divided, or the medulla oblongata destroyed, inhibition is not produced, however much either the intestine or the mesenteric nerves be stimulated. This shows that the phenomena are caused by impulses ascending along the mesenteric nerves to the medulla, and so affecting a portion of that organ as to give rise by reflex action to impulses which descend the vagi as inhibitory impulses. The portion of the medulla thus mediating between the afferent and efferent

impulses may be spoken of as the *cardio-inhibitory centre.* Reflex inhibition through one vagus may be brought about by stimulation of the central end of the other.

If the peritoneal surface of the intestine be inflamed, very gentle stimulation of the inflamed surface will produce marked inhibition ; and in general the alimentary tract seems in closer connection with the cardio-inhibitory centre than other parts of the body ; the injurious—sometimes fatal—effects of a violent blow on the stomach are known to all.   But apparently stimuli, if sufficiently powerful, will, through reflex action, produce inhibition from whatever be the part of the body to which they are applied.   Thus, crushing a frog's foot will stop the heart.   In ourselves, the fainting from emotion, or from severe pain, is the result of a reflex inhibition of the heart, the afferent impulses in the one case at least, and probably in both cases, reaching the medulla from the brain.   In succeeding pages we shall have occasion more than once in discussing the effects of stimulating a given nerve, to consider how far those effects are due to a reflex inhibition of the heart; and probably there are few events taking place in the body which have not a tendency thus to affect the central vascular pump, though it many cases the tendency is counteracted by interfering agencies.   But we must be careful to avoid falling into the error of supposing that every arrest, or slowing or weakening of the heart, is due to impulses descending the vagus fibres.   In many instances cardiac troubles are due to events originating in the heart itself, so far independent of the inhibitory processes which we are studying now, that they are in no way whatever counteracted by atropin.

Direct stimulation of the cardio-inhibitory centre itself, such as occurs during the destruction of or results from injury to the medulla, also produces inhibition.

And the question naturally arises, Has this cardio-inhibitory centre any constant automatic action ?

In the dog, and also, though to a far less extent, in the rabbit, section of both vagi is followed by a quickening of the heart's beat.   This result may be interpreted as showing that the centre in the medulla exercises a permanent restraining influence on the heart; that organ in fact being habitually curbed.   The argument that the effects of an artificial stimulation of the vagus soon wear off, and that, therefore, a permanent stimulation of the vagi, leading to permanent inhibitory action, would be impossible, may be met by the reflection that a natural stimulation is, possibly, not wholly identical with artificial stimulation, and its effects need not necessarily wear off.

We need not now stay to discuss the question whether this central action is really automatic—*i. e.*, kept up by molecular pro-

cesses originating in certain nerve cells, or reflex, that is, main-
tained by nervous impulses reaching it along certain or various
afferent nerves. Granting, however, the existence of a centre in
the medulla, which either automatically or otherwise is in per-
manent action, it is obviously open to us to speak of reflex
inhibition as being brought about by influences which augment
the action of that centre. But we have seen that active nervous
centres are subject, not only to augmentative, but also to inhibi-
tory influences. Hence the cardio-inhibitory centre might itself
be inhibited by impulses reaching it from various quarters. In
other words, the beat of the heart might be quickened by a les-
sening of the normal action of the inhibitory centre in the
medulla. It is in fact probable, that many cases of quickening
of the heart's beat are produced in this way; though the matter
requires further investigation.

Accelerator Nerves.—The heart's beat may in the mammal be
quickened, even after division of both vagi, by direct stimulation
of the cervical spinal cord. The effects produced, however, are
very complex, and led, on their first being made known, to much
discussion, one outcome of which was the discovery of certain
nerves of a very peculiar character, which pass from the cervical
spinal cord, frequently along the nerve accompanying the verte-
bral artery, and reach the heart through the last cervical and
first thoracic ganglia; these have been called the "accelerator
nerves." Their course is different in the rabbit and in the dog,
see Figs. 79 and 80, and indeed varies even in the same kind of
animal. Stimulation of these nerves with the interrupted current
causes a quickening of the heart's beat, in which what is gained
in rate is lost in force, for the blood-pressure is not necessarily
increased, but may remain the same, or even be diminished;
apparently not only is the diastole diminished but the systole is
actually shortened. Our knowledge of these "accelerator"
nerves is, however, too imperfect to be dwelt upon here.

Other Modifying Agents.—The beat of the heart may also be
modified by influences bearing directly on the nutrition of the
heart. The tissues of the heart, like all other tissues, need an
adequate supply of blood of a proper quality; if the blood vary
in quality or quantity the beat of the heart is correspondingly
affected. The excised frog's heart, as we have seen, continues to
beat for some considerable time, though apparently empty of
blood. After a while, however, the beats diminish and disap-
pear, and their disappearance is greatly hastened by washing
out the heart with a normal saline solution, which when allowed
to flow through the cavities of the heart readily permeates the

tissues on account of the peculiar construction of the ventricular walls. If such a "washed out" quiescent heart be fed in the manner described at p. 224, with diluted blood (of the rabbit, sheep, etc.) it may be restored to functional activity. A similar but less complete restoration may be witnessed if serum be used

FIG. 79.
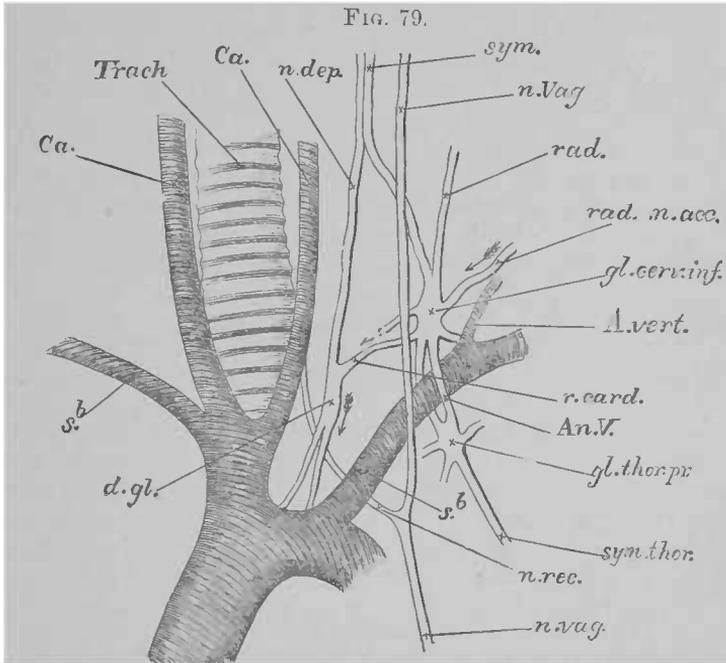
THE LAST CERVICAL AND FIRST THORACIC GANGLIA IN THE RABBIT.

(Left side. Somewhat diagrammatic, many of the various branches being omitted.)

Trach Trachea. *Ca* carotid artery *sb* subclavian artery. *n. Vag* the vagus trunk. *n. rec.* the recurrent laryngeal *sym.* the cervical sympathetic nerve ending in the inferior cervical ganglion, *gl. cerv. inf.* Two roots of the ganglion are shown, *rad.*, the lower of the two accompanying the vertebral artery, *A. vert.*, being the one generally possessing accelerator properties. *gl. thor. pr.* the first thoracic ganglion Its two branches communicating with the cervical ganglion surround the subclavian artery forming the annulus of Vieussens. *sym. thor.* the thoracic sympathetic chain *n dep.* depressor nerve, which, though running by the side of the sympathetic, is really a branch of the vagus, from which it separates higher up This is joined in its course by a branch from the lower cervical ganglion, there being a small ganglion at their junction, from which proceed nerves to form a plexus over the arch of the aorta. It is this branch from the lower cervical ganglion which possesses accelerator properties—hence the course of the accelerator fibres is indicated in the figure by the arrows.

instead of blood, and a heart fed regularly with fresh supplies of blood or even of serum, may be kept beating for a very great length of time. In treating of the skeletal muscles, we saw that in their case the exhaustion following upon withdrawal

of the blood-stream might be attributed either to an inadequate supply of new nutritive material and oxygen, or to an accumulation in the muscular substance of the products of muscular metabolism, or to both causes combined. And the same considerations hold good for the nervous and muscular structures of

Fig. 80.
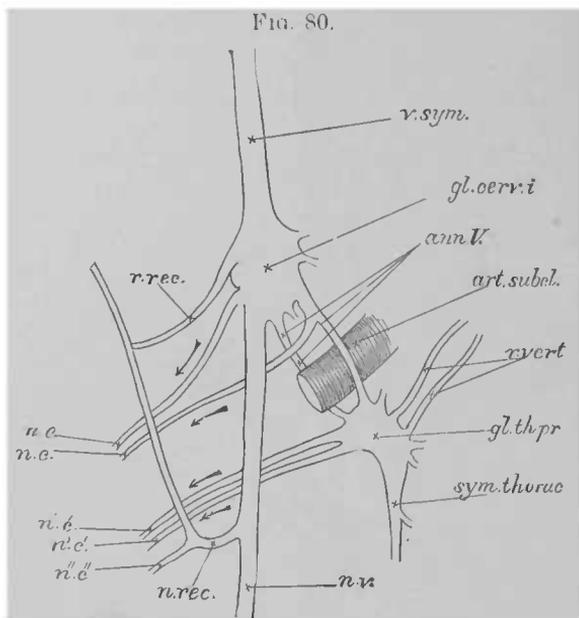
THE LAST CERVICAL AND FIRST THORACIC GANGLIA IN THE DOG.
The cardiac nerves of the dog. The figure is largely diagrammatic, and represents the left side.

v. sym. the united vagus and cervical sympathetic nerves. *gl. cerv. i.* the inferior cervical ganglion. *n. v.* the continuation of the trunk of the vagus. *ann. V.* the two branches forming the annulus of Vieussens round the subclavian artery, *art. subcl.*, and joining *gl. th. pr.*, the first thoracic or stellate ganglion (the branch running in front of the artery is considered by Schmiedeberg to be an especial channel of accelerator fibres . *sym. thorac.* the sympathetic trunk in the thorax. *v. vert.* communicating branches from the cervical nerves running along-side the vertebral artery, the rami vertebrales. *n. rec.* the recurrent laryngeal. *n. c.* cardiac branches from the lower cervical ganglion, accelerator nerves of Schmiedeberg. *n.' c.'* cardiac branches from the first thoracic ganglion, accelerator nerves of Cyon. *n." c."* cardiac branch from recurrent nerve. *r. rec.* branch from lower cervical ganglion to the recurrent nerve, often containing accelerator fibres.

the heart, though the subject has not yet been sufficiently well worked out to permit any very definite statements to be made. It seems probable, however, that an important factor in the matter is the accumulation in the muscular fibres and in the surrounding lymph of carbonic acid, and of the substances which give rise to the acid reaction.

When the frog's heart is thus "fed" with various substances the interesting fact is brought to light that some substances, such, for instance, as very dilute lactic acid, lead to increased expansion, and others, such, for instance, as very dilute solutions of sodium hydrate, to diminished expansion, or to continued contraction of the quiescent ventricle. It would appear that the muscular fibres of the ventricle over and above their rhythmic contractions are capable of varying in length, so that at one time they are longer, and the ventricle when pressure is applied to it internally dilates beyond the normal, while at another time they are shorter, and the ventricle with the same internal pressure is contracted beyond the normal. Further, in the frog at least, when the pause between two beats is lengthened the relaxation of the ventricle goes on increasing, so that apparently the ventricle when beating normally is already somewhat contracted when a new beat begins. In other words, the ventricle possesses what we shall speak of in reference to arteries as tonicity or tonic contraction, and the amount of this tonic contraction, and in consequence the capacity of the ventricle, varies according to circumstances.

When the frog's ventricle is thus artificially fed with serum, or even with blood, the beats, whether spontaneous or provoked by stimulation, are apt to become intermittent and to arrange themselves into groups. This intermittence is possibly due to the serum or blood being unable to carry on nutrition in a completely normal manner, and to the consequent production of abnormal chemical substances, and it is probable that cardiac intermittences seen during life have often a similar causation. Various chemical substances in the blood, natural or morbid, may thus affect the heart's beat by acting on its muscular fibres, or its nervous elements or both, and that probably in various ways, modifying in different directions the rhythm, or the individual contractions, or both.

The physical or mechanical circumstances of the heart also affect its beat ; of these, perhaps, the most important is the amount of the distention of its cavities. The contractions of cardiac muscle, like those of ordinary muscle (see p. 118), are increased up to a certain limit by the resistance which they have to overcome ; a full ventricle will, other things being equal, contract more vigorously than one less full ; though, as in ordinary muscle, the limit at which resistance is beneficial may be passed, and an over-full ventricle will cease to beat at all.

Under normal conditions, the ventricle probably empties itself completely at each systole. Hence, an increase in the quantity of blood in the ventricle would augment the work done in two ways : the quantity thrown out would be greater, and the in-

creased quantity would be ejected with greater force. Further, since the distention of the ventricle is (at the commencement of the systole, at all events) dependent on the auricular systole, the work of the ventricle (and so of the heart, as a whole) is in a measure governed by the auricle.

The Relation of the Heart's Beat to Blood-pressure.—When the blood-pressure is high, not only is the resistance to the ventricular systole increased, but, other things being equal, more blood flows (in the mammalian heart) through the coronary artery. Both these events would increase the activity of the heart, and we might expect that the increase would be manifest in the rate of the rhythm as well as in the force of the individual beats. As a matter of fact, however, we do not find this. On the contrary, as Marey has insisted, the relation of heart-beat to pressure may be put almost in the form of a law, that "the rate of the beat is in inverse ratio to the arterial pressure;" a rise of pressure being accompanied by a diminution, and fall of pressure with an increase of the pulse-rate. This, however, only holds good if the vagi be intact. If these be previously divided, then in whatever way the blood-pressure be raised—whether by injecting blood or clamping the aorta, or increasing the peripheral resistance, through that action of the vaso-motor nerves which we shall have to describe directly—or in whatever way it be lowered, no such clear and decided inverse relation between blood-pressure and pulse-rate is observed. It is inferred, therefore, that increased blood-pressure causes a slowing of the pulse, when the vagi are intact, because the cardio-inhibitory centre in the medulla is thereby stimulated, and the heart in consequence to a certain extent inhibited.

The Effects on the Circulation of Changes in the Heart's Beat.

Any variation in the heart's beat directly affects the blood-pressure unless some compensating influence be at work. The most extreme case is that of complete inhibition. Thus, if, while a tracing of arterial pressure is being taken, the beat of the heart be suddenly arrested, some such curve as that represented in Fig. 81 will be obtained. It will be observed that immediately after the last beat, there is a sudden rapid fall of the blood-pressure. At the pulse due to the last systole, the arterial system is at its maximum of distention ; forthwith the elastic reaction of the arterial walls propels the blood forward into the veins, and there being no fresh fluid injected from the heart, the fall of the mercury is unbroken, being rapid at first, but slower afterwards, as the elastic force of the arterial walls is more and more used

up. With the returning beats, the pressure correspondingly rises in successive leaps until the normal mean pressure is regained. The size of these returning leaps of the mercury may seem disproportionately large, but it must be remembered that by far the greater part of the force of the first few strokes of the heart is expended in distending the arterial system, a small portion only of the blood which is ejected into the arteries passing on into the veins. As the arterial pressure rises, more and more blood passes at each beat through the capillaries, and the rise of the pressure at each beat becomes less and less, until at last the whole contents

FIG. 81.
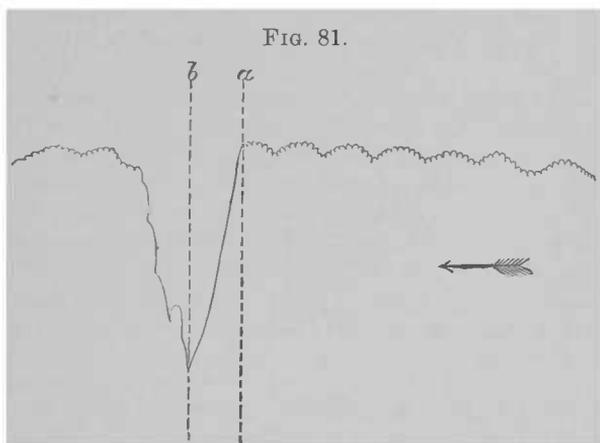
TRACING, SHOWING THE INFLUENCE OF CARDIAC INHIBITION ON BLOOD-PRESSURE. FROM A RABBIT.

The current was thrown into the vagus at *a* and shut off at *b*. It will be observed that one beat is recorded after the commencement of the stimulation. Then follows a very rapid fall, continuing after the cessation of the stimulus. With the returning beats, the mercury rises by leaps until the normal pressure is regained.

of the ventricle pass at each stroke into the veins, and the mean arterial pressure is established. To this it may be added, that, as we have seen, the force of the individual beats may be somewhat greater after than before inhibition. Besides, when the mercury manometer is used, the inertia of the mercury tends to magnify the effects of the initial beats,

Complete arrest of the heart-beats is not necessary to produce a fall of pressure. As is seen in Fig. 83, mere slowing of the beats will lower the mean pressure. And, speaking generally, we may say that, if while the force of the individual beats remains constant the frequency is increased or diminished, and *vice versa*, if while the frequency remains the same the force is increased or diminished, the result in both cases is that the pressure is proportionately increased or diminished. This clearly must be the

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case; but obviously it is quite possible that the beats might, while more frequent, so lose in force, or while less frequent, so
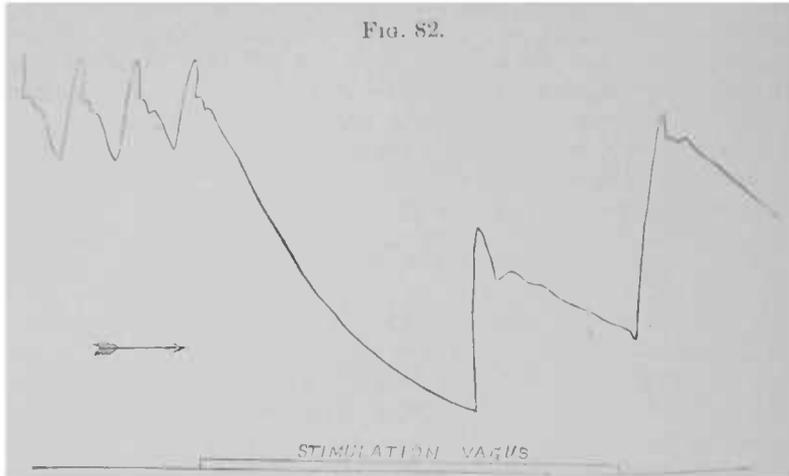
VAGUS STIMULATION.

Pulse-tracing from the carotid of rabbit, taken by a modification of the sphygmograph. The period of vagus stimulation is marked by the line below. One beat occurs after stimulation has begun. Shows the fall of blood-pressure, and the character of the first recommencing beats.

increase in force, that no difference in the mean pressure should result. And this, indeed, is not unfrequently the case—so much

STIMULATION OF VAGUS
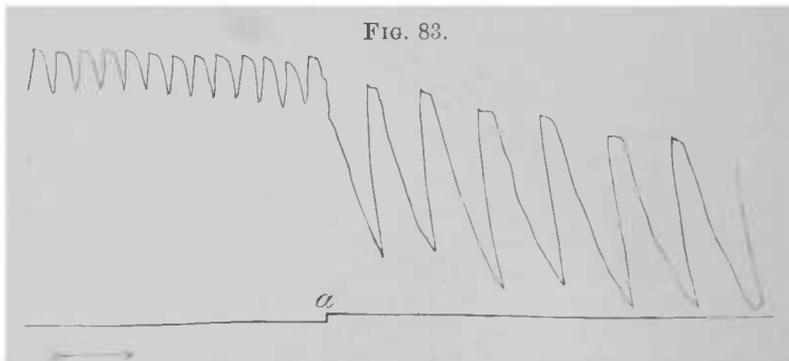
Blood-pressure curve taken with mercury manometer. The effect is to slow the rhythm rather than to bring about complete stand-still. With the slow pulse, the pressure still continues to fall. The beginning of stimulation is marked by *a*

so, that variations in the heart-beat must always be looked upon as a far less important factor of blood-pressure than variations in the peripheral resistance.

An increase in the quantity of blood ejected at each beat must necessarily augment, and a decrease diminish, the blood-pressure, other things remaining the same. But the quantity sent out at each beat, on the supposition that the ventricle always empties itself at each systole, will depend on the quantity entering into the ventricle during each diastole, and that will be determined by the circumstances not of the heart itself, but of some other part or parts of the body.

Sec. 5.—Changes in the Calibre of the Minute Arteries. Vaso-motor Actions.

The middle coat of all arteries contains circularly disposed plain muscular fibres. As the arteries become smaller, the muscular element becomes more and more prominent as compared with the elastic element, until, in the minute arteries, the middle coat consists entirely of a series of plain muscular fibres wrapped round the elastic internal coat. Nerve-fibres belonging to the sympathetic system are distributed largely to bloodvessels, but their terminations have not as yet been clearly made out. By galvanic, or still better by mechanical stimulation, this muscular coat may, in the living artery, be made to contract. During this contraction, which has the slow character belonging to the contractions of all plain muscle, the calibre of the vessel is diminished.

If the web of a frog's foot be examined under the microscope, any individual small artery will be found to vary in calibre, being sometimes narrowed and sometimes dilated. During the narrowing, which is obviously due to a contraction of the muscular coat of the artery, the attached capillary area and the corresponding veins become less filled with blood, and paler. During the stage of dilation, which corresponds to the relaxation of the muscular coat, the same parts are fuller of blood and redder. It is obvious that, the pressure at the entrance into any given artery remaining the same, more blood will enter the artery when relaxation takes place, and consequently the resistance offered by the artery is lessened, and less when contraction occurs and the resistance is consequently increased. The blood always flows in the direction of least resistance.

The small arteries frequently manifest what may be called spontaneous variations in their calibre, and these variations are very apt to take on a distinctly rhythmical character. If a small artery in the web of the frog be carefully watched, it will be seen from time to time to vary very considerably in width, without any obvious change taking place in the heart's beat or any events

occurring in the general vaso-motor system. Similar variations may be witnessed in the vessels of the mesentery of a mammal. The most striking and most easily observed instance of rhythmical constriction and dilation is to be found in the median artery of the ear of the rabbit. If the ear be held up before the light, it will be seen that at one moment the artery appears as a delicate, hardly visible, pale streak, the whole ear being at the same time pallid. After a while the artery slowly widens out, becomes thick and red, the whole ear blushing, and many small vessels previously invisible coming into view. Again, the artery narrows and the blush fades away; and this may be repeated at some-what irregular intervals several times a minute. The extent and regularity of the rhythm are usually markedly increased if the rabbit be held up by the ears for a short time previous to the observation. Similar rhythmic variations in the calibre of the arteries have been observed in several places—*ex. gr.*, in the saphena artery of the rabbit, in the axillary artery of the tortoise, and in the small arteries of the muscles of the frog; probably they are widely spread. They may be compared with the rhythmic movements of the veins in the bat's wing, and of the caudal vein of the eel.

The extent and intensity of the constriction or dilation which may be observed in the frog's web are found to vary very largely. Irregular variations of slight extent occur even when the animal is apparently subjected to no disturbing causes; while as the result of experimental interference the arteries may become either constricted—in some cases almost to obliteration—or dilated until they acquire double or more than double their normal diameter. This constriction or dilation may be brought about not only by treatment applied directly to the web, but also by changes affecting the nerve of the leg. Thus, section of the sciatic nerve is generally followed by a dilation which may be slight, or which may be very marked, and which is sometimes preceded by a passing constriction; while stimulation of the peripheral stump of the divided nerve by an interrupted current of moderate intensity generally gives rise to constriction, often so great as almost to obliterate some of the minute arteries.

These facts show that the contractile elements of the minute arteries of the web of the frog's foot are capable by contraction or relaxation of causing constriction or dilation of the calibre of the arteries; and that this condition of constriction or dilation may be brought about through the agency of nerves.

Vaso-motor Nerves.—In warm-blooded animals, though we cannot readily, as in the frog, watch the circulation under the microscope, we have abundant evidence of the influence of the

nervous system on the calibre of the arteries. Thus, in the mammal, division of the cervical sympathetic on one side of the neck causes a dilation of the minute arteries of the head of the same side, shown by an increased supply of blood to the parts. If the experiment be performed on a rabbit, the effect on the circulation in the ear is very striking. The whole ear of the side operated on is much redder than normal, its arteries are obviously dilated, its veins unusually full, innumerable minute vessels before invisible come into view, and the temperature may be more than a degree higher than on the other side.

Division of the sciatic nerve in a mammal causes a similar dilation of the small arteries of the foot and leg. Where the condition of the circulation can be readily examined, as, for instance, in the hairless balls of the toes, especially when these are not pigmented, the vessels are seen to be dilated and injected ; and a thermometer placed between the toes shows a rise of temperature amounting, it may be, to several degrees.

The quantity of blood present in the bloodvessels of the mammal may sometimes be observed directly, but has frequently to be determined indirectly. The temperature of passive structures subject to cooling influences, such as the skin, is largely dependent on the supply of blood the more abundant the supply, the warmer the part. Hence, in these parts variations in the quantity of blood may be inferred from variations of temperature; but, in dealing with more active structures, there are obviously sources of error in the possibility of the treatment adopted, such as the stimulation of a nerve, giving rise to an increase of temperature due to increased metabolism, independent of variations in blood-supply.

The quantity of blood may also be determined by the plethysmograph. In this instrument, a part of the body, such as the arm, is introduced into a closed chamber filled with fluid—ex. gr., a large glass tube, the opening by which the arm is introduced being secured with a stout caoutchouc membrane. An increase or decrease of blood sent into the arm will lead to an increase or decrease of the volume of the arm, and this will make itself felt by an increase or diminution of pressure in the fluid of the closed chamber, which may be registered and measured in the usual way. We shall have to speak again of a modification of this instrument when we are dealing with the kidney.

Division of the brachial plexus produces a similar dilation of the bloodvessels of the front limb. Division of the splanchnic nerve produces a dilation of the bloodvessels of the intestines and other abdominal viscera. Division in the mammal of the hypoglossal nerve on one side causes a dilation of the vessels in the corresponding half of the tongue. Division of a nerve supplying a muscle causes a large and sudden increase in the venous flow from the muscle, indicating that the muscular arteries have become dilated ; and in the frog this dilation, consequent on

section of the nerve, may be actually observed by placing a thin muscle, such as the mylo-hyoid, under the microscope, and watching the calibre of the small arteries and the circulation of the blood through them while the nerve is being cut.

We find, in fact, that in almost all parts of the body certain " vascular areas " stand in such a relation to certain nerves that the division of one of these nerves causes a dilation of the minute arteries in, and consequently an increased supply of blood to, a corresponding vascular area.   We may speak of these nerves as " vaso-motor " nerves, or, more correctly, since in the vast majority of cases the nerves in question have other functions than that of governing arteries, as containing vaso-motor fibres, much in the same way as an ordinary spinal nerve is spoken of as containing sensory and motor fibres ; and from what has been said above, it is evident that these vaso-motor fibres are found sometimes in sympathetic, sometimes in cerebro-spinal nerves.

Since division of a vaso-motor nerve, or nerve containing vaso-motor fibres, leads to the dilation of the arteries of its appropriate vascular area, it is obvious that previous to that division these arteries were in a state of permanent constriction, due to a permanent contraction of their muscular coats.   This permanent constriction, which may vary considerably in degree (the dilating effects of section of the vaso-motor nerve correspondingly varying in amount), is spoken of as "tone," " arterial tone."   Arteries in such a state of permanent constriction as under ordinary circumstances is normal to arteries whose vaso-motor fibres have not been divided and which are otherwise in a normal condition, are said to " possess tone."   When, as after division of the vaso-motor fibres, the constriction gives place to dilation, the arteries are said to have " lost tone ;" and when, under various circumstances which we shall study hereafter, the constriction becomes greater than normal, their tone is said to be increased.

A very little consideration will show that this arterial tone is a most important factor in the circulation.   In the first place, the whole flow of blood in the body is adapted to and governed by what we may call the *general tone* of the arteries of the body at large.   In a normal condition of the body, if not all, at least the great majority of the minute arteries of the body are in a state of tonic—*i. e.*, of moderate—constriction, and it is the narrowing due to this constriction which forms a large item of that peripheral resistance which we have seen (p. 170) to be one of the two great factors of blood-pressure.   The normal general blood-pressure, and therefore the normal flow of blood, is, in fact, dependent on the " general tone " of the minute arteries.   In the second place, changes in *local tone*—*i. e.*, the tone of any particular vascular area, have very decided effects on the circulation.

These effects are both local and general, as the following considerations will show.

Let us suppose that the artery A is in a condition of normal tone, is midway between extreme constriction and dilation. The flow through A is determined by the resistance in A and in the vascular tract which it supplies, in relation to the mean arterial pressure, which again is dependent on the way in which the heart is beating and on the peripheral resistance of all the small arteries and capillaries, A included. If, while the heart and the rest of the arteries remain unchanged, A be constricted, the peripheral resistance in A will increase, and this increase of resistance will lead to an increase of the general arterial pressure. This increase of pressure will tend to cause the blood in the body at large to flow more rapidly from the arteries into the veins. The constriction of A, however, will prevent any increase of the flow through it—in fact, will make the flow through it less than before. Hence the whole increase of discharge from the arterial into the venous system must take place through channels other than A. Thus, as the result of the constriction of any artery there occur (1) diminished flow through the artery itself, (2) increased general arterial pressure, leading to (3) increased flow through the other arteries. If, on the other hand, A be dilated, while the heart and other arteries remain unchanged, the peripheral resistance in A is diminished. This leads to a lowering of the general arterial pressure, which in turn causes the blood to flow less rapidly from the arteries into the veins. The dilation of A, however, permits, even with the lowered pressure, more blood to pass through it than before. Hence the diminished flow tells all the more on the rest of the arteries. Thus, as the result of the dilation of any artery, there occur (1) increased flow of blood through the artery itself, (2) diminished general pressure, and (3) diminished flow through the other arteries. Where the artery thus constricted or dilated is small, the local effect, the diminution or increase of flow through itself, is much more marked than the general effects, the change in blood-pressure and the flow through other arteries. When, however, the area the arteries of which are affected is large, the general effects are very striking. Thus if while a tracing of the blood-pressure is being taken by means of a manometer connected with the carotid artery, the splanchnic nerves be divided, a conspicuous but steady fall of pressure is observed, very similar to that which is seen in Fig. 84. The section of the splanchnic nerves causes the mesenteric and other abdominal arteries to dilate, and these being very numerous, a large amount of peripheral resistance is taken away, and the blood-pressure falls accordingly; a large increase of flow into the portal veins takes place,

and the supply of blood to the face, arms, and legs is proportionally diminished. It will be observed that the dilation of the arteries is not instantaneous but somewhat gradual, the pressure sinking not abruptly but with a gentle curve.

Arterial tone, then, both general and local, is a powerful instrument for determining the flow of blood to the various organs and tissues of the body, and thus becomes a means of indirectly influencing their functional activity. We should accordingly expect to find that the vaso-motor nerves were connected with, and arterial tone regulated by the central nervous system, in order that the calibre of the arteries of, and the supply of blood sent to, this or that vascular area might be varied according to the varying needs of the economy. And experiment proves this to be the case.

We stated that section of the cervical sympathetic in the neck causes dilation or loss of tone in the bloodvessels of the head and face. This is true at whatever point of the course of the nerve from the upper to the lower cervical ganglion, both included, the section be made. No such dilation of the vessels of the head and face takes place when the thoracic sympathetic chain is divided anywhere below the upper thoracic ganglion; but dilation does occur after division of certain of the *rami communicantes* connecting the spinal cord with the cervical sympathetic through the lower cervical or upper thoracic ganglion. Hence it is clear that the normal tone of the arteries of the head and face is maintained by influences (whose exact nature we shall study presently) proceeding from the central nervous system, passing through certain *rami communicantes* (the exact path being somewhat uncertain or possibly not constant) into the cervical sympathetic, and ascending to the head and face by that nerve. In other words, the vaso-motor fibres of the vessels of the head and face may be traced down the sympathetic to the lower cervical ganglion, and thence by *rami communicantes* into the spinal cord.

In a similar manner the vaso-motor fibres of the splanchnic nerves governing the mesenteric and other abdominal arteries can also be traced into the spinal cord, as may also those of the sciatic governing the bloodvessels of the hind limb and of the brachial nerve governing those of the forelimb. In fact, all the vaso-motor fibres (with certain special exceptions which will be discussed presently) may thus be traced into the spinal cord; they are all connected with the central nervous system. There is at present some uncertainty in certain cases as to the exact manner in which the fibres pass from the spinal cord to this or that nerve, as, for instance, along which nerve-roots the vaso-motor fibres eventually joining the sciatic trunk run, whether they all

pass on their way into the abdominal sympathetic or no, and the like; but these are questions which need not delay us now; in whichever way they may be settled, they do not affect the important fact that in some way or other all vaso-motor fibres spring from the central nervous system, and that (with certain special exceptions) what we have called the normal tone of the various vascular areas is maintained by influences proceeding from the central nervous system.

Far more important, however, than the maintenance of a normal tone, which indeed might be at once and for ever arranged for by the proper natural calibre of the elastic bloodvessels, is the power which the central nervous system possesses of varying the tone of this or that artery or group of arteries, of increasing it or of diminishing it, of producing constriction or dilation in those arteries, and thus, as we have seen, of effecting changes in general or local blood-pressure, or in both, and consequently of determining a flow of blood in this or that direction, according to the needs of the economy. And the exercise of this carefully arranged manipulation of the muscular walls of the arteries may be called forth in either direction, in the way of constriction, or in the way of dilation (or of both at the same time, one in one area and the other in others), by means of nervous impulses either originating in the central nervous system itself, or started by afferent impulses passing up to the central nervous system from some sentient surface.

Blushing is a familiar instance of vascular dilation brought about by the action of the central nervous system. Nervous impulses started in some parts of the brain by an emotion produce certain changes in the central nervous system (the exact nature and locality of these changes we shall discuss presently) which have in turn an effect on the vaso-motor fibres of the cervical sympathetic almost exactly the same as that produced by section of the nerve. In consequence, the muscular walls of the arteries of the head and face relax, the arteries dilate, and the whole region becomes suffused. Sometimes an emotion gives rise not to blushing, but to the opposite, viz., to pallor. In a great number of cases this has quite a different cause, being due to a sudden diminution or even temporary arrest of the heart's beats; but in some cases it may occur without any change in the beat of the heart, and is then due to a condition the very converse of that of blushing—that is, to an increased arterial constriction; and this increased constriction, like the dilation of blushing, is effected through the agency of the central nervous system and the cervical sympathetic. These are familiar examples, but we have in abundance exact experimental evidence of the effect of afferent impulses in inducing through the central nervous system

vaso-motor changes, and thus bringing about sometimes constriction, sometimes dilation, sometimes the two together. The action of the so-called depressor nerve is a striking instance of reflex dilation, as it may be called.

If in the rabbit, while the pressure in an artery such as the carotid is being registered, the depressor nerve, which is a branch of the vagus running alongside the carotid artery and sympathetic nerve (Fig. 79, *n. dep.*), be divided, and its central end— *i. e.*, the one connected with the brain—be stimulated with the interrupted current, a gradual but marked fall of pressure in the carotid is observed, lasting, where the period of stimulation is short, some time after the removal of the stimulus (Fig. 84).

FIG. 84.
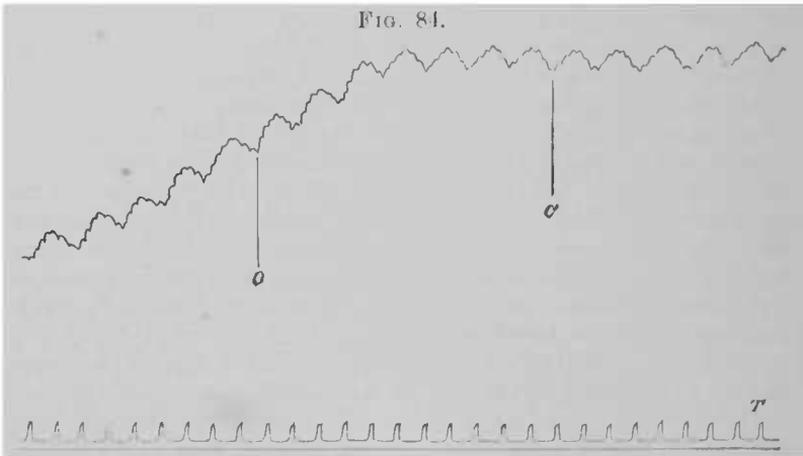
TRACING, SHOWING THE EFFECT ON BLOOD-PRESSURE OF STIMULATING THE CENTRAL END OF THE DEPRESSOR NERVE IN THE RABBIT. (To be read from right to left.)

T indicates the rate at which the recording surface was travelling; the intervals marked correspond to seconds. *C*, the moment at which the current was thrown into the nerve; *O*, the moment at which it was shut off. The effect is some time in developing, and lasts after the current has been taken off. The larger undulations are the respiratory curves; the pulse-oscillations are very small.

Since the beat of the heart is not markedly changed, the fall of pressure must be due to the diminution of peripheral resistance occasioned by the dilation of some arteries. And there is evidence that the arteries thus dilated are chiefly if not exclusively those arteries of the abdominal viscera which are governed by the splanchnic nerve. For if both the splanchnic nerves are divided previous to the experiment, the fall of pressure when the depressor is stimulated is very small—in fact, almost insignificant. The inference from this is clear; the afferent impulses passing along the depressor have so affected some part of the

central nervous system that the influences which, in a normal condition of things, passing along the splanchnic nerves keep the minute arteries of the abdominal viscera in a state of moderate tonic constriction, fail altogether, and those arteries in consequence dilate just as they do when the splanchnic nerves are divided the effect being possibly increased by the similar dilation of other smaller vascular areas.

The condition of the splanchnic or other vascular areas may, moreover, be changed, and thus the general blood-pressure modified by afferent impulses passing along other nerves than the depressor, the modification taking on, according to circumstances, the form either of decrease or of increase.

Thus, if in an animal (dog) placed under the influence of urari the central stump of the divided sciatic nerve be stimulated, an increase of blood-pressure, almost exactly the reverse of the decrease brought about by stimulating the depressor, is observed. The curve of the blood-pressure, after a latent period during which no changes are visible, rises steadily without any corresponding change in the heart's beat, reaches a maximum and after a while slowly falls again, the fall sometimes beginning to appear before the stimulus has been removed. There can be no doubt that the rise of pressure is due to the constriction of certain arteries ; the arteries in question being those of the splanchnic area certainly, and possibly of other vascular areas as well. The effect is not confined to the sciatic ; stimulation of any nerve containing afferent fibres may produce the same rise of pressure, and so constant is the result that the experiment has been made use of as a method for determining the existence of afferent fibres in any given nerve, and even the paths of centripetal impulses through the spinal cord.

If, on the other hand, the animal be under not urari but chloral, instead of a rise of blood-pressure, a fall, quite similar to that caused by stimulating the depressor, is observed when an afferent nerve is stimulated. The condition of the central nervous system seems to determine whether the reflex effect on the vaso-motor fibres is in the direction of constriction leading to a rise, or of dilation leading to a fall of blood-pressure.

Stimulation of a sentient surface in many cases causes a similar rise in blood-pressure as shown in Fig. 85, where a rise of blood-pressure follows irritation of the nostrils. In this case, however, the rise in blood-pressure is accompanied by changes in respiration and in the cardiac rhythm.

In the instances just quoted, the effect of the stimulation of the afferent nerve may be spoken of as a general one ; it is the general blood-pressure which is diminished or increased ; though

in the case of the depressor, at all events, it is chiefly in the
splanchnic area that the constriction or dilation takes place.

There are, however, some remarkable cases where a local effect
can be readily distinguished from the general effect, because the
two are in opposite directions.   Thus, if in a rabbit under urari,
the central stump of the auricularis magnus nerve or of the
auricularis posterior be stimulated, the rise of general pressure,
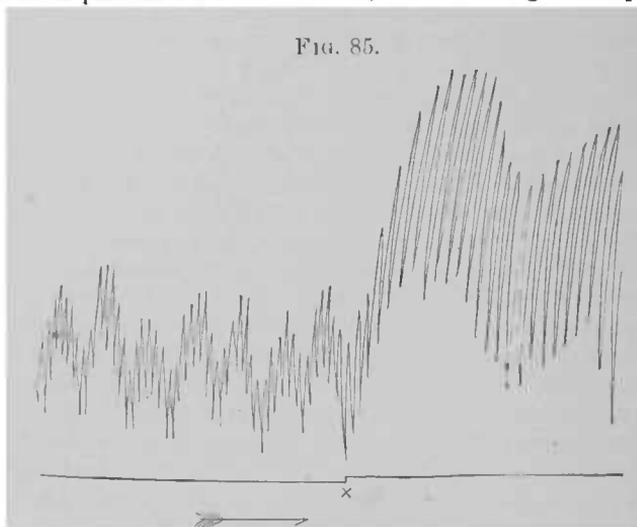
RISE OF BLOOD-PRESSURE FROM STIMULATION ON NOSTRIL WITH SMOKE.
The respiration and cardiac rhythm are at the same time rendered more slow.
The mark x indicates the time of the stimulation.

which is caused by the stimulation of this as of any other afferent
nerve, is accompanied by a dilation of the artery of the ear.
That is to say, the afferent impulses passing along the auricular
nerve while affecting the central nervous system in an ordinary
way, so as to cause constriction of many of the arteries of the
body (but chiefly, probably, the splanchnic vessels), at the same
time so affect some particular part of the central nervous system,
more especially connected with the vaso-motor fibres governing
the artery of the ear, as to lead to the dilation of that vessel.

So, also, in the same animal stimulation of branches of the
tibial nerve causes dilation of the saphena artery, together with
constriction of other arteries, as shown by the concomitant rise
of pressure.   And there are, probably, innumerable instances of
the same kind of action going on in the body during life, for it
is evident that the object of the local dilation—viz., the increased
flow of blood to the organ—must be assisted if a general con-
striction is at the same time taking place in other regions.

The general effect may not always be obvious—may, perhaps, be absent, so that the local dilation or constriction, as the case may be, is the only obvious result of the vaso-motor action. When the ear of the rabbit is gently tickled, the effect that is seen is a blushing of the ear, and though this may be in part due, as we shall see, to the action of a local mechanism, the case we have just cited shows that the central nervous system must be largely engaged. When the right hand is dipped in cold water, the temperature of the left hand falls, on account of a reflex constriction of the vessels of the skin of that hand caused by the stimulus applied to the other. Many more instances might be quoted, and we shall again and again come upon examples. The numerous pathological phenomena classed under sympathetic action, such as the affection of one eye by disease in the other, are probably in part, at least, the results of reflex vaso-motor action.

We have said enough to show that the calibre of the small arteries, which by determining the peripheral resistance forms one important factor regulating the flow of blood, is subject to influences proceeding from all parts of the body, and that these influences reach the arteries in a reflex manner by means of the central nervous system, the afferent impulses being for the most part carried by ordinary sensory nerves, while the efferent impulses pass along special vaso-motor fibres, which, though the centre of the reflex action lies in the cerebro-spinal axis, have a great tendency to run in sympathetic tracts.

The afferent impulses, of course, need not start from the peripheral nerve-endings. They may, for instance, arise in the brain. Thus, as we have seen, an emotion originating in the cerebrum may by vaso-motor action give rise either to blushing or to pallor. Nay, more, changes may be induced in the central nervous system itself without the need of any impulses reaching it from without. When we come to discuss the relations of respiration to the circulation, we shall see reason to think that the vaso-motor action of the central nervous system may be directly affected by the condition of the blood passing through it, so that if the quantity of oxygen in the blood be reduced, a general arterial constriction takes place, and a rise of blood-pressure follows; while with a return of oxygen to the blood, the vessels dilate and pressure falls. And it is more than probable that many substances introduced into the blood, or arising in the blood from natural or morbid changes, may affect blood-pressure by acting directly on the centres in the central nervous system. They may also, however, act on the peripheral structures. We shall return to these phenomena later on.

In many ways, then, and to a varying degree and extent, the

central nervous system can bring about arterial constriction or dilation, general or local. We have now to study the question, What is more exactly the nature of the nervous influences which lead to constriction and dilation, respectively? How do those which cause constriction differ from those which cause dilation?

In the fundamental experiment of the cervical sympathetic, when arterial dilation has followed upon section of the nerve, if the peripheral stump of the divided nerve be stimulated, the dilation gives place to constriction, the blush is replaced by pallor. If the stimulus be very strong the constriction is greater than normal, but by carefully adjusting the strength of the stimulus, the circulation may be brought to quite a normal condition, the "loss of tone" consequent on the severance of the vaso-motor fibres from the central nervous system may be replaced, and not more than replaced, by an artificial tone generated by the action of the stimulus on the sympathetic nerve. The most natural interpretation, therefore, of the vaso-motor action in this case is to suppose that the normal tone of the arteries of the face is maintained by "tonic" constrictive impulses of a certain intensity which pass from the central nervous system along the sympathetic, and that the dilation of the same arteries is due simply to a diminution or absence of these constrictive impulses, an increased constriction or pallor being similarly due to an increase beyond what is normal of these same impulses. In other words, the nervous influences leading to arterial dilation and constriction differ in degree only, not in kind, and may be considered as being merely phases (of decrease or of increase, as the case may be) of the same action. And if we turn to the splanchnic nerve we find a similar interpretation equally valid. Stimulation of the splanchnic nerve causes constriction of the arteries governed by that nerve, apparently because the stimulation supplies artificially the constrictive impulses which, so long as the nerve is intact, pass down it from the central nervous system, giving the requisite tone to its vascular area, and the loss of which by division of the nerve gives rise to dilation. So that were we to stop our inquiries at this point, our explanation of vaso-motor action would be very simple. We might speak of constrictive impulses as passing from the central nervous system to the various vascular areas, to such an extent as to constitute normal tone, but as being susceptible either of inhibition, complete or partial, thus leading to greater or less arterial dilation, or of augmentation, thus leading to excessive constriction.

But this simple view appears insufficient when we push our studies further.

In the first place, such a conception does not cover all the facts connected even with the two nerves just mentioned. For the

dilation or loss of tone which follows upon section of the cervical sympathetic (and the same is true of the splanchnic) is not permanent; after a while—it may be not until after several days, it may be sooner—the dilation disappears and the arteries regain their usual calibre. This recovery is not due to any regeneration of vaso-motor fibres in the sympathetic, for it may be observed when the whole length of the nerve, including the superior cervical ganglion is removed. When recovery of tone has thus taken place, dilation or increased constriction may be occasioned by local treatment; the ear may be made to blush or to pale by the application of heat or cold, by gentle stroking or rough handling, and the like; but neither the one nor the other condition can be brought about by the intervention of the central nervous system. So, also, the spontaneous rhythmic variations in the calibre of the arteries of the ear of which we spoke on p. 243, though they cease for a time after division of the cervical sympathetic, eventually reappear, even if the superior cervical ganglion be removed. And the analogous rhythmic variations of the veins of the bat's wing have been proved experimentally to go on vigorously when all connection with the central nervous system has been severed; they may continue, in fact, in isolated pieces of the wing. From this it is clear that what we have spoken of as the tone of the vessels of the face, though influenced by and in a measure dependent on the central nervous system, is not simply the result of an effort of that system. The muscular walls of the arteries are not mere passive instruments worked by the cerebro-spinal axis through the cervical sympathetic; obviously they have an intrinsic tone of their own, dependent possibly on some local nervous mechanism, though in the ear at least no such mechanism has yet been found: and it seems natural to suppose that when the central nervous system causes dilation or constriction of the vessels of the face, it makes use, in so doing, of this intrinsic local tone. But, if so, then the simple view entertained above, that arterial dilation and constriction are simply determined by the decrease or increase of tonic constrictive impulses passing directly from the central nervous system, is not a complete representation of the facts.

In the second place, if we turn from the sympathetic or splanchnic to other nerves containing vaso-motor fibres, we meet with still greater difficulties. To take, for instance, a nerve supplying a muscle, such as that going, in the frog, to the mylohyoid muscle. Here, as in the cervical sympathetic, section of the nerve produces dilation, but that dilation is even more transient than in the case of the sympathetic; the vessels speedily return to their former calibre. And then it is found that stimulation of whatever strength of the peripheral portion of the

divided nerve brings about not constriction but dilation. A similar dilation is seen when the nerve of a mammalian muscle is stimulated, and probably occurs in the case of all muscular nerves. There are, therefore, in the body, nerves, stimulation of which, as well as mere section, always brings about arterial dilation.

There are other nerves in the body of a mixed character, intermediate between the cervical sympathetic on the one hand, and the muscular nerves on the other, stimulation producing now constriction, now dilation. Such a nerve is the sciatic of a mammal. We have already seen that section of this nerve produces dilation of the vessels of the foot: but the dilation so caused after a few days disappears; the foot on the side on which the nerve was divided becomes not only as cool and pale, but frequently cooler and paler than the foot on the sound side. If the peripheral portion of the divided nerve be stimulated with an interrupted current, immediately or very shortly after division, the dilation due to the division gives place to constriction; the sciatic acts then quite like the cervical sympathetic, except, perhaps, that this artificial constriction cannot be maintained for so long a time, and is very apt to be followed by increased dilation. If, however, the stimulation be deferred for some days, until the dilation has given place to a returning constriction, the effect is not constriction, but dilation; the nerve then acts, as far as its vaso-motor fibres are concerned, like a muscular nerve, and not like the cervical sympathetic. In fact, by variations in the attendant circumstances, and in the mode of stimulation, into the details of which we cannot enter now, stimulation of the divided sciatic may, at the will of the experimenter, be made to produce either arterial dilation or arterial constriction.

In all the above cases, section of the nerve produces dilation, whether the subsequent stimulation causes constriction or dilation; the dilation after section may be sometimes not very marked, but is always present to some extent or other. But there are certain nerves, section of which produces no marked changes in the vascular areas to which they are distributed, and yet stimulation of which brings about dilation often of an extreme character. A striking example of this is seen in the so-called nervi erigentes. The erection of the penis is, putting aside the subsidiary action of muscular bands in restraining the outflow through the veins, chiefly due to the dilation of branches of the pudic arteries, whereby a large quantity of blood is discharged into the venous sinuses. Erection may, in the dog, be artificially produced by stimulating the *peripheral* ends of the divided nervi erigentes, which are branches from the first and second, and sometimes from the third, sacral nerve passing across the pelvis.

On applying the interrupted current to the peripheral ends of these nerves, the corpora cavernosa at once become turgid. And yet simple section of these nervi erigentes will not in itself give rise to erection.

A similar case is presented by the submaxillary gland. As will be explained more in detail in treating of secretion, this gland is supplied by two nerves, by branches of the chorda tympani reaching it along its duct, and by branches of the cervical sympathetic reaching it along its arteries. Neither section of the chorda tympani nor section of the cervical sympathetic produces any very marked effect in the circulation of the gland. Yet stimulation of the former will bring about a most striking dilation, of the latter a no less striking constriction, of the arteries of the gland.

How can we construct a view of the action of vaso-motor nerves which will be consistent with all these various facts?

In the first place, we must admit the existence of a local tone in the several vascular areas, independent of the central nervous system. In such cases as the corpora cavernosa of the penis, and the submaxillary gland, this independence is unmistakable; in other regions it is not at first sight so apparent, but, as we have already urged, must be admitted even for these.

In the second place, as is strikingly shown by the case of the submaxillary gland, there are nerves which, since stimulation of them always causes dilation, may be called *vaso-dilator* nerves, and nerves which, since stimulation of them always causes constriction, may be called *vaso-constrictor* nerves. Examples of the first are seen in the nervi erigentes, the chorda tympani, the nerves of muscles, etc.; of the second, in the cervical sympathetic, the splanchnic, etc. Or, to be more exact, we may say that the vaso-motor fibres of the former are vaso-dilator, of the latter, vaso-constrictor.

In the third place, the cases of the corpora cavernosa of the penis and the submaxillary gland suggest the idea that dilation is the result of the complete or partial loss of local tone; that, in fact, vaso-dilators act by inhibiting, and vaso-constrictors by augmenting, the activity of the local mechanism (whatever it be) which gives rise to the local tone. The erection of the penis which follows stimulation of the nervi erigentes, and the injection of the submaxillary gland which follows stimulation of the chorda tympani, present a very close analogy to the inhibition of the heart by stimulation of the vagus. Just as the rhythmic contraction of the cardiac fibre is stopped by the vagus, so the tonic contraction of the arterial fibre (and this tonic contraction is, indeed, at bottom an obscure rhythmic contraction) is stopped by the chorda or the nervi erigentes. And it seems to be very

natural to draw the conclusion that dilation is in all cases mere inhibition, and constriction in all cases mere augmentation, of local tone.   But tempting as this view is, and useful, perhaps, as it may be as a working hypothesis, it must not be regarded as definitely proved.   It is quite possible that dilation may be brought about in different ways in different cases ; and so, also, with constriction.

Further, the occurrence of dilation after simple section of a nerve raises an interesting question.   Do the arteries in such a case dilate because the very section of the nerve acts as a stimulus to vaso-dilator fibres, or because the local tone is insufficient to keep up an adequate arterial constriction unless it be supplemented by additional tonic impulses reaching the local mechanism from the central nervous system, which supplement is lost by section of the nerve?   Obviously, if mere section behaves as a stimulus to vaso-dilator fibres of such a potency as to give rise to a dilation lasting hours, or it may be days, all evidence of " tonic" impulses proceeding from the central nervous system is done away with.   We can, then, only speak of dilation and constriction as being the result of the action of vaso-dilator and vaso-constrictor fibres, respectively, both worked in a reflex manner by the central nervous system.   Into the discussion whether such an interpretation of the effects of simple section is justified by facts or not, and into the allied controversy concerning the reason why the vaso-motor effects of stimulating the efferent fibres of the sciatic and other nerves vary so much under different circumstances, we cannot enter here.   We must content ourselves with the general conclusion that though local tone may exist independently of the central nervous system, the condition of the various vascular areas, in the living body in a normal condition, is arranged and modified to meet passing or permanent needs, by the central nervous system, through the agency of vaso-motor nerves, and that these vaso-motor nerves in some cases, since they are used to give rise to dilation only, may be spoken of as vaso-dilator nerves, or as containing vaso-dilator fibres, in other cases may similarly be called vaso-constrictor, and in yet a third class of cases be regarded as mixed in character, since, according to circumstances, they give rise either to dilation or to constriction.

The Course of Vaso-motor Fibres.—Leaving out of consideration local vaso-motor mechanisms, such as those which may be supposed to exist in the submaxillary gland, we may make the general statement that vaso-motor influences may be traced back to the spinal cord.   The exact paths taken by the vaso-motor fibres have not, however, as yet been fully worked out.

Most observers are agreed that the fibres leave the spinal cord by the anterior roots of the spinal nerves ; but in the majority of

cases, at all events as far as the mammal is concerned, the fibres do not run in a direct course to their destination in company with the ordinary motor fibres passing to the same structures as themselves. Thus, the vaso-motor fibres of the hind limbs do not pass directly with the anterior roots into the sciatic nerve, but, largely at all events, turn aside, to join through the rami communicantes the abdominal sympathetic; and it is only after they have traversed a certain length of sympathetic nerve that they again return to the spinal nerves, enter into the sciatic plexus, and thus become part of the nerves of the leg. So, also, the vaso-motor fibres for the forelimb pass in large measure from the anterior roots of the upper dorsal nerves to the thoracic sympathetic chain, and thence by the first thoracic ganglion to the brachial plexus, and so on to the forelimb. And we have already seen that the vaso-motor fibres for the head and face, pass from the lower cervical or lower dorsal spinal cord to the first thoracic or to the last cervical ganglion, and by the cervical sympathetic upwards.

When, as in the case of the submaxillary gland, the presence of distinct and antagonistic vaso-constrictor and vaso-dilator nerves is conspicuous in the same organ, the dilator fibres are generally found running in a cerebro-spinal and the constrictor fibres in a sympathetic nerve, but we cannot at present say that such a contrast is invariable. We cannot as yet trace out such distinct courses for the dilator and constrictor fibres of either the fore or hind limb; and in the tongue, while dilator fibres run into the lingual nerve, constrictor fibres appear in the hypoglossal, which is no less clearly a spinal nerve than the fifth, of which the lingual is a branch.

Vaso-motor Centres.—There remains the important question, What part of the central nervous system is it which intermediates as a nervous vaso-motor centre or centres, either of purely reflex or of partly reflex and partly automatic action, between various afferent impulses and the efferent vaso-motor impulses leading either to dilation or constriction?

We have seen that stimulation of the central stump of the divided sciatic gives rise, in an animal under urari, to an increase of general blood-pressure, brought about chiefly, if not entirely, by an augmentation of constrictive impulses passing along the splanchnic nerves. This increase of blood-pressure is manifested, with (in satisfactory experiments) undiminished intensity, even when the whole of the brain, down to a certain limit in the medulla oblongata, has been removed. But if the removal be carried beyond this limit, or if a small area of the medulla oblongata lying above the calamus scriptorius be removed, the effect on the general blood-pressure of stimulating the central stump of

the sciatic—we might add, of any other afferent nerve—is comparatively insignificant. The simplest view to take of these facts is to suppose that this small portion of the medulla oblongata acts as a *vaso-motor centre*, by the action of which ordinary afferent impulses coming from the sciatic or any other afferent nerve are transformed into vaso-motor impulses of constrictive (or as in the case of an animal under chloral, of dilating) effect and so discharged along the splanchnic nerves.

The lower limit of this region, which we may call the medullary vaso-motor centre has been placed in the rabbit at a horizontal line drawn about 4 or 5 mm. above the point of the calamus scriptorius, and the upper limit at about 4 mm. higher up— *i. e.*, about 1 or 2 mm. below the corpora quadrigemina. When transverse sections of the brain are carried successively lower and lower down, an effect on blood-pressure in the way of lowering it and also of diminishing the rise of blood-pressure resulting from stimulation of the sciatic, is first observed when the upper limit is reached. On carrying the sections still lower, the effect of stimulating the sciatic becomes less and less, until when the lower limit is reached no effects at all are observed. The centre appears to be bilateral, the halves being placed not in the middle line, but more sideways and rather nearer the anterior than the posterior surface. It may, perhaps, be more closely defined as a small prismatic space in the forward prolongation of the lateral columns after they have given off their fibres to the decussating pyramids. This space is largely occupied by a mass of gray matter, called by Clarke the antero-lateral nucleus, and containing large multipolar cells.

Whether this medullary vaso-motor centre has any distinct automatic action, whether it may be regarded as continually generating out of its own molecular oscillations, and discharging along the vaso-motor fibres, impulses whereby the general arterial tone is maintained, is a question which, like the allied question mooted on p. 235, need not be discussed here. Granting even the existence of such automatic function, they must be of secondary importance. As we have already urged, the great use of the whole vaso-motor system is not to maintain a general arterial tone, but to modify according to the needs of the economy the condition of this or that vascular area.

The impulse passing down the vaso-motor fibres of the cervical sympathetic, and of many other nerves, may similarly be traced back to this same region of the medulla oblongata. Whether all vaso-motor fibres are actually in functional connection with it may perhaps be doubted; but at all events the fibres passing to so many vascular areas, and those of such magnitude and importance, are by means of it brought into functional relationship

with so many afferent nerves of the body, that it may fairly be spoken of as the general vaso-motor centre.

But the use of this phrase must not be understood to imply that this small portion of the medulla oblongata is the only part of the central nervous system which can act as a vaso-motor centre. In the frog reflex vaso-motor effects may be obtained by stimulating various afferent nerves after the whole medulla has been removed, and, indeed, even when only a comparatively small portion of the spinal cord has been left intact and connected, on the one hand, with the afferent nerve which is being stimulated, and, on the other, with the efferent nerves in which run the vaso-motor fibres whose action is being studied. In the mammal such effects do not so readily appear, but may with care and under special conditions be obtained. Thus in the dog, when the spinal cord is divided in the dorsal region, the arteries of the hind limbs and hinder part of the body become dilated. This one would naturally expect as the result of their severance from the general medullary vaso-motor centre. But if the animal be kept in good condition for some time, a normal or nearly normal arterial tone is after a while reëstablished; and the tone thus regained may be modified in the direction certainly of dilation, and possibly, but this is by no means so certain, of constriction by afferent impulses reaching the lumbar cord. Erection of the penis through the nervi erigentes may then be still brought about by suitable stimulation of sensory surfaces, and dilation of various vessels of the limbs readily produced by stimulation of the central stump of one or another nerve.

These remarkable results, which, though they are most striking in connection with the lumbar cord, hold good apparently for the dorsal cord also, and indeed for all parts of the spinal cord, naturally suggest a doubt whether the explanation just given above of the effects of section of the medulla oblongata is a valid one. When we come to study the central nervous system, we shall again and again see that the immediate effect of operative interference with these delicate structures is a temporary suspension of nearly all their functions. This is often spoken of as "shock," and may be regarded as an extreme form of inhibition. And the question may fairly be put whether the effects of cutting and injuring the structures, which we have spoken of as the medullary vaso-motor centre, are not in reality simply those of shock. The case of the dog with the divided dorsal cord, and other similar cases, clearly prove that parts of the spinal cord, other than the particular region of the medulla oblongata of which we are speaking, may act as vaso-motor centres. And we may very fairly at least put forward the view, that the vascular dilation which follows upon sections of the so-called medullary vaso-motor centre, comes about

because section of or injury to this region exercises a strong inhibitory influence on all the vaso-motor centres situated in the spinal cord below. Owing to the special function of the medulla oblongata in carrying on the all-important work of respiration, a mammal whose medulla has been divided cannot be kept alive for any length of time. We cannot, therefore, put the matter to the simple experimental test of extirpating the supposed medullary vaso-motor centre, and seeing what happens when the animal has completely recovered from the effects of the operation, we have to be guided in our decision by more or less indirect arguments. We must not attempt to discuss the matter fully here, but may say that, after all due weight has been attached to the play of inhibitory impulses, there still remains a balance of evidence in favor of the view that the region of the medulla of which we are speaking does act as a general vaso-motor centre. It is not, however, to be regarded as the single vaso-motor centre, whither afferent impulses from all parts of the body must always travel before they can start vaso-motor impulses along this or that nerve. We are rather to suppose that the spinal cord along its whole length, contains, interlaced with the reflex and other mechanisms by which the skeletal muscles are governed, vaso-motor centres and mechanisms of varied complexity, the details of whose functions and topography have yet largely to be worked out. As in the absence of the sinus venosus the auricles and ventricle of the frog's heart may still continue to beat, so in the absence of the medulla oblongata, these spinal vaso-motor centres provide for the vascular emergencies which arise. As, however, in the normal entire frog's heart, the sinus, so to speak, gives the work and governs the work of the whole organ, so the medullary vaso-motor centre rules and coördinates the lesser centres of the cord, and through them presides over the chief vascular areas of the body. It is possible, moreover, that the medullary centre is specially connected with the splanchnic nerves, and thus with the capacious vascular area of the abdominal viscera, and, in consequence, possesses an additional importance. By means of these vaso-motor central mechanisms, by means of the head centre in the medulla, and the subsidiary centres in the spinal cord, the delicate machinery of the circulation, which determines the blood-supply, and so the activity of each tissue and organ is able to respond by narrowing or widening arteries to the ever-varying demands, and to meet by compensating changes the shocks and strains of daily life.

Vaso-motor Nerves of the Veins. — Although the veins are provided with muscular fibres, and are distinctly contractile, and although rhythmic variations of calibre due to contractions may

be seen in the great veins opening into the heart, in the veins of the bat's wing, and elsewhere, and similar rhythmic variations, also possibly due to active rhythmic contractions, but possibly, also, of an entirely passive nature, have been observed in the portal veins, very little is known of any nervous arrangements governing the veins. When in the frog the brain and spinal cord are destroyed, very little blood comes back to the heart as compared with the normal supply, and the heart, in consequence, appears almost bloodless, and beats feebly. This has been interpreted as indicating the existence of a normal tone in the veins dependent on the central nervous system. When the latter is destroyed, the veins become abnormally distended, and a large quantity of blood becomes lodged and hidden, as it were, in them.

The Effects of Local Vascular Constriction or Dilation.

Whatever be determined ultimately to be the *modus operandi* of vaso-motor mechanisms, the following fundamental facts remain of prime importance.

The tone of any given vascular area may be altered, positively in the direction of augmentation (constriction), or negatively in the way of inhibition (dilation), quite independently of what is going on in other areas. The change may be brought about by (1) a stimulus applied to the spot itself, and, acting either directly on some local mechanism, or indirectly by reflex action through the general central nervous system ; (2) by a stimulus applied to some other sentient surface, and acting by reflex action through the central nervous system ; (3) by a stimulus (chemical, arising in or carried by the blood) acting directly on the central nervous system ; (4) by some part of the central nervous system acting on the vaso-motor centre, as in emotions.

The effects of local dilation are local and general.

The local effects are as follows. The arteries in the area being dilated, offer less resistance than before to the passage of blood. Consequently, more blood than usual passes through them, filling up the capillaries and distending the veins. Owing to the diminution of the resistance, the fall of pressure in passing from the arteries to the veins will be less marked than usual ; that in the small arteries themselves will be lowered ; that in the corresponding veins heightened. The lowering of the pressure in the arteries means that their elastic coats are not put to the stretch as much as usual—*i. e.*, their elasticity is not called into play to the same extent as before. Now, as has been seen, every portion of the arterial wall has its share in destroying the pulse by converting the intermittent into a continuous flow. Hence, the dilated

arteries, their elasticity not being called into play so much as
before, will not contribute their usual share towards destroying
the pulsations which reach them at the cardiac side. The pul-
sations will travel through them less changed than before, and may,
in certain cases, pass right on into the veins. This is frequently
seen in the submaxillary gland, when the chorda tympani is
stimulated. The channels being wider, resistance being less, and
the force of the heart behind remaining the same, more blood than
before passes through the area in a given time; or, put differ-
ently, the same quantity of blood passes through the area in a
shorter time. The blood, consequently, as it passes into the veins
is less changed than in the normal condition of the area. Usually
the flow is so rapid that the oxyhæmoglobin of the corpuscles is
deoxidized to a much less extent than usual, and the venous blood
still possesses an arterial hue. On the other hand, since more
blood passes in a given time, there is an opportunity for an in-
crease in the total interchange between the blood and the tissue.
Thus the total work may be greater, though the share borne by
each quantity of blood is less.

The general effects of dilation are briefly these. Supposing
that the total quantity of blood issuing from the ventricle remains
the same—that is to say, supposing that the quantity of blood
put into circulation is constant, the surplus passing through the
dilated area must be taken away from the rest of the circulation.
Consequently the fulness of the dilated area will lead to an
emptying of the other areas. This is seen very clearly when the
dilated area is a capacious one. At the same time, local dilation
causes a local diminution of peripheral resistance. This in turn
causes a lowering of the general arterial pressure ; to this we
have already called attention.

The effects of local constriction, similarly local and general,
are naturally the reverse of those of dilation. In the vascular
area directly affected, less blood passes through the capillaries
in a given time, and in consequence less total interchange
between the blood and the tissues takes place, though each unit-
volume of blood which does pass through is more deeply affected.
The blood-pressure in the corresponding arteries is increased,
and, if the area be large, the pressure in even distant arteries
may be heightened.

Thus, to indicate results in a general manner, local dilation
encourages a copious flow of blood through the area where the
dilation is taking place, and, by reducing the blood-pressure,
hinders the flow of blood into other areas. Local constriction,
on the other hand, lessens the flow of blood in the particular
area, and by heightening the blood-pressure tends to throw the
mass of the blood on to other areas. Hence the great regulative

value of the vaso-motor system. By augmenting or inhibitory influences (constrictor or dilating) applied either to peripheral mechanisms or to cerebro-spinal centres, and called forth by stimuli either intrinsic and acting through the blood, or extrinsic and acting through nervous tracts, the supply of blood to this or that organ or tissue may be increased or reduced ; the surplus or deficit being carried away to, or brought up from, either the rest of the body generally or some other special organ or tissue.

Sec. 6.—Changes in the Capillary Districts.

We have already seen (p. 151) that the capillary channels vary very much in width from time to time ; but the capillaries do not, like the arteries, possess a distinct muscular coat, and the mechanism by which they are brought, now to a dilated, now to a constricted condition has not been worked out so thoroughly as in the case of the arteries. On the one hand there can be no doubt that the changes in their calibre are, in part, of a passive nature. They are expanded when a large supply of blood reaches them through the supplying arteries, and, by virtue of their elasticity, shrink again when the supply is lessened or withdrawn.

On the other hand, there is an increasing amount of evidence that the capillary walls are really contractile. The constituent epithelioid cells have been seen to change their form under the influence of stimuli ; and there is much reason for believing that the calibre of a capillary canal may vary, quite independently of the arterial supply or the venous outflow, in consequence of changes in form of the epithelioid cells, allied to the changes in a muscle-fibre or muscle-cell which constitute a contraction. Though the matter requires further investigation, it is probable that these active changes play an important part in determining the quantity of blood passing through a capillary area ; but there is as yet no evidence that they, like the corresponding changes in the arteries, are governed by the nervous system.

Over and above these changes of form, the capillaries and minute vessels also possess other active properties, which cause them to play an important part in the work of the circulation. They are concerned in assisting to maintain a vital equilibrium between the intravascular blood and the extra-vascular tissue, an equilibrium which is the central fact of a normal capillary circulation, of a normal interchange between the blood and the tissue, and thus of a normal life of the tissue. The existence of this equilibrium is best shown when it is overthrown or modified, as in inflammation and allied conditions.

If an irritant, such as a drop of chloroform or a little diluted
oil of mustard, be applied to a small portion of a frog's web, a
frog's tongue, or some other transparent tissue, the following
changes may be observed under the microscope. The first effect
that is noticed is a dilation of the arteries, accompanied by a
quickening of the stream. The capillaries become filled with
corpuscles, and many passages, previously invisible or nearly so
on account of their containing no corpuscles, now come into view.
The veins at the same time appear enlarged and full. The in-
crease of width is most marked in the arteries, next so in the
veins, and least of all in the capillaries. If the stimulus be very
slight, this may all pass away, the arteries gaining their normal
constriction, and the capillaries and veins returning to their
normal condition; in other words, the effect of the stimulus in
such a case is simply a temporary blush. Unless, however, the
chloroform or mustard be applied with especial care, the effects
are much more profound and lasting. In the case of the frog's
web a condition is set up known under the name of *stasis*. This
has been considered as merely a phase of inflammation, since in
the frog's web, in which inflammation has been largely studied,
the agents which produce inflammation frequently produce
stasis. But in the frog's tongue, and elsewhere, true inflamma-
tion may be set up and produce all its results without any stasis
making its appearance; and though the two conditions are in
several respects similar, they appear to be distinct; stasis being
the result of the profounder action of the irritant, and the fore-
runner of local death or necrosis.

It is this stasis which particularly illustrates the points to
which we wish to call attention. When, as the result of the
irritant, the initial blush passes into stasis, the following events
may be observed: The quickening of the stream gives way to a
slackening; this is not due to any returning constriction of the
arteries, for they still continue dilated. It will further be ob-
served that the red blood-corpuscles, instead of being in the larger
capillaries and smaller arteries and veins confined to the axial
stream, are diffused and, indeed, crowded over the whole width
of the channels. The capillaries and veins get more and more
crowded with corpuscles, the white corpuscles being scattered
irregularly among the more numerous red ones; and, though the
channels get wider and wider, becoming frequently even enor-
mously distended, the stream becomes slower and slower, until at
last the movement of the blood in the affected area ceases alto-
gether. The phase of accelerated flow has given place to stasis.
The capillaries, veins, and small arteries are choked with corpus-
cles, and it may now be remarked that the red corpuscles seem to
run together, so that their outlines are no longer distinguishable;

they appear to have become fused into a homogeneous mass. Except in cases where the stimulus produces permanent mischief, this peculiar condition after a while subsides. The outlines of the corpuscles become once more distinct, those on the venous side of the block gradually drop away into the neighboring currents, little by little the whole obstruction is removed, the current through the area is reëstablished, and though the arteries and capillaries remain dilated for some considerable time, they eventually return to their normal calibre.

The stasis, the arrest of the current here seen, is not due to any lessening of the heart's beat; the arterial pulsations, or at least the arterial flow, may be seen to be continued down to the affected area, and there to cease very suddenly. It is not due to any increase of peripheral resistance caused by constriction of the small arteries, for these continue dilated rather than constricted. It must therefore be due to some new and unusual resistance occurring in the capillary area itself. The increase of resistance is not caused by any change confined to the corpuscles themselves; for if after a temporary delay one set of corpuscles has managed to pass away from the affected area, the next set of corpuscles is subjected to the same delay and the same apparent fusion. The cause of the resistance must therefore lie in the capillary walls, or in the tissue of which they form a part. We are driven to conclude that the walls of the capillaries (and of the other vessels) exert in health a certain attraction on the corpuscles, maintain a certain adhesiveness between them and themselves, thereby determining the normal flow, with its axial stream and plasmatic layer, and offering a normal resistance to the pressure of the arterial system; and that in stasis, for reasons which we cannot as yet explain, this attraction, this adhesiveness is largely and progressively increased. Hence the early disappearance of the distinction between the axial stream and plasmatic layer, the tarrying of the corpuscles in spite of the widening of their path, and finally their agglomeration and fusion in the even enormously distended channels.

That the increased adhesion is due to the vascular walls and not primarily to the corpuscles themselves is further shown by the fact that if in the frog, an artificial blood of normal saline solution to which milk has been added be substituted for normal blood, a stasis may by irritants be induced in which oil-globules play the part of corpuscles, and by their aggregation bring about an arrest of the flow through the capillaries.

In true inflammation the course of events is different. The vessels become dilated, but the loss of distinction between the axial stream and the plasmatic layer does not occur. On the

contrary the plasmatic layer appears even more striking on account of the large number of white corpuscles which gather in it and become adherent to the inner surface of the walls of the veins and venous capillaries. In the normal circulation only a few white corpuscles are from time to time seen in this situation slowly moving on in jerks; but now the walls of the veins seem to be more and more thickly lined with white corpuscles, which are at first completely stationary. At the same time white corpuscles become also very abundant in the capillaries. Very soon these white corpuscles may be seen, either through stomata at the junctions of the epithelioid cells forming the lining of the vessels, or by temporary breaches which are rapidly repaired, making their way through the walls of the veins and capillaries, and escaping into the surrounding tissues. Through the walls of the capillaries and smaller veinlets, red corpuscles pass as well as white. And this takes place to such an extent that very soon the tissue around the veins and capillaries becomes crowded with white corpuscles, and to a less extent with red corpuscles which have made their way out of the vessels. At the same time a large quantity of coagulable lymph, which since it appears also to have passed from the blood-stream through the walls of the bloodvessels is spoken of as exudation, makes its appearance in the interstices of the inflamed tissue. While however these changes are going on there is not, as in stasis, a delay and final arrest of the blood-stream. On the contrary, the flow through the widened channels continues during the whole time to remain accelerated. By comparing the outflow from the veins of the inflamed foot of a dog, with the outflow from the veins of the healthy foot, it has been ascertained that a larger quantity of blood passes through the inflamed foot than through the healthy foot in the same time.

We must not however pursue this subject of inflammation any further. We have simply brought it forward as affording another illustration of the action of the walls of the bloodvessels; for, though the matter is perhaps not definitely settled, it seems probable that the aggregation, in inflammation, of the white corpuscles upon the lining surface of the vessels is due to a special attraction which the bloodvessels exert on the white corpuscles, without producing that general adhesion of all the corpuscles which is the mark of stasis, and that the migration of the corpuscles is also at least facilitated by similar intrinsic changes in the vascular walls.

We cannot say at present whether the vascular walls are also capable of modifying the passage of the fluid parts as distinguished from the corpuscular elements of the blood, though we know by experiment that the flow of fluid through capillary

tubes may be modified on the one hand by changes in the substance of which the tubes are composed, and on the other hand by changes in the chemical nature (even independent of the specific gravity) of the fluid which is used. We have said enough to show that the peripheral resistance in the capillaries (and consequently all that depends on that peripheral resistance) is not merely a matter of the mechanical friction of the blood against the smooth walls of the bloodvessels, but is concerned with the vital condition of the tissues. When the tissue is in health, a certain resistance is offered to the passage of blood through the capillaries, and the whole vascular mechanism is adapted to overcome this resistance to such an extent that a normal circulation can take place. When the tissue becomes affected, the disturbance of the equilibrium between the tissue and the blood may, as in inflammation, so modify the flow as to lead to the abnormal escape from the blood of various constituents, or, as in stasis, so augment the resistance that the passage of the blood becomes difficult or impossible. And it is quite open to us to suppose that there are conditions the reverse of stasis, in which the resistance may be lowered below the normal, and the circulation in the area quickened.

Thus the vital condition of the tissue becomes a factor in the maintenance of the circulation; and it is possible, though not yet proved, that these vital conditions are directly under the dominion of the nervous system.

It is perhaps hardly necessary to observe that the considerations urged above are quite distinct from what is sometimes spoken of under the name of "capillary" force, as an agent of the circulation. If by capillary force it is intended to refer to the rise of fluids in capillary tubes, it is evident that since such phenomena are the results of adhesions, capillarity can only be a greater or less hindrance to the flow of blood, seeing that this is propelled by a force (the heart's beat) which has been proved by experiment to be equal to the task of driving the blood from ventricle to auricle through the capillary regions. If by capillary force it is meant that the tissues have some vital power of withdrawing the fluid parts of the blood from the small arteries and thus of assisting an onward flow, it becomes necessary also to assume that they have as well the power of returning the fluid parts to the veins. Both these assumptions are unnecessary and without foundation.

Sec. 7.—Changes in the Quantity of Blood.

In an artificial scheme, changes in the total quantity of fluid in circulation will have an immediate and direct effect on the arterial pressure, increase of the quantity heightening, and decrease diminishing, it. This effect will be produced partly by the pump being more or less filled at each stroke, and partly by

the peripheral resistance being increased or diminished by the greater or less fulness of the small peripheral channels. The venous pressure will, under all circumstances, be raised with the increase of fluid, but the arterial pressure will be raised in proportion only so long as the elastic walls of the arterial tubes are able to exert their elasticity.

In the natural circulation, the direct results of change of quantity are obscured by compensatory arrangements. Thus, experiment shows that when an animal with normal blood-pressure is bled from one carotid, the pressure in the other carotid sinks so long as the bleeding is going on,[1] and remains depressed for a brief period after the bleeding has ceased. In a short time, however, it regains or nearly regains the normal height. This recovery of blood-pressure, after hemorrhage, is witnessed so long as the loss of blood does not amount to more than about 3 per cent. of the body-weight. Beyond that, a large and frequently a sudden dangerous permanent depression is observed.

The restoration of the pressure after the cessation of the bleeding is too rapid to permit us to suppose that the quantity of fluid in the bloodvessels is repaired by the withdrawal of lymph from the extra-vascular elements of the tissues. In all probability the result is gained by an increased action of the vaso-motor nerves, increasing the peripheral resistance, the vaso-motor centres being thrown into increased action by the diminution of their blood-supply. When the loss of blood has gone beyond a certain limit, this vaso-motor action is insufficient to compensate the diminished quantity (possibly the vaso-motor centres in part become exhausted), and a considerable depression takes place; but at this epoch the loss of blood frequently causes anæmic convulsions.

Similarly, when an additional quantity of blood is injected into the vessels, no marked increase of blood-pressure is observed so long as the vaso-motor centre in the medulla oblongata is intact. If, however, the cervical spinal cord be divided previous to the injection, the pressure, which on account of the removal of the medullary vaso-motor centre, is very low, is permanently raised by the injection of blood. At each injection the pressure rises, falls somewhat afterwards, but eventually remains at a higher level than before. This rise continues until the amount of blood in the vessels above the normal quantity reaches from 2 to 3 per cent. of the body-weight. Beyond this point there is no further rise of pressure.

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[1] Chiefly in consequence of free opening in the vessel from which the bleeding is going on, cutting off a great deal of the peripheral resistance, and so leading to a general lowering of the blood-pressure.

These facts show, in the first place, that when the volume of the blood is increased, compensation is effected by a lessening of the peripheral resistance by means of a vaso-dilator action of the vaso-motor centres, so that the normal blood-pressure remains constant. They further show that a much greater quantity of blood can be lodged in the bloodvessels than is normally present in them. That the additional quantity injected does remain in the vessels is proved by the absence of extravasations, and of any considerable increase of the extra-vascular lymphatic fluids. It has already been insisted that, in health, the veins and capillaries must be regarded as being far from filled, for were they to receive all the blood which they can, even at a low pressure, hold, the whole quantity of blood in the body would be lodged in them alone. In these cases of large addition of blood, the extra quantity appears to be lodged in the small veins and capillaries (especially of the internal organs), which are abnormally distended to contain the surplus.

We learn from these facts the two practical lessons, first, that blood-pressure cannot be lowered directly by bleeding, unless the quantity removed be dangerously large; and, secondly, that there is no necessary connection between a high blood-pressure and fulness of blood, or plethora, since an enormous quantity of blood may be driven into the vessels without any marked rise of pressure.

Sec. 8.—The Mutual Relations and the Co-ordination of the Vascular Factors.

The foregoing considerations show how complicated and sensitive, and therefore how useful, is the vascular mechanism. It may be worth while briefly to summarize the relations of the different factors, and to point out the manner in which they are made to work in harmony for the good of the body.

Two facts stand out prominent above all others: (1) the heart's beat may be made slow by vagus inhibition, and, on the other hand, quickened either by withdrawal of the constant inhibitory influence exercised by the cardio-inhibitory centre, or by the direct action of accelerating mechanisms. (2) The peripheral resistance may be increased or diminished, the increase and decrease being due either to increased or diminished action of the vaso-motor centres which preside over arterial tone, or to the action of special constrictor or dilator fibres.

These two facts are, by the mediation of the nervous system, placed in mutual regulative dependence on each other. Thus, if with a given peripheral resistance, and proportionate blood-

pressure, the heart begins to beat violently, afferent impulses passing up the depressor nerves diminish peripheral resistance (by opening the splanchnic flood-gates), and prevent the rise of blood-pressure which would otherwise take place. In this way a delicate organ—such, for instance, as the retina—is sheltered from the turbulence of the heart by the flow of blood being diverted to the less noble organs of the abdomen. Conversely, if peripheral resistance be in any area increased, the general blood-pressure is prevented from rising too high by reason of the actual increase of blood-pressure so affecting the medulla, that inhibitory impulses descend the vagus, and, by producing a less frequent, possibly a weaker pulse, tone down the distention of the arteries.

The more we learn of the working of the body, the more aware we become of the fact that it is crowded with regulative and compensating arrangements no less striking and exquisite than the two we have just described. Some of these will be seen in the following almost tabular statement of the various modifications of the vascular factors, and of their causes:

A. The *Beat of the Heart* is affected

1. By the amount of distention of the ventricular cavities preceding the systole. This will depend on

a. The quantity of blood reaching the heart and passing into its cavities during the diastole. This, in turn, is determined by the flow of blood through the veins, the flow itself being influenced by the arterial pressure, respiratory movements, etc.

b. The force of the auricular contractions.

c. The amount of resistance which has to be overcome by the systole. This is determined by the mean arterial pressure, and is influenced by everything which influences that.

2. By the quantity of the blood passing through the coronary arteries. In the frog the thin walls of the auricle and the spongy texture of the ventricle permit the nourishment of the cardiac substance to be carried on by direct contact with the blood in the cavities. In mammals this mode of nutrition must be insignificant. In them the condition of the cardiac muscles and nervous appendages depends almost exclusively on the blood distributed by the coronary arteries. The coronary circulation, however, is peculiar, and is largely determined by the action of the heart itself.

3. By the quality of the blood passing through the coronary arteries, and acting upon simply the muscular tissue, or upon the various nervous mechanisms, or upon both. This is illustrated by the action of poisons. The quantitative relations of the normal, and the presence of abnormal, constituents of the blood, must of necessity profoundly affect the heart's beat.

4. Through the inhibitory fibres of the vagus.

a. By the blood directly stimulating the endings of the vagus fibres. This is only seen in the case of poisons.

b. By the blood directly affecting the cardio-inhibitory centre in the medulla oblongata, either positively by augmenting the normal inhibitory influences, and so slowing the heart, or negatively by depressing those influences, and so quickening the heart.

c. By reflex stimulation of the same centre. Cases of exaltation through reflex stimulation have already been quoted. Instances of depression leading to quickening of the heart's beat are not so clear. The afferent impulses may be started in any part of the body ; but, as we have seen, there seems to be a special connection between this centre and the alimentary canal.

5. By the accelerator nerves. We have, however, at present no very satisfactory evidence of the natural activity of these nerves.

B. The *Peripheral Resistance* is affected—

1. By the vital—*i.e.*, the nutritive—condition of the tissue of the part. This is again influenced by

a. The quality (and quantity ?) of the blood brought to it.

b. Through the agency of the nervous system, as is seen in cases of inflammation caused by nervous influences.

Both these points are very obscure.

2. By the varying calibre (constriction, dilation) of the minute arteries, brought about

a. By the blood or other stimulus acting directly on the peripheral vaso-motor mechanism.

b. By the blood or other stimulus acting directly on the vaso-motor centres in the central nervous system.

c. By reflex stimulation of the vaso-motor centres.

d. By the quantity of blood supplied to the vaso-motor centre, this being in turn dependent on the blood-pressure in the arteries supplying the centre. Thus, a regulative mechanism is established for cases when the quantity of blood, as distinguished from its quality, is changed (see p. 271).

Through these intricate ties it comes to pass that an event which takes place in one part of the body is felt, to a greater or less extent, by all parts. To take a simple instance : a change in the condition of the skin at any one spot, such as that produced by the application of cold or heat, may lead.

α. By direct local action to a constriction or dilation of the vessels of the part, giving rise to local pallor or suffusion.

β. By reflex action through the central nervous system, to an increase of the same local effects, and in addition to a change in the calibre of the bloodvessels in other parts. This distant reflex

change may be of the same or the opposite nature as the local change.

γ. By reflex action to a quickening or slowing of the heart's beat, though the heart is in this respect less intimately connected with the skin than with other parts.

Out of these primary effects there may arise secondary effects; the constriction or dilation produced locally will affect the general blood-pressure, which in turn will produce all its effects.

The modifications of the heart's beat will not only affect the general blood-pressure, but in a reflex manner may affect the peripheral resistance, and hence the flow of blood in particular areas (e. g., the splanchnic area). The modifications of the flow through the area directly, and also through those secondarily, affected, will influence the temperature and chemical changes of the blood, and variations in these will, in turn, produce their effects everywhere. And so on.

On the other hand, the turbulence which would be the natural outcome of all these events is softened down, by the compensating effects of which we have spoken, into the smoothness which we call health. Still, the greatness of the possibilities of change which lie hidden in the body are clearly enough shown by the violence of disease, when compensation fails of accomplishment.

BOOK II.

THE TISSUES OF CHEMICAL ACTION WITH THEIR RE-SPECTIVE MECHANISMS—NUTRITION.

CHAPTER I

[THE EPITHELIA.

THE epithelia are found in the body as single or multiple layers of nucleated protoplasmic cells. They have a large area of distribution in the economy, and play a very important part in many of the vital processes. These cells are more or less

Fig. 86.—Fragments of Epithelium from a Serous Membrane (peritoneum) Magnified 410 diam. *a*, cell ; *b*, nucleus ; *c*, nucleoli. HENLE.

Fig. 87.—Epithelium Scales from the inside of the Mouth. Magnified 260 diam. HENLE.
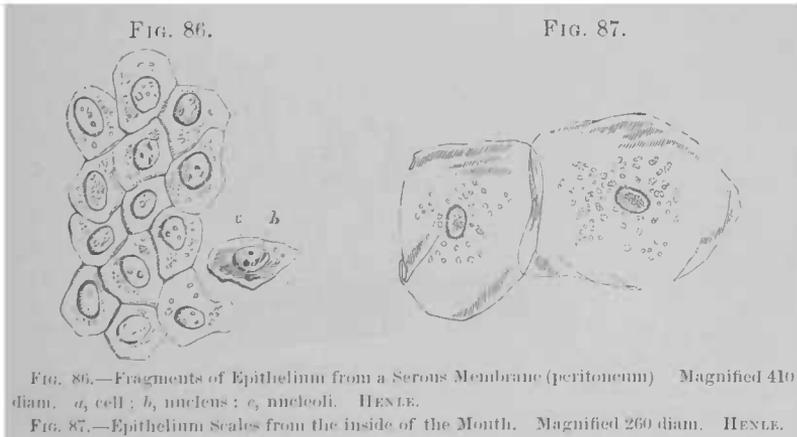
modified in form and structure in the different epithelia, and so differentiated in their "amœbiform units" as to perform very diverse functions.

They have been divided into four principal varieties, distinguished by certain characteristic appearances of the cells. They

are generally known as *pavement, tessellated,* or *squamous; columnar* or *cylindrical: ciliated;* and *spheroidal* epithelia.

Pavement, tessellated, or *squamous* epithelium is found widely distributed, forming the epidermal covering, the lining of the bloodvessels, serous sacs, many of the mucous membranes, etc. This form of epithelium consists of irregular, polygonal, flattened cells, which are overlapped, or more or less merged into each other at their edges. (Figs. 86 and 87.)
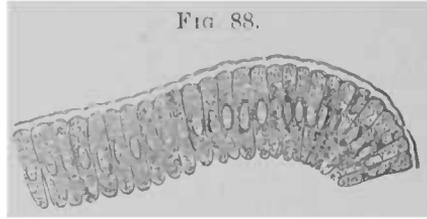
FIG. 88.

CYLINDRICAL EPITHELIUM FROM INTESTINAL VILLUS OF A RABBIT. Magnified 300 diam. After KOLLIKER.

Columnar or *cylindrical* epithelium (Fig. 88) is found in the form of elongated cylindrical cells, which are more or less angular on their sides from mutual compression; they are placed parallel with each other, and vertically on the basement
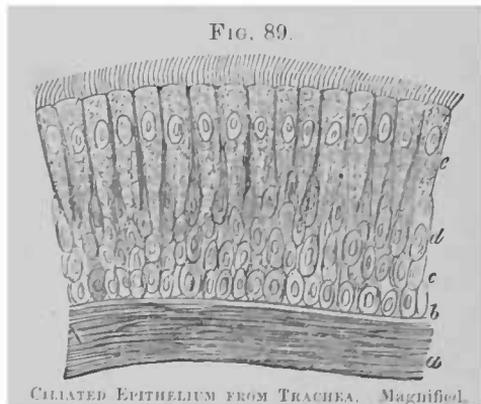
FIG. 89.

CILIATED EPITHELIUM FROM TRACHEA. Magnified.

a, basement membrane; *b, c, d,* cells in the several stages of development, and which will ultimately be fully developed ciliated cells, and take the place of the matured ones which will be thrown off; *e,* shows fully developed cells.

membrane. This form of epithelium is found principally as a lining of the mucous membrane of the gastro-intestinal tract, and of many of the ducts.

Ciliated epithelium (Fig. 89) usually is found in a form

similar to that of the columnar variety. These cells have projecting from their free extremities very numerous hair-like bodies or *cilia*. If these cells are examined with a microscope during life or immediately after death, the cilia will be seen to be in a state of constant vibratile motion. This form of epithelium is found in the greater portion of the respiratory tract, in the Fallopian tubes, etc.

Spheroidal or *glandular* (Fig. 98) epithelium is in the form of somewhat globular or spheroidal cells, which are more or less angular on their sides, from compression of adjoining cells. This epithelium is found principally in the secretory portions of the glands, and in many, if not in all of them, forms the essential physiological constituent.

The functions of these different epithelia are as diverse as are their forms and structures. Pavement epithelium is so distributed that its use often appears to be of a mere *mechanical* or *physical* character. Thus in the skin it consists of numerous stratifications of cells which form a tough, more or less impermeable layer, which protects the true skin from effects of friction, and at the same time protects the body from overloss of water by evaporation. The horns of animals, the nails and hairs, are all modifications of this form of epithelium. In the bloodvessels it forms a smooth lining membrane and seems to be endowed with a vital property in preventing an intravascular coagulation of the blood. In the capillaries it also plays a very important part in the interchange of the secretive and excretive materials which are conveyed in the blood. In both the systemic and pulmonic capillaries it is an active agent in the interchange of gases, and is, therefore, a *respiratory* tissue. In the bladder, where its form is somewhat modified, it forms a membrane which prevents the reabsorption of urine.

Other epithelia, such as the spheroidal, are principally *secretive*, and possess the power of selecting certain elements from the blood, and by a process of metabolism convert them into new substances. In certain glands these cells themselves undergo certain metamorphoses and are elaborated as elements of the secretion. The function of this epithelium in some of the glands is *excretory*. The spheroidal and columnar varieties are the principal secretory epithelia.

Absorption is the principal function of others. The intestinal villi, which are covered with a layer of columnar epithelial cells, are intimately connected with the function of absorption. It is through these cells that the chyle passes to reach the lacteals, and through which other products of digestion pass to reach the intestinal capillaries of the portal vein. The cells in this position are somewhat modified by possessing a striated outer surface

(Fig. 90). The striæ were supposed by some physiologists to be minute canals which lead into the intracellular protoplasm. These cells during fasting contain clear granular protoplasm, but during digestion they are seen to contain very numerous fat-globules. They will be referred to more fully hereafter.

The ciliated epithelia possess a special function by virtue of their ciliary appendages. In the respiratory tract they assist in the expulsion of mucus and foreign bodies, also in the expiration

FIG. 90.
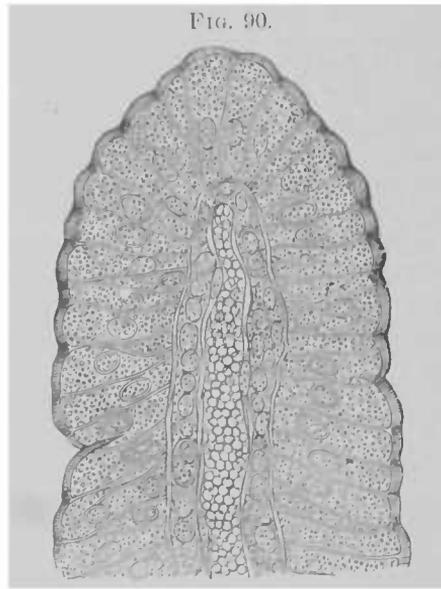
SECTION OF A VILLUS FROM THE INTESTINE OF A RABBIT.

Above *a* is the central canal bounded on either side by the matrix *b*, which again is covered by long columnar cells *a*, containing a nucleus and granules. The outer surface of these cells is seen to be striated.

of air. In the Fallopian tubes they are probably active agents in propelling the ovule along the interior of the tubes to the uterine cavity.

The epithelia have no bloodvessels, and must, therefore, obtain their nutriment by diffusion from the adjoining tissues.

After epithelium cells are matured, and no longer capacitated for the performance of their proper functions, they are cast off and replaced by cells which are produced beneath. (See Fig. 89.)]

THE TISSUES AND MECHANISMS OF DIGESTION.

The food, in passing along the alimentary canal, is subjected to the action of certain juices which are the products of the secretory activity of the epithelium cells of the alimentary mucous membrane itself, or of the glands which belong to it. These juices (viz., saliva, gastric juice, bile, pancreatic juice, succus entericus, and the secretion of the large intestine), poured upon and mingling with the food, produce in it such changes that from being largely insoluble, it becomes largely soluble, or otherwise modify it in such a way that the larger part of what is eaten passes into the blood, either directly by means of the capillaries of the alimentary canal, or indirectly by means of the lacteal system, while the smaller part is discharged as excrement.

We have, therefore, to consider—1st, the properties of the various juices, and the changes they bring about in the food eaten; 2d, the nature of the processes by means of which the various epithelium cells of the various glands and various tracts of the canal are able to manufacture so many various juices out of the common source, the blood, and the manner in which the secretory activity of the cells is regulated and subjected to the needs of the economy; 3d, the mechanisms, here as elsewhere, chiefly of a muscular nature, by which the food is passed along the canal, and most efficiently brought in contact with successive juices; and 4th and lastly, the means by which the nutritious digested material is separated from the indigested or excremental material, and absorbed into the blood.

SEC. 1.—THE PROPERTIES OF THE DIGESTIVE JUICES.

[*Physiological Anatomy of the Salivary Glands.*

The saliva is a compound secretion, being the product of four distinct sets of glands. Three of these exist in pairs, and are termed respectively the *parotid*, *submaxillary*, and *sublingual*. The fourth set comprises the simple follicular glands, which are very numerous and found in the buccal mucous membrane.

The larger salivary glands are composed of lobes, which are subdivided into lobules. The lobules are composed of smaller vesicular divisions, which are termed the *alveoli*. The clustered appearance of the alveoli, which compose the lobule, resembles somewhat the form of a bunch of grapes, hence they have been termed *racemose* glands. (Fig. 91). The alveoli are composed of a delicate basement membrane, lined by spheroidal epi-

thelium, which is the proper secretory portion of the organ. These cells contain non-granular protoplasm, with an eccentric nucleus. In some of the alveoli granular protoplasmic cells,

FIG. 91.
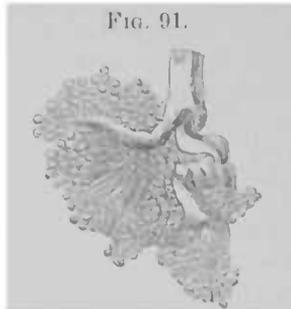
LOBULE OF PAROTID GLAND OF A NEWBORN INFANT, INJECTED WITH MERCURY.   (Magnified.)

with centric nuclei are found.   (Fig. 92.)   Within the alveolar vesicles containing the spheroidal cells there are frequently found halfmoon-shaped cells which are called *demilune* cells.

FIG. 92.
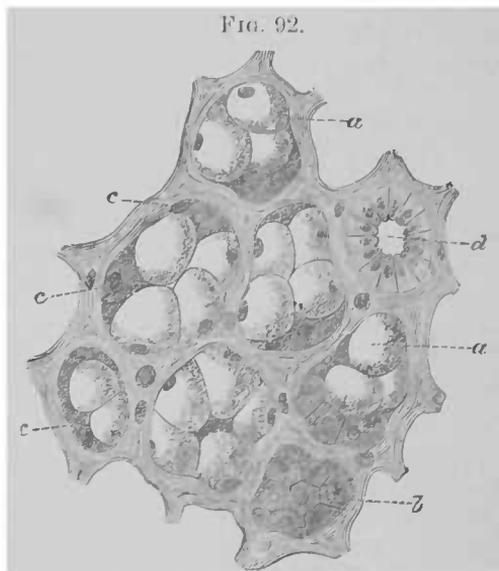
SUBMAXILLARY GLAND OF A DOG.
a, mucous cells ; b, protoplasmic cells ; c, demilune cells ; d, transverse section of an excretory duct, with its peculiar columnar epithelial cells.

These are always found external to the spheroidal cells, and are supposed to be young spheroidal cells in rapid growth, which will replace the old cells when they have matured.   The alveoli of a

lobule empty their secretion by a common duct, which by uniting
with the ducts from other lobules forms the common duct or ducts
of the gland.   These ducts are all lined by columnar epithelium.
The sublingual gland has multiple ducts.   The parotid and sub-
maxillary glands each have a single duct.

Fig. 93.
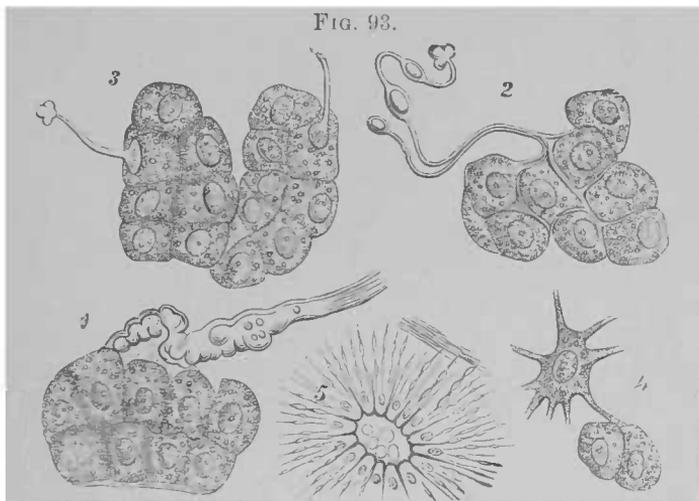
MODES OF TERMINATION OF THE NERVES IN THE SALIVARY GLANDS.
1 and 2, branching of the nerves between the salivary cells ; 3, termination of the nerve in
the nucleus; 4, union of a ganglion cell with a salivary cell ; 5, varicose nerve fibres enter-
ing the cylindrical cell of the excretory ducts.

   The alveoli are surrounded by dense plexuses of capillaries,
in the meshes of which arise the lymphatics.   The substance of
the gland is closely bound together by a fibro-areolar tissue.
The mode by which the nerves terminate in these glands is, as
yet, undetermined.   Pflüger believes that the medulla of the
nerve penetrates the cells and unites with the nucleus (Fig. 93,
1 and 2); that others (4) (probably from the *sympathetic system*)
terminate in multipolar ganglion cells, which send prolongations
into the nuclei of the gland-cell; other nerves (3) terminate in
an expanded extremity, which he considers an intermediate
organ ; others (5) terminate in the columnar cells lining the
ducts.   Whether these supposed terminations of the nerves are
the real ones or not is still a question involved in much doubt.]

Saliva.

   Mixed saliva, as it appears in the mouth, is a thick, glairy,
generally frothy and turbid fluid.   Under the microscope it is
seen to contain, beside the molecular débris of food (and fre-

quently cryptogamic spores), epithelium scales, mucus-corpuscles
aud granules, and the so-called salivary corpuscles. (Fig. 94.)
Its relation in a healthy subject is alkaline, especially when the
secretion is abundant. When the saliva is scanty, or when the
subject suffers from dyspepsia, the reaction of the mouth may be
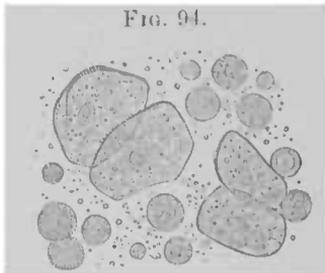
FIG. 94.

SALIVARY CORPUSCLES, EPITHELIAL SCALES AND GRANULES.

acid. Saliva contains but little solid matter—on an average,
probably, about 0.5 per cent.—the specific gravity varying from
1.002 to 1.006. Of these solids, rather less than half—about 0.2
per cent.—are salts (including a small quantity of potassium
sulphocyanide).

[Analysis of Human Saliva:

Water		995.16
Epithelium		1.62
Soluble organic matter		1.34
Sodium, calcium, and magnesium phosphates	0.98	
Potassium chloride ⎱ Sodium chloride ⎰	0.84	
Potassium sulphocyanide	0.06	
	——	1.88]

The organic bodies which can be recognized in it are chiefly
mucin, with small quantities of globulin and serum-albumin.

The chief purpose served by the saliva in digestion is to moisten
the food, and to assist in mastication and deglutition. In some
animals this is its only function.   In other animals and in man
it has a specific solvent action on some of the food-stuffs. Such
minerals as are soluble in slightly alkaline fluids are dissolved
by it. On fats it has no effect save that of producing a very
feeble emulsion. On proteids it has also no action. Its char-
acteristic property is that of converting starch into some form of
sugar.

Action of Saliva on Starch.—If to a quantity of boiled starch,
which is always more or less viscid and somewhat opaque or

turbid, a small quantity of saliva be added, it will be found after a short time that an important change has taken place, inasmuch as the mixture has lost its previous viscidity and become thinner and more transparent. In order to understand this change, the reader must bear in mind the existence of the following bodies (described more fully in the Appendix), all belonging to the class of carbo-hydrates : 1. *Starch*, which forms with water not a true solution but a more or less viscid mixture, and gives a characteristic blue color with iodine. 2. *Dextrin*, differing from starch in forming a clear solution and in giving a red color with iodine. 3. *Dextrose*, also called glucose or grape-sugar, giving no coloration with iodine, but characterized by the power of reducing cupric and other metallic salts; thus, when dextrose is boiled with a fluid often known as Fehling's fluid,[1] which is a solution of cupric sulphate with an excess of sodium hydrate, the cupric salt is reduced and a red or yellow deposit of cuprous oxide is thrown down. This reaction serves with others as a convenient test for dextrose. Neither starch nor dextrin, nor that commonest form of sugar known as cane-sugar, gives this reaction. 4. *Maltose*, very similar to dextrose, and like it capable of reducing cupric salts. Besides having a slightly different formula, it differs from dextrose chiefly in its smaller reducing power—*i. e.*, a given quantity will not convert so much cupric oxide into cuprous oxide as will the same weight of dextrose, and in having a stronger rotatory action on rays of light (see Appendix). Besides the above, we may mention the peculiar body, *achroodextrin*, which differs from dextrin in giving no coloration at all with iodine, and the so-called *soluble starch*, which like dextrin forms a clear solution with water, but unlike dextrin gives a blue color with iodine.

Hence when a quantity of starch is boiled with water we may recognize in the viscid imperfect solution on the one hand the presence of starch, by the blue color which the addition of iodine gives rise to, and on the other hand the absence of sugar (dextrose, maltose), by the fact that when boiled with Fehling's fluid no reduction takes place and no cuprous oxide is precipitated.

If, however, the boiled starch be submitted for a while to the action of saliva, especially at a somewhat high temperature such as 35° or 40° C., it is found that the subsequent addition of iodine

[1 (1) Dissolve 8.66 grams of pure crystallized cupric sulphate in 40 cc. of distilled water.

(2) Dissolve 43 grams of pure crystallized potassic-sodic tartrate in 150 to 185 grams of sodic hydrate, sp. gr. 1.12.

Then add together, and add sufficient distilled water to make one-fourth of a litre.

The solution spoils by keeping, and should frequently be made fresh.]

gives no blue color at all, or very much less color, showing that the starch has disappeared or diminished ; on the other hand the mixture readily gives a precipitate of cuprous oxide when boiled with Fehling's fluid, showing that dextrose or maltose is present. That is to say, the saliva has converted the starch into dextrose or maltose, and there are reasons, which we need not enter into here, for thinking that while some dextrose is formed, the greater part of the sugar which appears is in the form of maltose. As the conversion of the starch by the saliva is going on the addition of iodine frequently gives rise to a red or violet color instead of a pure blue, but when the conversion is complete no coloration at all is observed. The appearance of this red or violet color indicates the presence of dextrin.

The temporary appearance of dextrin shows that the action of the saliva on the starch is somewhat complex ; and this is still further proved by the fact that even when the saliva has completed its work the whole of the starch does not reappear as dextrose or maltose. There are probably several other bodies formed out of the starch besides these, the relative proportions varying according to circumstances. The change, therefore, though perhaps we may speak of it in a general way as one of hydration, cannot be exhibited under a simple formula, and we may rest content for the present with the statement that starch when subjected to the action of saliva is converted chiefly into the sugar known as maltose with a comparatively small quantity of dextrose, dextrin appearing temporarily in the process, and other bodies on which we need not dwell being formed at the same time.

Raw unboiled starch undergoes a similar change, but at a much slower rate. This is due to the fact that in the curiously formed starch grain the true starch, or *granulose*, is invested with coats of *cellulose*. This latter material, which requires previous treatment with sulphuric acid before it will give the blue reaction, on the addition of iodine, is apparently not acted upon by saliva. Hence the saliva can only get at the granulose by traversing the coats of cellulose, and the conversion of the former is thereby much hindered and delayed.

The conversion of starch into sugar, and this we may speak of as the amylolytic action of saliva, will go on at the ordinary temperature of the atmosphere. The lower the temperature the slower the change, and at about $0°$ C. the conversion is indefinitely prolonged. After exposure to this cold for even a considerable time the action recommences when the temperature is again raised. Increase of temperature up to about $35°$ to $40°$, or even a little higher, favors the change, and the greatest activity is said to be witnessed at about $40°$. Much beyond this,

however, increase of temperature becomes injurious, markedly so at 60° or 70°, and saliva which has been boiled for a few minutes not only has no action on starch while at that temperature, but does not regain its powers on cooling. By being boiled the amylolytic activity of saliva is permanently destroyed.

The action of saliva on starch needs for its development a slightly alkaline or at least a neutral reaction of the mixture; it is hindered or arrested by a distinctly acid reaction. Indeed the presence of even a very small quantity of free acid, at all events of hydrochloric acid, at the temperature of the body not only suspends the action but speedily leads to permanent abolition of the activity of the juice. The bearing of this will be seen later on.

The action of saliva is hampered by the presence in a concentrated state of the product of its own action—that is, of sugar. If a small quantity of saliva be added to a thick mass of boiled starch, the action will after a while slacken, and eventually come to almost a stand-still long before all the starch has been converted. On diluting the mixture with water, the action will recommence. If the products of action be removed as soon as they are formed, a small quantity of saliva will, if sufficient time be allowed, convert into sugar a very large—one might almost say an indefinite—quantity of starch. Whether the particular constituent on which the activity of saliva depends is at all consumed in its action has not at present been definitely settled.

On what constituent do the amylolytic virtues of saliva depend?

If saliva, filtered and thus freed from mucus and other formed constituents, be treated with ten or fifteen times its bulk of alcohol, a precipitate takes place containing, besides other substances, all the proteid matters. Upon standing under the alcohol for some time (several days, or, better, weeks), the proteids thus precipitated become coagulated and insoluble in water. Hence, an aqueous extract of the precipitate, made after this interval, contains very little proteid material, and yet is exceedingly active. Moreover, by other more elaborate methods there may be obtained from saliva solutions which appear to be almost entirely free from proteids, and yet are intensely amylolytic. But even these, probably, contain other bodies besides the really active constituent. Whatever the active substance be in itself, it exists in such extremely small quantities that it has never yet been satisfactorily isolated; and, indeed, the only evidence we have of its existence is the manifestation of its peculiar powers.

The salient features of this body, which we may call *ptyalin*, are then—1st, its presence in minute and almost inappreciable quantity; 2d, the close dependence of its activity on temperature; 3d, its permanent and total destruction by a high tempera-

ture and by various chemical reagents; 4th, the want of any clear proof that it itself undergoes any change during the manifestation of its powers—that is to say, the energy necessary for the transformation which it effects *does not come out of itself*; if it is at all used up in its action, the loss is rather that of simple wear and tear of a machine, than that of a substance expended to do work; 5th, the action which it induces is probably of such a kind (splitting up of a molecule with assumption of water) as is effected by the agents called catalytic, and by that particular class of catalytic agents called hydrolytic.

These features mark out the amylolytic active body of saliva as belonging to the class of *ferments*[1]; and we may henceforward speak of the amylolytic ferment of saliva.

Mixed saliva. whose properties we have just discussed, is the result of the mingling in various proportions of saliva from the parotid, submaxillary, and sublingual glands with the secretion from the buccal glands. These constituent juices have their own special characters, and these are not the same in all animals. Moreover, in the same individual the secretion differs in composition and properties according to circumstances; thus, as we shall see in detail hereafter, the saliva from the submaxillary gland secreted under the influence of the chorda tympani nerve is very different from that which is obtained from the same gland by stimulating the sympathetic nerve.

In man pure parotid saliva may easily be obtained by introducing a fine canula into the opening of the Stenonian duct, and submaxillary saliva, or rather a mixture of submaxillary and sublingual saliva, by similar catheterization of the Whartonian duct In animals the duct may be dissected out and a canula introduced.

Parotid saliva in man is clear and limpid, not viscid; the reaction of the first drops secreted is often acid, the succeeding portions, at all events when the flow is at all copious, are alkaline; that is to say, the natural secretion is alkaline, but this may be obscured by acid changes taking place in the fluid which has been retained in the duct. On standing, it becomes turbid from a precipitate of calcic carbonate, due to an escape of carbonic acid. It contains globulin and some other forms of albu-

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[1] Ferments may, for the present at least, be divided into two classes, commonly called *organized* and *unorganized*. Of the former yeast may be taken as a well-known example. The fermentative activity of yeast which leads to the conversion of sugar into alcohol, is dependent on the life of the yeast-cell. Unless the yeast-cell be living and functional, fermentation does not take place; when the yeast-cell dies fermentation ceases, and no substance obtained from yeast, by precipitation with alcohol or otherwise, will give rise to alcoholic fermentation. The salivary ferment belongs to the latter class; it is a substance, not a living organism like yeast.

min, with little or no mucin. Potassium sulphocyanate may also sometimes be detected, but structural elements are absent.

Submaxillary saliva, in man and in most animals, differs from parotid saliva in being more alkaline and, from the presence of mucus, more viscid; it contains, often in abundance, salivary corpuscles, and amorphous masses of proteid material. The so-called chorda saliva in the dog, of which we shall presently speak, is, under ordinary circumstances, thinner and less viscid, contains less mucus, and fewer structural elements, than the so-called sympathetic saliva, which is remarkable for its viscidity, its structural elements, and for its larger total of solids.

Sublingual saliva is more viscid, and contains more mucin and more total solids (in the dog 2.75 per cent.) than even the submaxillary saliva.

The action of saliva varies in intensity in different animals. Thus, in man, the pig, the guinea-pig, and the rat, both parotid and submaxillary and mixed saliva are amylolytic; the submaxillary saliva being in most cases more active than the parotid. In the rabbit, while the submaxillary saliva has scarcely any action, that of the parotid is energetic. The saliva of the cat is much less active than the above, and that of the dog still less; indeed, the parotid saliva of the dog is wholly inert. In the horse, sheep, and ox, the amylolytic powers of either mixed saliva, or of any one of the constituent juices, are extremely feeble.

Where the saliva of any gland is active, an aqueous infusion of the same gland is also active. The importance and bearing of this statement will be seen later on. From the aqueous infusion of the gland, as from saliva itself, the ferment may be approximately isolated. In some cases, at least, some ferment may be extracted from the gland, even when the secretion is itself inactive.

The readiest method, indeed, of preparing a highly amylolytic liquid tolerably free from proteid and other impurities, is to mince finely a gland known to have an active secretion, such, for instance, as that of a rat, dehydrate it by allowing it to stand under absolute alcohol for some days, and then, having poured off most of the alcohol, and removed the remainder by evaporation at a low temperature, to cover the pieces of gland with strong glycerine. A mere drop of such a glycerine extract rapidly converts starch into sugar.

[Physiological Anatomy of the Mucous Membrane of the Stomach.

The mucous membrane of the stomach is soft and velvety, and of a pale, grayish color. It is lined throughout with columnar

epithelium. When the stomach is empty, the muscular walls
contract and cause the mucous membrane to form numerous
longitudinal folds, which are termed rugæ. If the surface be
examined with the aid of a lens, numerous vascular ridges or
processes will be seen, at the bases of which are numbers of
minute openings, which are the orifices of the *gastric follicles* or
glands (Fig. 95). If a vertical section be made of the membrane
(Fig. 96), it will be seen to consist of tubuli closely arranged side

FIG. 95.

FIG. 96.
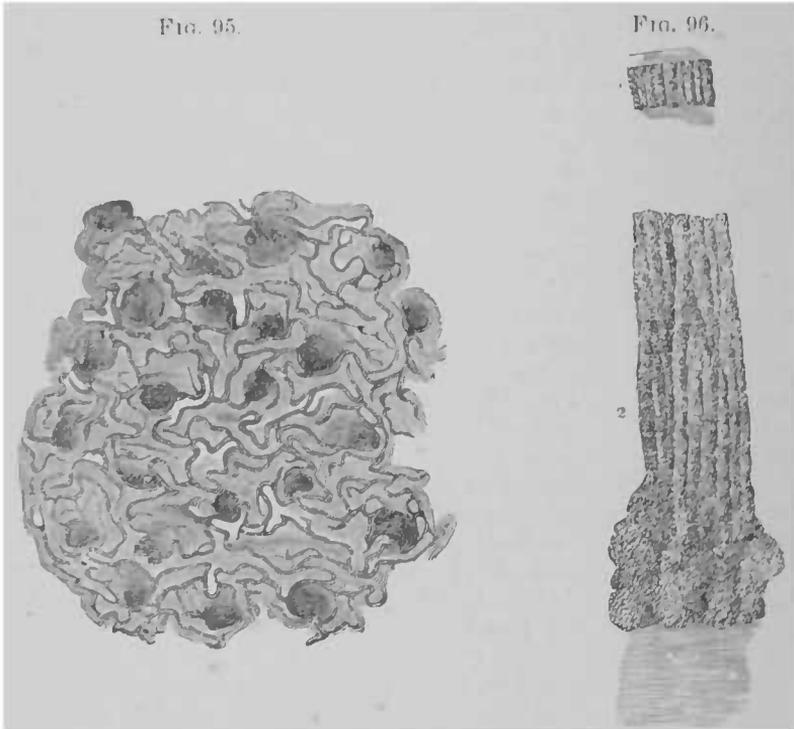
Capillary Network of the Lining Membrane of
the Stomach, with the Orifices of the Gastric Fol-
licles.

Vertical Section of the Mucous
Membrane of the Stomach, near
the Pylorus. Magnified 20 times.

by side, and resting upon a submucous fibrous tissue which con-
tains a layer of unstriated muscular fibres, called the *muscularis
mucosæ*. These muscular fibres are entirely distinct from the
muscles forming the stomachal walls. The tubuli or gastric
glands form the greater portion of the thickness of the mucous
membrane, and, according to Sappey, number about five millions.
They are bound together by an adenoid tissue, and surrounded
by plexuses of capillaries. The nerves are derived from the
pneumogastric and sympathetic.

The gastric glands consist of two principal kinds: the *acid* and *peptic*. The acid glands (Figs. 97 and 98) are distributed over nearly the whole area of the mucous membrane; but near the pylorus are absent. They consist of a trunk with its branching divisions and terminal canals, or cæca. The trunk at the superficial extremity has an open orifice on the surface of the

FIG. 97.　　FIG. 98.　　FIG. 99.
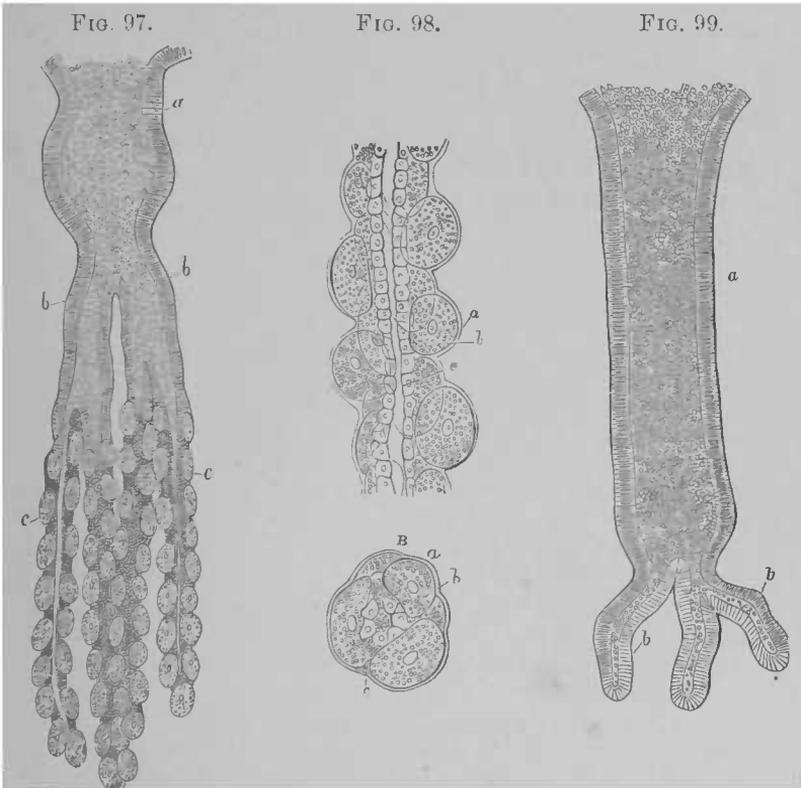
FIG. 97.—Acid Gastric Gland　*a*, common trunk; *b, b,* its chief branches; *c, c,* terminal cæca with spheroidal or "peptic" gland-cells.

FIG. 98.—Portions of one of the Cæca more highly magnified, as seen longitudinally (A), and in transverse section (B). *a,* basement membrane; *b,* large glandular or peptic cell; *c,* small "central" epithelium cells surrounding the cavity.

FIG. 99.—Peptic Gastric Gland, with Columnar Epithelium. *a,* wide trunk; *b, b,* its cæcal appendages.

membrane, at the other extremity it terminates in two or more branching divisions; these divisions are again subdivided into small canals, which are the cæca. The canals are lined by a wall of small epithelium cells. Surrounding this wall is a compact layer of larger spheroidal or ovoidal nucleated granular proto-

25

plasmic cells. These glands are probably the ones which especially secrete the acid of the gastric juice. The trunk and its primary divisions are lined with columnar epithelium.

The peptic glands are found in greatest number about the region of the cardia and pylorus. Their principal structural difference from the acid glands is in the cæcal appendages and in the epithelial lining. (Fig. 99.) The cæcal appendages are very short as compared with those of the acid glands, and the glands are lined throughout with columnar epithelium. The function of the peptic glands, and probably of the columnar epithelium of the acid glands, is to secrete pepsin.

Within the membrane are found a variable number of small *lenticular glands.* These are closed sacs, and are similar in structure to the solitary glands of the small intestines. They are probably accessories of the lymphatic system.]

Gastric Juice.

There is no difficulty in obtaining what may fairly be considered as a normal saliva; but there are many obstacles in the way of determining the normal characters of the secretion of the stomach. When no food is taken, the stomach is at rest and no secretion takes place. When food is taken, the characters of the gastric juice secreted are obscured by the food with which it is mingled. The gastric membrane may, it is true, be artificially stimulated, by touch for instance, and a secretion obtained. This we may speak of as gastric juice, but it may be doubted whether it ought to be considered as normal gastric juice. And indeed, as we shall see, even the juice which is poured into the stomach during a meal, varies as digestion is going on. Hence the characters which we shall give of gastric juice must be considered as having a general value only.

Gastric juice, obtained by artificial stimulation from the healthy stomach of a fasting dog, by means of a gastric fistula, is a thin, almost colorless fluid with a sour taste and odor.

[Analysis of gastric juice (Bidder and Schmidt):

Water . .		973.062
Ferment (pepsin) .	17.127	
Free hydrochloric acid (?)	3 050	
Potassium, sodium, calcium, and ammonium chlorides .	4.724	
Calcium, iron, and magnesium phosphates	2 037	
	————	26.938]

In the operation for gastric fistula, an incision is made through the abdominal walls, along the *linea alba,* the stomach is opened, and the lips of the gastric wound securely sewn to those of the incision in the abdomi-

nal walls. Union soon takes place, so that a permanent opening from the exterior into the inside of the stomach is established. A tube of proper construction, introduced at the time of the operation, becomes firmly secured in place by the contraction of healing. Through the tube the contents of the stomach can be received, and the mucous membrane stimulated at pleasure.

When obtained from a natural fistula in man, its specific gravity has been found to differ little from that of water, varying from 1.001 to 1.010, and the amount of solids present to be correspondingly small. In animals, pure gastric juice seems to be equally poor in solids, the higher estimates which some observers have obtained being probably due to admixture with food, etc.

Of the solid matters present, about half are inorganic salts, chiefly alkaline (sodium) chlorides, with small quantities of phosphates. The organic material consists of pepsin, a body to be described immediately, mixed with other substances of undetermined nature. In a healthy stomach, gastric juice contains a very small quantity only of mucus, unless some submaxillary saliva has been swallowed.

The reaction is distinctly acid, and the acidity is normally due to free hydrochloric acid. This is shown by various proofs, among which we may mention the fact that the amount of hydrochloric acid is more than can be neutralized by the bases, and the excess corresponds to the quantity of free acid present. Lactic and butyric and other acids when present are secondary products, arising either by their respective fermentations from articles of food, or from the decomposition of their alkaline or other salts. In man, the amount of free hydrochloric acid in healthy juice may be stated about 0.2 per cent., but in some animals it is probably higher.

On starch, gastric juice has *per se* no effect whatever; indeed, the acidity of the juice tends to weaken, or may be sufficient to arrest and even destroy, the amylolytic action of any saliva with which it may be mixed.

On dextrose, healthy gastric juice has no effect. And its power of inverting cane-sugar seems to be less than that of hydrochloric acid diluted to the same degree of acidity as itself. In an unhealthy stomach, however, containing much mucus, the gastric juice is very active in converting cane-sugar into dextrose. This power seems to be due to the presence in the mucus of a special ferment, analogous to, but quite distinct from, the ptyalin of saliva. An excessive quantity of cane-sugar introduced into the stomach causes a secretion of mucus, and hence provides for its own conversion.

On fats, gastric juice has, at most, a limited action. When adipose tissue is eaten, the chief change which takes place in the

stomach is that the proteid and gelatiniferous envelopes of the fat cells are dissolved, and the fats set free. Though there is experimental evidence that emulsion of fats to a certain extent does take place in the stomach, the great mass of the fat of a meal is not so changed.

Such minerals as are soluble in free hydrochloric acid are for the most part dissolved; though there is a difference in this and in some other respects between gastric juice and simple free hydrochloric acid diluted with water to the same degree of acidity as the juice, the presence either of the pepsin or other bodies apparently modifying the solvent action of the acid.

The essential property of gastric juice is the power of dissolving proteid matters, and of converting them into a substance called peptone.

Action of Gastric Juice on Proteids.—The results are essentially the same whether natural juice obtained by means of a fistula or artificial juice—*i. e.*, an acid infusion of the mucous membrane of the stomach, be used.

Artificial gastric juice may be prepared in any of the following ways:

1. The mucous membrane of a pig's or dog's stomach is removed from the muscular coat, finely minced, rubbed in a mortar with pounded glass and extracted with water. The aqueous extract filtered and acidulated (it is in itself somewhat acid), until it has free acidity corresponding to 0.2 per cent. of hydrochloric acid, contains but little of the products of digestion such as peptone, but is fairly potent.

2. The mucous membrane similarly prepared and minced, allowed to digest at 35° C. in a large quantity of hydrochloric acid diluted to 0.2 per cent. The greater part of the membrane disappears, shreds only being left, and the somewhat opalescent liquid can be decanted and filtered. The filtrate has powerful digestive (peptic) properties, but contains a considerable amount of the products of digestion (peptone, etc.), arising from the digestion of the mucous membrane itself.[1]

3. From the mucous membrane, similarly prepared and minced, the superfluous moisture is removed with blotting paper, and the pieces are thrown into a comparatively large quantity of concentrated glycerine, and allowed to stand. The membrane may be previously dehydrated by being allowed to stand under alcohol, but this is not necessary. The decanted clear glycerine, in which a comparatively small quantity of the ordinary proteids of the mucous membrane are dissolved, if added to hydrochloric acid of 0.2 per cent. (about 1 c.c. of glycerine to 100 c.c. of the dilute acid are sufficient), makes an artificial juice tolerably free from ordinary proteids and peptone, and of remarkable potency, the presence of the glycerine not interfering with the results.

If a few shreds of fibrin, obtained by whipping blood, after being thoroughly washed and boiled, be thrown into a quantity

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[1] These, however, may be removed by concentration at 40° C., and subsequent dialysis.

of gastric juice, and the mixture be exposed to a temperature of from 35° to 40° C., the fibrin will speedily, in some cases in a few minutes, be dissolved. The shreds first swell up and become transparent, then gradually dissolve, being especially liable to fall to pieces into flakes when the vessel containing them is shaken, and finally disappear, with the exception of some granular débris, the amount of which, though generally small, varies according to circumstances.

If small morsels of coagulated albumin, such as white of egg, be treated in the same way, the same solution is observed. The pieces become transparent at their surfaces; this is especially seen at the edges, which gradually become rounded down, and solution steadily progresses from the outside of the piece inwards.

If any other form of coagulated albumin (*e. g.*, precipitated acid- or alkali-albumin, suspended in water and boiled) be treated in the same way, a similar solution takes place. The readiness with which the solution is effected will depend, *cæteris paribus*, on the smallness of the pieces, or rather on the amount of surface as compared with bulk, which is presented to the action of the juice.

Gastric juice, then, readily dissolves coagulated proteids, which otherwise are insoluble, or soluble only, and that with difficulty, in very strong acids.

Nature of the Change as Shown by the Products of the Action.—If raw white of egg, largely diluted with water and strained, be treated with a sufficient quantity of dilute hydrochloric acid, the opalescence or turbidity which appeared in the white of egg on dilution, and which is due to the precipitation of various forms of globulin, disappears, and a clear mixture results. If a portion of the mixture be at once boiled, a large deposit of coagulated albumin occurs. If, however, the mixture be exposed to 50° or 55° C. for some time, the amount of coagulation which is produced by boiling a specimen becomes less, and finally, produces no coagulation whatever. By neutralization, however, the whole of the albumin (with such restrictions as the presence of certain neutral salts may cause) may be obtained in the form of acid-albumin or syntonin, the filtrate after neutralization containing no proteids at all (or a very small quantity). Thus the whole of the albumin present in the white of egg is converted, by the simple action of dilute hydrochloric acid, into acid-albumin or syntonin.

If the same white of egg be treated with gastric juice instead of simple dilute hydrochloric acid, the events for some time seem the same. Thus after a while boiling causes no coagulation, while neutralization gives a considerable precipitate of a proteid

body, which, being insoluble in water and in dilute sodium chloride solutions, and soluble in dilute alkali and acids, at least closely resembles syntonin. But it is found that only a portion of the proteids originally present in the white of egg can thus be regained by precipitation. A great deal is still retained in the filtrate after neutralization, in the form of what is called *peptone*, and, on the whole, the longer the digestion is carried on, the greater is the proportion borne by the peptone to the precipitate thrown down on neutralization, indeed, in some cases at all events, all the proteids are brought into the condition of peptone.

Peptone is a proteid, having the same approximate elementary composition as other proteids, and giving most of the usual proteid reactions.

It is distinguished from other proteids by the following marked features:

1st. Though soluble in distilled water and in neutral saline solutions, even the most dilute, and therefore not precipitated from its acid or alkaline solutions by neutralization, it is not, like the other similarly soluble proteids, coagulated by heat.

2d. It is diffusible, passing through membranes with considerable ease. The diffusion is not so rapid as that of salts, sugar, and other similar substances, but is very marked as compared with that of other proteids; these pass through membranes with the greatest difficulty. (For other less important reactions see Appendix.)

The neutralization precipitate resembles, in its general characters, acid-albumin or syntonin. Since, however, it probably is distinguishable from the body or bodies produced by the action of simple acid on muscle or white of egg, it is best to reserve for it the name of *parapeptone*. Thus the digestion by gastric juice of white of egg results in the conversion of all the proteids present into peptone and parapeptone, of which the former must be considered as the final and chief product, the latter a bye-product or initial product of variable occurrence and importance. The gastic digestion of fibrin, either raw or boiled, and of all forms of coagulated albumin, gives rise to the same products, peptone and parapeptone. Milk when treated with gastric juice is first of all coagulated or curdled. This is the result partly of the action of the free acid, but chiefly of the special action of a particular constituent of gastric juice, of which we shall speak hereafter. The coagulum consists of a proteid, *casein*, and of fat; and the casein is subsequently dissolved with the same appearance of peptone and parapeptone as in the case of other proteids. In fact, the digestion by gastric juice of all the varieties of proteids consists in the conversion of the proteid

into peptone, with the concomitant appearance of a certain variable amount of parapeptone.

Circumstances Affecting Gastric Digestion.—The solvent action of gastric juice on proteids is modified by a variety of circumstances. The nature of the proteid itself makes a difference, though this is determined probably by physical rather than by chemical characters. Hence in making a series of comparative trials the same proteid should be used, and the form of proteid most convenient for the purpose is fibrin. If it be desired simply to ascertain whether any given specimen has any digestive powers at all, it is best to use boiled fibrin, since raw fibrin is eventually dissolved by dilute hydrochloric acid alone, probably on account of some pepsin present in the blood becoming entangled with the fibrin during coagulation. But in estimating quantitatively the peptic power of two specimens of gastric juice under different conditions, raw fibrin prepared by Grünzter's method is the most convenient.

Portions of well-washed fibrin are stained with carmine and again washed to remove the superfluous coloring matter. A fragment of this colored fibrin thrown into an active juice, on becoming dissolved, gives up its color to the fluid, and if the same stock of colored fibrin be used in a series of experiments, the amount of fibrin dissolved may be fairly estimated by the depth of tint given to the fluid. Fibrin thus colored with carmine may be preserved in ether.

Since, if sufficient time be allowed, even a small quantity of gastric juice will dissolve at least a very large if not an indefinite quantity of fibrin, we are led to take, as a measure of the activity of a specimen of gastric juice, not the quantity of fibrin which it will ultimately dissolve, but the rapidity with which it dissolves a given quantity.

The greater the surface presented to the action of the juice, the more rapid the solution, hence minute division and constant movement favor digestion. And this is probably, in part at least, the reason why a fragment of spongy filamentous fibrin is more readily dissolved than a solid clump of boiled white of egg of the same size. Neutralization of the juice wholly arrests digestion ; fibrin may be submitted for an almost indefinite time to the action of neutralized gastric juice without being digested. If the neutralized juice be properly acidified, it may again become active; in gastric juice, however, which has been made alkaline, and kept at a temperature of 35°, the solvent powers are not only suspended but actually destroyed. Digestion is most rapid with dilute hydrochloric acid of 0.2 per cent. (the acidity of natural gastric juice). If the juice contains much

more or much less free acid than this, its activity is visibly impaired. Other acids, lactic, phosphoric, etc., may be substituted for hydrochloric, but they are not so effectual, and the degree of acidity most useful varies with the different acids. The presence of neutral salts, such as sodium chloride in excess, is injurious. The action of mammalian gastric juice is most rapid at 35° to 40° C.; at the ordinary temperature it is much slower, and at about 0° C. ceases altogether. The juice may be kept, however, at 0° C. for an indefinite period without injury to its powers. The gastric juice of cold-blooded vertebrates is relatively more active at low temperatures than that of warm-blooded mammals or birds.

At temperatures much above 40° or 45° the action of the juice is impaired. By boiling for a few minutes the activity of the most powerful juice is irrevocably destroyed. The presence in a concentrated form of the products of digestion hinders the process. If a large quantity of fibrin be placed in a small quantity of juice, digestion is soon arrested ; on dilution with the normal hydrochloric acid (2 per cent.), or, if the mixture be submitted to dialysis, to remove the peptones formed, and its acidity be kept up to the normal, the action recommences. By removing the products of digestion as fast as they are formed, and by keeping up the acidity to the normal, a given amount of gastric juice may be made to digest a very large quantity of proteid material. Whether the quantity is really unlimited is disputed ; but in any case the energies of the juice are not rapidly exhausted by the act of digestion.

Nature of the Action.—All these facts go to show that the digestive action of gastric juice on proteids, like that of saliva on starch, is a ferment-action ; in other words, that the solvent action of gastric juice is essentially due to the presence in it of a ferment-body. To this ferment-body, which as yet has been only approximately isolated, the name of *pepsin* has been given. It is present not only in gastric juice, but also in the glands of the gastric mucous membrane, especially in certain parts, and under certain conditions which we shall study presently. The glycerine extract of gastric mucous membrane, especially of that which has been dehydrated, contains a minimal quantity of proteid matter, and yet is intensely active. Other methods, such as the elaborate one of Brücke, give us a material which, though containing nitrogen, exhibits none of the ordinary proteid reactions, and yet in concert with normal dilute hydrochloric acid is peptic in the highest degree. We seem, therefore, justified in asserting that pepsin is not a proteid, but it would be hazardous to make any dogmatic statement concerning a substance, obtained in small

quantity only, probably mixed with other bodies, and the chemical characters of which we know as yet very little. At present the manifestation of peptic powers is our only safe test of the presence of pepsin.

In one important respect pepsin, the ferment of gastric juice, differs from ptyalin, the ferment of saliva. Saliva is active in a perfectly neutral medium, and there seems to be no special connection between the ferment and any alkali or acid. In gastric juice, however, there is a strong tie between the acid and the ferment, so strong that some writers speak of pepsin and hydrochloric acid as forming together a compound, pepto-hydrochloric acid.

In the absence of exact knowledge of the constitution of proteids, we cannot state distinctly what is the precise nature of the change into peptone. Judging from the analogy with the action of saliva on starch, we may fairly suppose that the process is at bottom one of hydration; but we have no exact proof of this, and it is at least quite as probable that peptone arises by a simple splitting up of larger proteid molecules. Peptone closely resembling, if not identical with, that obtained by gastric digestion, may be obtained by the action of strong acids, by the prolonged action of dilute acids, especially at a high temperature, or simply by digestion with super-heated water in a Papin's digester. The *role* of pepsin, therefore, is only to facilitate a change which may be effected without it.

All proteids, so far as we know, are converted by pepsin into peptone. Of its action on other nitrogenous substances not truly proteid in nature, we need only say that mucin, nuclein, and the chemical basis of horny tissues, are wholly unaffected by it, but that the gelatiniferous tissues are dissolved and changed into a substance so far analogous with peptone, that the characteristic property of gelatinization is entirely lost. Chondrin and the elastic tissues are also dissolved.

Action of Gastric Juice on Milk.—It has long been known that an infusion of calves' stomach, called *rennet*, has a remarkable effect in rapidly curdling milk, and this property is made use of in the manufacture of cheese. Gastric juice has a similar effect; milk when subjected to the action of gastric juice is first curdled and then digested. If a few drops of gastric juice be added to a little milk in a test-tube, and the mixture exposed to a temperature of $40°$, the milk will curdle into a complete clot in a very short time. If the action be continued, the curd or clot will be ultimately dissolved and digested. Milk contains, besides albumin, fats, milk, sugar, and various salines, a peculiar proteid

called *casein*,[1] a body allied to the so-called alkali-albumin. In natural milk casein is present in solution, and "curdling" consists essentially in the casein becoming insoluble and being precipitated in a solid form, a great deal of the fat being generally carried down with it. Now casein is readily precipitated from milk upon the addition of a small quantity of acid, and it might be supposed that the curdling effect of gastric juice was due to its acid reaction. But this is not the case, for neutralized gastric juice, or neutral rennet, is equally efficacious. Moreover, the substance thrown down by an acid is not quite exactly the same as that which appears in curdling.

The effect is closely dependent on temperature, being like the peptic action of gastric juice favored by a rise of temperature up to about 40° Moreover, the curdling action is destroyed by previous boiling of the juice or rennet. These facts suggest that a ferment is at the bottom of the matter; and, indeed, all the features of the action support this view. The ferment, however, is not pepsin, but some other body; and the two may be separated by cautiously adding magnesium carbonate to gastric juice or to an infusion of calves' stomach. The clear fluid, left above the precipitate thus formed, readily curdles milk, but even when acidified has no peptic action on proteids, showing that the precipitate caused by the addition of the magnesium carbonate has carried down all the pepsin, but left behind at least a good deal of the rennet-ferment.

Rennet-ferment seems to be present in variable quantity in the gastric juice of most animals, and may also be obtained from the gastric mucous membrane of many though not all animals. It is especially abundant in the stomach of the calf.

It has been suggested that the ferment might act by inducing a fermentation in the sugar of milk, giving rise to lactic acid, which precipitates the casein by virtue of its being an acid. But this view is disproved not only by the difference in the product mentioned above, but also by the fact that casein precipitated from milk by neutral salts, washed free from milk sugar and redissolved, forms a fluid which is readily curdled by rennet like natural milk. It seems probable that the ferment really acts on the casein, converting it in some way from a soluble to an insoluble form.

[*Physiological Anatomy of the Liver.*

The liver is the largest gland in the body. It is very vascular, receiving not only the arterial blood from the hepatic artery for its own nutrition, but also the blood of the portal vein, which

[1] See Appendix.

centains the great portion of the products of digestion. The blood is conveyed from the liver by the hepatic veins which empty into the inferior vena cava. The bile, which is the principal secretion of the organ, is conducted from the liver through two ducts which unite to form the hepatic duct.

The liver is covered with a delicate areolar tissue which sends processes or trabeculæ into its substance between the lobules. A prolongation of this areolar tissue accompanies the vessels as a sheath into the organ, and is called Glisson's capsule. The liver is partially covered with peritoneum, which by its reduplications forms the hepatic ligaments which suspend the viscus in the abdominal cavity.

The substance of the liver is composed of lobules having a polygonal outline. These lobules are made up of irregular poly-hedral rounded cells, which are granular and nucleated, some-times containing two or more nuclei (Fig. 100). The cell contents

FIG. 100.
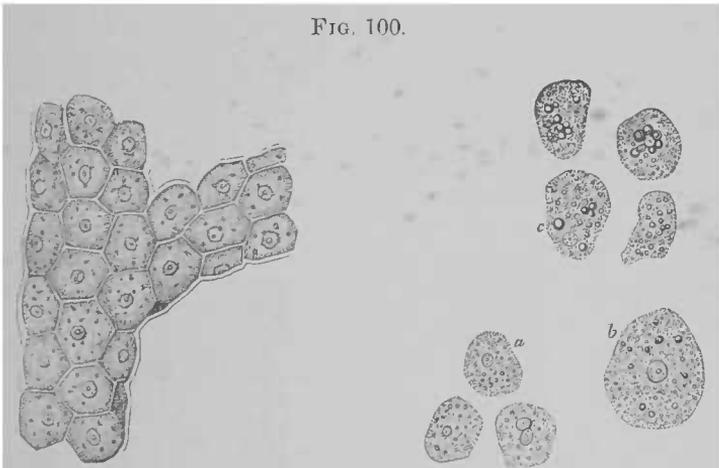
A, Portion of a Hepatic Column, from Human Liver, showing its component secreting cells. B Secreting cells detached. a, in their normal state ; b, a cell more highly magnified, showing the nucleus and distinct oil-particles ; c, in various stages of fatty degeneration.

are viscid, yellowish, and contain oil-globules. These cells com-prise the secretory portion of the liver.

The lobules are extremely vascular, and the distribution of the bloodvessels to them is very complex. They are observed to have a large vessel in the centre, which, through its capillaries, communicates with the capillaries of an intricate plexus of ves-sels coming from the circumference. The portal vein, hepatic artery, and hepatic duct run in company in their distribution. The hepatic vein and its ramifications run independently of the

FIG. 101.
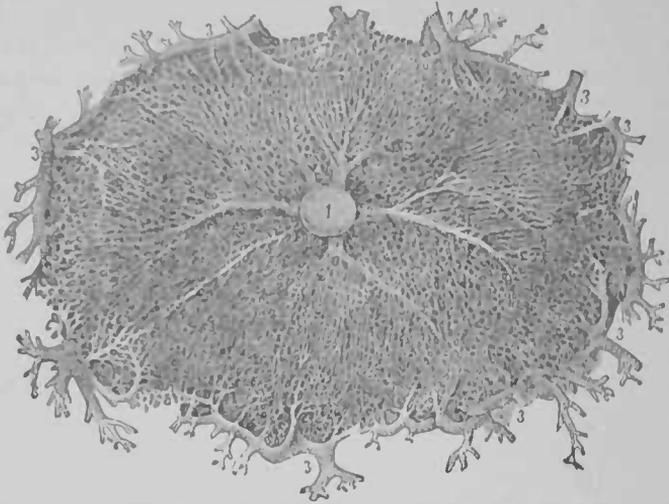
Cross-section of a Lobule of the Human Liver, in which the capillary network between the Portal and Hepatic Veins has been fully injected (from Sappey) $\frac{6.9}{1}$. 1, section of the *intra*-lobular vein; 2, its smaller branches collecting blood from the capillary network; 3, *inter*-lobular branches of the vena portæ with their smaller ramifications passing inwards towards the capillary network in the substance of the lobule. After KIRKE.

FIG. 102.
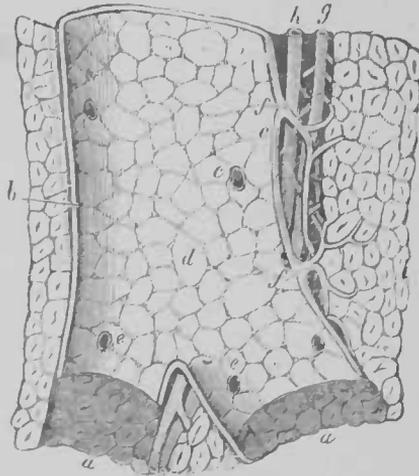
Longitudinal Section of a small Portal Vein and Canal. *a*, portions of the canal from which the vein has been removed; *b*, the side of the portal vein in contact with the canal; *c*, the side of the vein which is separated from the canal by the hepatic artery and duct, with areolar tissue (Glisson's Capsule); *d*, internal surface of the portal vein, through which are seen the outlines of the lobules and the openings (*e*) of the interlobular veins; *f*, vaginal veins of Kiernan; *g*, hepatic artery; *h*, hepatic duct.

other vessels. In Fig. 102 is shown a longitudinal section of a portal canal, which contains a portal vein, hepatic artery, and hepatic duct.

The portal vein sends its branches between the lobules, which are called the *inter*lobular veins. The veins form a dense plexus of capillaries in the substance of the lobule, and are seen to communicate with other capillaries which converge and form one large vein in the centre, termed an *intra*lobular vein. Between

FIG. 103.
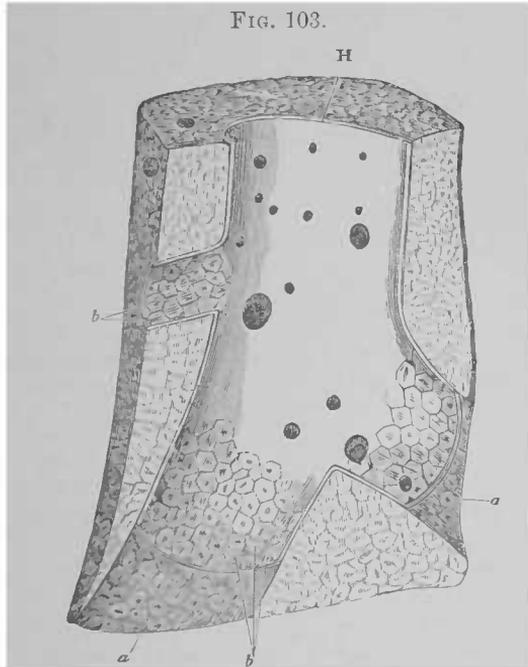
Section of a Portion of Liver passing longitudinally through a large Hepatic Vein, from the Pig (after Kiernan) $\frac{5}{1}$. *H*, hepatic venous trunk, against which the sides of the lobules are applied; *b*, sublobular hepatic veins, on which the bases of the lobules rest, and through the coats of which they are seen as polygonal figures; *a, a*, walls of the hepatic venous canal, formed by the polygonal bases of the lobules.

the meshes of this intralobular capillary plexus are found the hepatic cells (Fig. 101). The *intra*lobular vein empties into a larger vein at the base of the lobule, which is called a *sub*lobular vein. These sublobular veins unite to form the hepatic veins (Fig. 103). The walls of the hepatic veins are very thin, and, unlike the portal veins, have no areolar investment. The distribution of the hepatic artery and of the larger branches of the hepatic duct, is similar to that of the portal vein.

The larger branches of the hepatic ducts are lined with cylin-

drical epithelium ; the smaller branches are lined with spheroidal
epithelium.   The relation which the terminal filaments of the
duct bear to the cells has not as yet been definitely determined.
The smaller biliary ducts form a capillary plexus, within the
meshes of which are the hepatic cells (Fig. 104).   The ultimate
biliary ducts are supposed to be mere intercellular passages,
having no cell-wall, and measuring about 2.5 mm. in diameter
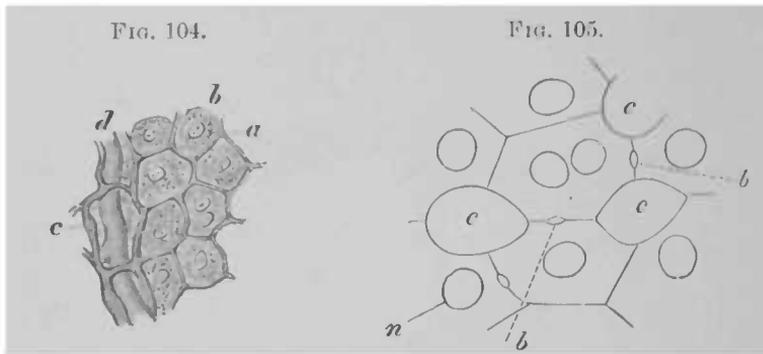
Fig. 104. —Injected Biliary Capillaries of the Liver of the Rabbit   Part of a lobule show-
ing the arrangement of the biliary ducts in relation to the hepatic cells.   a, capillaries of the
biliary ducts ; b, hepatic cells ; c, biliary ducts ; d, capillary bloodvessels.

Fig. 105.—Section of Rabbit's Liver Injected   c, blood capillaries ; b, bile passages ; n,
nucleus of hepatic cell.

(Fig. 105).   The liver is supplied with nerves from the sym-
pathetic, the pneumogastric (the left, especially), and the right
phrenic.
    On the inferior surface of the liver is an accessory organ, called
the gall-bladder, which, during the intervals of digestion, serves
as a receptacle for the bile.   The mechanism by which the bile
is carried into the gall-bladder is somewhat obscure.   The bile is
conveyed from the liver through the hepatic duct, which, uniting
with the cystic duct of the gall-bladder, forms the *ductus com-
munis choledochus*, which conveys the bile during digestion to the
duodenum.   The mechanism by which the bile gets into the gall-
bladder is probably due to both a tonic condition of sphincteric
muscular fibres surrounding the outlet of the *ductus communis
choledochus*, and a reversed peristalsis of the muscular fibres in
the wall of the duct.
    The function of the liver is both secretive and excretive.   Its
principal secretions are the bile and a peculiar amyloid substance
called glycogen.   Its principal excretion is an alcohol termed
cholesterin.   It is supposed by Prof. A. Flint, Jr., that this sub-
stance is converted in the intestine into a new substance which he
calls stercorin.]

Bile.

The quantity of bile varies much, not only in different animals, but in the same animal at different times. It is, moreover, affected by the length of the sojourn in the gall-bladder; bile taken direct from the hepatic duct, especially when secreted rapidly, contains little or no mucus; that taken from the gall-bladder, as of slaughtered oxen or sheep, is loaded with mucus. The color of the bile of carnivorous and omnivorous animals, and of man, is a bright golden-red; of graminivorous animals, a golden-green, or a bright green, or a dirty green, according to circumstances, being much modified by retention in the gall-bladder. The reaction is alkaline. The following may be taken as the average composition of human bile (Frerichs):

	In 1000 parts.
Water	859.2
Solids:	
Bile salts	91.4
Fats, etc.	9.2
Cholesterin	2.6
Mucus and pigment	29.8
Inorganic salts	7.8
	—— 140.8

The entire absence of proteids is a marked feature of bile. With regard to the inorganic salts, the points of interest are the presence of a large quantity of sodium chloride (0.2 to 0.27 per cent.), the presence of phosphates, of iron (about 0.006 per cent.), manganese, and, occasionally, at all events, of copper. The ash contains soda in a very large amount, and also sulphates, both coming from the bile-salts. The peculiar body cholesterin is conspicuous by its quantity and constancy, but its physiological functions are obscure. The constituents which deserve chief attention are the pigments and the bile-salts.

Pigments of Bile.— The natural golden-red color of normal human or carnivorous bile, is due to the presence of *Bilirubin*. This, which is also the chief pigmentary constituent of gall-stones, and occurs largely in the urine of jaundice, may be obtained in the form either of an orange-colored powder, or of well-formed rhombic tablets and prisms. Insoluble in water, and but little soluble in ether and alcohol, it is readily soluble in chloroform, and in alkaline fluids. Its composition is $C_{16}H_{18}N_2O_3$. Treated with oxidizing agents, such as nitric acid yellow with nitrous acid, it displays a succession of colors in the order of the spectrum. The yellowish golden-red becomes green, this a greenish-blue,

then blue, next violet, afterwards a dirty red, and finally a pale yellow. This characteristic reaction of bilirubin is the basis of the so-called Gmelin's test for bile-pigments. Each of these stages represents a distinct pigmentary substance. An alkaline solution of bilirubin, exposed in a shallow vessel to the action of the air, turns green, becoming converted into *Biliverdin* ($C_{16}H_{20}N_2O_5$ or $C_{16}H_{18}N_2O_4$, Maly), the green pigment of herbivorous bile. Biliverdin is also found at times in the urine of jaundice, and is probably the body which gives to bile which has been exposed to the action of gastric juice, as in biliary vomits, its characteristic green hue. It is the first stage of the oxidation of bilirubin in Gmelin's test. Treated with oxidizing agents biliverdin runs through the same series of colors of bilirubin, with the exception of the initial golden-red.

The Bile Salts.—These consist, in man and many animals, of *sodium glycocholate* and *taurocholate;* the proportion of the two varying in different animals. In man, both the total quantity of bile salts and the proportion of the one bile salt to the other seem to vary a good deal, but the glycocholate is said to be always the more abundant. In ox-gall, sodium glycocholate is abundant, and taurocholate scanty. The bile salts of the dog, cat, bear, and other carnivora, consist exclusively of the latter.

Insoluble in ether, but soluble in alcohol and in water, the aqueous solutions having a decided alkaline reaction, both salts may be obtained by crystallization in fine acicular needles. They are exceedingly deliquescent. The solutions of both acids have a dextro-rotatory action on polarized light.

Preparation.—Bile, mixed with animal charcoal, is evaporated to dryness and extracted with alcohol. If not colorless, the alcoholic filtrate must be further decolorized with animal charcoal, and the alcohol distilled off. The dry residue is treated with absolute alcohol, and to the alcoholic filtrate anhydrous ether is added as long as any precipitate is formed. On standing, the cloudy precipitate becomes transformed into a crystalline mass at the bottom of the vessel. If the alcohol be not absolute, the crystals are very apt to be changed into a thick syrupy fluid. This mass of crystals has been often spoken of as *bilin.* Both salts are thus precipitated, so that in such a bile as that of the ox or man, bilin consists both of sodium glycocholate and sodium taurocholate. The two may be separated by precipitation from their aqueous solutions with sugar of lead, which throws down the former much more readily than the latter. The acids may be separated from their respective salts by dilute sulphuric acid, or by the action of lead acetate and sulphydric acid.

On boiling with dilute acids (sulphuric, hydrochloric), or caustic potash, or baryta water, glycocholic acid is split up into

cholalic (cholic) acid and glycin. Taurocholic acid may similarly be split up into cholalic acid and taurin. Thus

Glycoholic acid.   Cholalic acid.   Glycin.

$$C_{26}H_{43}NO_6 + H_2O = C_{24}H_{40}O_5 + C_2H_5NO_2$$

Taurocholic acid.   Cholalic acid.   Taurin.

$$C_{26}H_{45}NSO_7 + H_2O = C_{24}H_{40}O_5 + C_2H_7NSO_3.$$
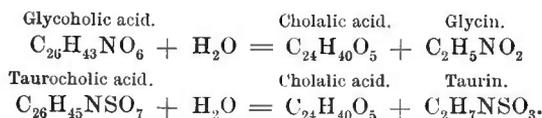
Both acids contain the same non-nitrogenous acid, cholalic acid; but this acid is in the first case associated or conjugated with the important nitrogenous body glycin, or amido-acetic acid—that is, a compound formed out of ammonia, and one of the series of fatty acids, viz., acetic ; and in the second case with taurin, or amido-isethionic acid—that is, a compound formed out of ammonia, a member of the ethyl group, and sulphuric acid. The decomposition of the bile acids into cholalic acid and taurin or glycin respectively takes place naturally in the intestine, the glycin and taurin being absorbed, so that from the two acids, after they have served their purpose in digestion, the two ammonia compounds are returned into the blood. Either of the two acids, or cholalic acid alone, when treated with sulphuric acid and cane-sugar, gives a magnificent purple color (Pettenkofer's test) with a characteristic spectrum. A similar color may often be produced by the action of the same bodies on albumin, amyl alcohol, and some other organic bodies.

Action of Bile on Food. In some animals at least bile contains a ferment capable of converting starch into sugar ; but its action in this respect is wholly subordinate.

On proteids bile has no direct digestive action whatever, but since it is at least often alkaline it tends to neutralize the acid contents of the stomach as they pass into the duodenum and so prepares the way for the action of the pancreatic juice. To peptic action it is distinctly antagonistic ; the presence of a sufficient quantity of bile renders gastric juice inert towards proteids. Moreover when bile, or a solution of bile-salts, is added to a fluid containing the products of gastric digestion, a precipitate takes place, consisting of parapeptone, peptone, and bile salts. The precipitate, however, is redissolved in an excess of bile or solution of bile salts. Concerning the purpose of this precipitation, which actually takes place in the duodenum, we shall speak hereafter.

With regard to the action of bile on fats, the following statements may be made :

Bile has a slight solvent action on fats, as seen in its use by painters. It has by itself a slight but only slight emulsifying

power : a mixture of oil aud bile separates after shaking rather less rapidly than a mixture of oil and water. With free fatty acids, bile forms soaps. It is moreover a solvent of solid soaps, and it would appear that the emulsion of fats is under certain circumstances at all events facilitated by the presence of soaps in solution. Hence bile is probably of much greater use as an emulsion agent when mixed with pancreatic juice than when acting by itself alone. To this point we shall return. Lastly, the passage f fats through membranes is assisted by wetting the membranes th bile, or with a solution of bile salts. Oil passes with conside .ble ease through a filter-paper kept wet with a solution of bile salts, whereas it passes with extreme difficulty through one kept constantly wet with distilled water.

Lastly bile possesses so-called antiseptic qualities. Out of the body its presence hinders various putrefactive processes ; and when it is prevented from flowing into the alimentary canal, the contents of the intestine undergo changes different from those which take place under normal conditions, and leading to the appearance of various products, especially of ill-smelling gases.

These various actions of bile seem to be dependent on the bile salts and not on the pigmentary or other constituents.

The Physiological Anatomy of the Pancreas.

The physiological anatomy of the pancreas is essentially that of the salivary glands. The lobes are composed of lobules, which are made up of alveoli. It possesses a single duct, which conveys the pancreatic fluid into the intestine either through an individual orifice, or by one common to it and the ductus communis choledochus.]

Pancreatic Juice.

Natural healthy pancreatic juice obtained by means of a temporary pancreatic fistula differs from the preceding fluids in the comparatively large quantity of proteids which it contains. Its composition varies according to the rate of secretion, for, with the more rapid flow, the increase of total solids does not keep pace with that of the water, though the ash remains remarkably constant.

By an incision through the linea alba the pancreatic duct (or ducts) can easily be found either in the rabbit or in the dog, and a canula secured in it. There is no difficulty about a temporary fistula, but Bernard found that with permanent fistulæ the secretion altered in nature, and lost many of its characteristic properties. Others, however, have succeeded in obtaining permanent fistulæ without any impairment of the secretion.

Healthy pancreatic juice is a clear viscid fluid, frothing when shaken. It has a very decided alkaline reaction, and contains few or no structural constituents.

The average amount of solids in the pancreatic juice of the dog when obtained from a temporary fistula is about 8 to 10 per cent.; but in the thoroughly active secretion from a permanent fistula it is not more than about 2 to 5 per cent., 0.8 being inorganic matter, and this is probably the normal amount. The important constituents are albumin, a peculiar form of casein or alkali-albumin (precipitable by saturation with magnesium sulphate), peptone, leucin and tyrosin, a small amount of fats and soaps, and a comparatively large quantity of sodium carbonate, to which the alkaline reaction of the juice is due, and which seems to be peculiarly associated with the albumin.

Since, as we shall presently see, pancreatic juice contains a ferment acting energetically on proteid matters in an alkaline medium, it rapidly digests itself; and, when kept, speedily changes in character. Perfectly fresh juice appears to contain a substance not unlike myosin, giving rise to a sort of coagulation, but the coagulum is soon dissolved. Perfectly fresh juice is also said to be almost entirely free from leucin, tyrosin, and peptone, which also seem to be the products of self-digestion.

Action on Food-stuffs.—On *starch*, raw or boiled, pancreatic juice acts with great energy, rapidly converting it into sugar (chiefly maltose). All that has been said in this respect concerning saliva might be repeated in the case of pancreatic juice, except that the activity of the latter is far greater than that of the former. Pancreatic juice and the aqueous infusion of the gland are always capable of converting starch into sugar, whether the animal from which they were taken be starving or well fed. From the juice, or, by the glycerine method, from the gland itself, an amylolytic ferment may be approximately isolated.

On *proteids*, pancreatic juice also exercises a solvent action, so far similar to that of gastric juice that by it proteids are converted into peptone. If a few shreds of fibrin are thrown into a small quantity of pancreatic juice, they speedily disappear, especially at a temperature of 35° C., and the mixture is found to contain peptone. The activity of the juice in thus converting proteids into peptone, is favored by increase of temperature up to 40° or thereabouts, and hindered by low temperatures; it is permanently destroyed by boiling. The digestive powers of the juice, in fact, depend, like those of gastric juice, on the presence of a ferment; to this ferment the name *trypsin* has been given. A glycerine extract of pancreas, prepared in the same method as that of the

gastric mucous membrane, is (under appropriate conditions) active on proteids, like the native juice.

The appearance of fibrin undergoing pancreatic digestion is, however, different from that undergoing peptic digestion. In the former case the fibrin does not swell up, but remains as opaque as before, and appears to suffer corrosion rather than solution. But there is a still more important distinction between pancreatic and peptic digestion of proteids. Peptic digestion is essentially an acid digestion; we have seen that the action only takes place in the presence of an acid, and is arrested by neutralization. Pancreatic digestion, on the other hand, may be regarded as an alkaline digestion; the action is most energetic when some alkali is present; and the activity of an alkaline juice is hindered or delayed by neutralization, and arrested by acidification, at least with mineral acids. The glycerine extract of pancreas is, under all circumstances, as inert in the presence of free mineral acid as that of the stomach in the presence of alkalies. If the digestive mixture be supplied with sodium carbonate to the extent of 1 per cent., digestion proceeds rapidly, just as does a peptic mixture when acidulated with hydrochloric acid to the extent of 0.2 per cent. Sodium carbonate of 1 per cent. seems, in fact, to play in pancreatic digestion a part altogether comparable to that of hydrochloric acid of 0.2 per cent. in gastric digestion. And, just as pepsin is rapidly destroyed by being heated to about 40° with a 1 per cent. solution of sodium carbonate, so trypsin is rapidly destroyed by being similarly heated with dilute hydrochloric acid of 0.2 per cent. Alkaline bile, which arrests peptic digestion, seems, if anything, favorable to pancreatic digestion.

Corresponding to this difference in the helpmate of the ferment, there is in the two cases a difference in the nature of the products. In both cases peptone is produced, and such differences as can be detected between pancreatic and gastric peptones are comparatively slight; but in pancreatic digestion the bye-product is not, as in gastric digestion, a kind of acid-albumin, but a body having more analogy with alkali-albumin. Before solution has actually taken place, the fibrin becomes altered in character. It is soluble not only in dilute acids and alkalies, but also in a 10 per cent. solution of sodium chloride, and the solutions obtained by the latter reagent are coagulable on boiling and on the addition of strong nitric acid. The first action of the pancreatic juice, therefore, seems to be to convert the proteid under digestion into a body intermediate between alkali-albumin and ordinary native albumin.

But though the general characters of pancreatic and gastric digestion are on the surface similar, it is more than probable that profound differences do exist between them. This is shown by

the appearance, in the pancreatic digestion of proteids, of two remarkable nitrogenous crystalline bodies, *leucin* (Fig. 106) and *tyrosin* (Fig. 107). When fibrin (or other proteid) is submitted to the action of pancreatic juice, the amount of peptone which can be recovered from the mixture falls far short of the original

[FIG. 106.

FIG. 107.

Leucin.

Tyrosin.]
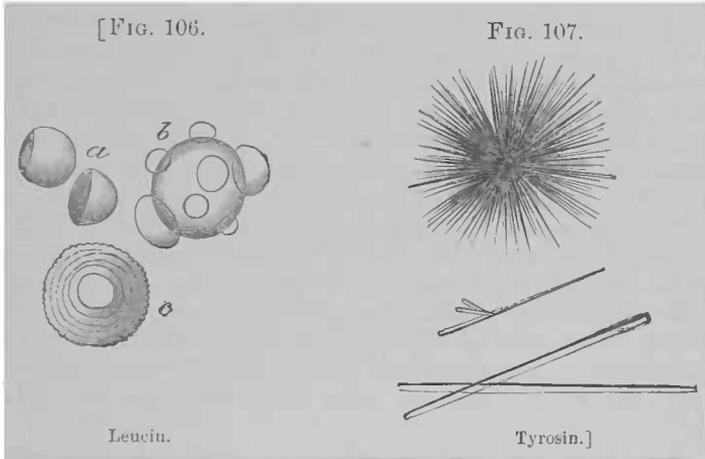
amount of proteids, much more so than in the case of gastric juice; and the longer the digestive action, the greater is this apparent loss. If a pancreatic digestion mixture be freed from the alkali-albumin by neutralization, and after concentration by evaporation be treated with excess of alcohol, most of the peptone will be precipitated. The alcoholic filtrate when concentrated, gives, on cooling, crystals of tyrosin, and the mother liquor from these crystals will afford abundance of crystals of leucin. Thus by the action of the pancreatic juice a considerable amount of the proteid, which is being digested, is so broken up as to give rise to products which are no longer proteid in nature. From this breaking up of the proteid there arise leucin, tyrosin, and probably several other bodies, such as fatty acids and volatile substances.

As is well known, leucin and tyrosin are the bodies which make their appearance when proteids or gelatin are acted on by dulute acids, alkalies, or various oxdizing agents. Now leucin is amido-caproic acid, and thus belongs distinctly to the fatty bodies; while tyrosin is a member of the aromatic group, being closely related to benzoic acid. So that in pancreatic digestion we have the large complex proteid molecule split up into its constituent fatty acid and aromatic molecules, and into its other less distinctly known components. In gastric digestion such a profound destruction of proteid material occurs to a much less

extent or not at all; neither leucin nor tyrosin can at present be considered as natural products of the action of pepsin.

Among the supplementary products of pancreatic digestion may be enumerated a body which gives a violet color with chlorine water (this reaction is often seen in the juice itself), and *indol*, to which apparently the strong and peculiarly fecal odor which makes its appearance during pancreatic digestion is due. Indol, however, unlike leucin and tyrosin, is not a product of pure pancreatic digestion, but of an accompanying decomposition due to the action of organized ferments. A pancreatic digestive mixture soon becomes swarming with bacteria, in spite of careful precautions, when natural juice or an infusion of the gland is used. When isolated ferment is used, and atmospheric germs are excluded, or when pancreatic digestion is carried on in the presence of salicylic acid, which prevents the development of bacteria and like organisms, but permits the action of the trypsin, no odor is perceived, and no indol is produced.

After long-continued digestion, especially when accompanied by putrefactive decomposition, the amount of proteids which are carried beyond the peptone stage and broken up, may be very great.

On the gelatiniferous elements of the tissues in their normal condition pancreatic juice appears to have no solvent action. In this respect it affords a striking contrast to gastric juice. But when they have been previously treated with acid or boiled so as to become converted into actual gelatine, trypsin is able to dissolve them, apparently changing them much in the same way as does pepsin. Trypsin unlike pepsin, will dissolve mucin. Like pepsin, it is inert towards nuclein, horny tissues, and the so-called amyloid matter.

On *Fats* pancreatic juice has a twofold action: it emulsifies them, and it splits up neutral fats into their respective acids and glycerine. If hog's lard be gently heated till it melts and be then mixed with pancreatic juice before it solidifies, on cooling a creamy emulsion, lasting for almost an indefinite time, is formed. So also when olive oil is shaken up with pancreatic juice, the separation of the two fluids takes place very slowly, and a drop of the mixture under the microscope shows that the division of the fat is very minute. An alkaline aqueous infusion of the gland has similar emulsifying powers. If perfectly neutral fat be treated with pancreatic juice, especially at the body-temperature, the emulsion speedily takes on an acid reaction, and by appropriate means not only the corresponding fatty acids but glycerine may be obtained from the mixture. When an alkali is present, the fatty acids thus set free form their corresponding soaps. Pancreatic juice contains fats, and is consequently apt

after collection to have its alkalinity reduced; and an aqueous infusion of a pancreatic gland (which always contains a considerable amount of fat) very speedily becomes acid.

Thus pancreatic juice is remarkable for the power it possesses of acting on all the food-stuffs, on starch, fats, and proteids.

The action on starch and on proteids, and the splitting up of fatty acids appear to be due to the presence of three distinct ferments, and methods have been suggested for isolating them. The emulsifying power, on the other hand, is connected with the general composition of the juice (or of the aqueous infusion of the gland), being probably in large measure dependent on the alkali-albumin present. The proteolytic ferment trypsin as ordinarily prepared seems to be proteid in nature, and capable of giving rise, by digestion, to peptones; but it may be doubted, as in the case of pepsin, etc., whether the pure ferment has yet been isolated. There are no means of distinguishing the amylolytic ferment of the pancreas from ptyalin. The term *pancreatin* has been variously applied to many different preparations from the gland, and its use had perhaps better be avoided.

The action of pancreatic juice, or of the infusion or extract of the gland, on starch, is seen under all circumstances, whether the animal be fasting or not. The same may probably be said of the action on fats. On proteids the natural juice, when secreted in a normal state, is always active. The glycerine extract or aqueous infusion of the gland, on the contrary, differs at different times; prepared from an animal some four to ten hours after food has been taken, it is very powerful; prepared from a fasting animal, it is said to exhibit scarcely any action at all. To this point, however, we shall return immediately.

[*Physiological Anatomy of the Mucous Membrane of the Small Intestine.*

The mucous membrane lining the small intestine is thrown into numerous transverse folds, which are called *valvulæ conniventes*. These folds are best marked near the pyloric end, and are relatively few in the ileum. They afford a greater surface for the contact of food with the absorbing structures, while at the same time its passage along the intestinal walls is retarded. The surface of the membrane has a soft, velvety appearance, and if seen by the aid of a lens, it appears thickly studded with innumerable finger-like projections, which are called *villi*. At the bases of these villi are numerous minute apertures, which are the openings of the secreting glands. These glands are of three kinds: *Brunner's* or *racemose*, simple *follicles* or *glands of Lieberkühn*, and the *agminate*. The *glands of Brunner* (Fig. 108) are

racemose glands, and are confined to the duodenum. They are partially embedded in the submucous tissue. In their physiology they are closely allied to the pancreatic glands.

The *glands of Lieberkühn* or *simple follicles* resemble the finger

FIG. 108.
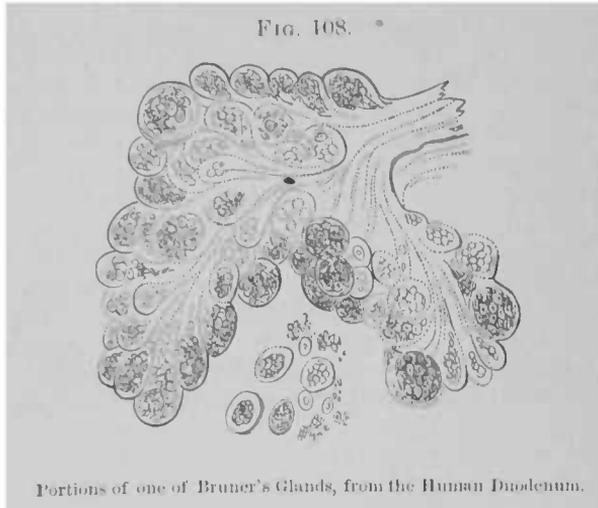
Portions of one of Bruner's Glands, from the Human Duodenum.

of a glove inverted. They are profusely distributed in both the large and small intestine, and appear as simple depressions of the

FIG. 109.

A Gland of Lieberkühn.

mucous membrane. Like the whole of the intestine, they are lined by columnar epithelium. They are surrounded by capillary plexuses of bloodvessels and lymphatics, and are the principal glands concerned in the secretion of the *succus entericus* (Fig. 109).

The *agminate glands,* or Peyer's patches, occur as localized collections of small white *sacculi.* (Fig. 110.) These sacculi are surrounded by dense capillary plexuses of bloodvessels, which send numerous vascular loops into the interior to form a framework for the stroma of the organ. The stroma consists of an adenoid tissue containing in its meshes lymph-corpuscles and an opaque substance with oil-globules.

These sacculi are embedded in the submucous tissue, and generally project more or less above the free surface of the membrane. Each sacculus is sometimes surrounded at its free surface by an annular depression or fossa, and encircled by a zone of openings, which are the orifices of the intestinal follicles. (Fig. 111.) Villi are sometimes seen on their surface. When the sacculi exist singly, they are termed *solitary glands* (Fig. 112).

The function of the agminate glands is not known, but it is probable that they are accessories of the lymphatic system, and are actively concerned in absorption.

FIG. 110.
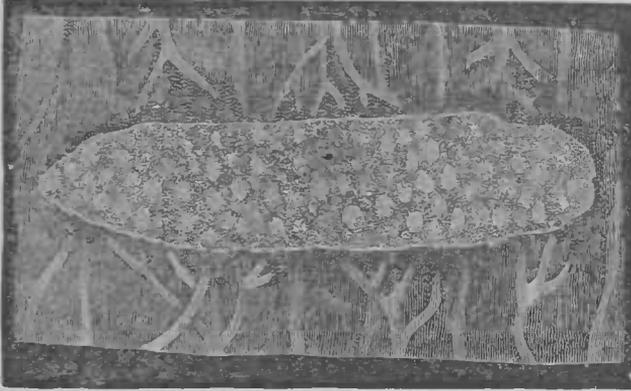
Agminate Follicles, or Peyer's Patch, in a state of distention. Magnified about 5 diam. After BOEHM.

The villi are covered with columnar epithelium, which is continuous with the intestinal lining, but is somewhat modified on
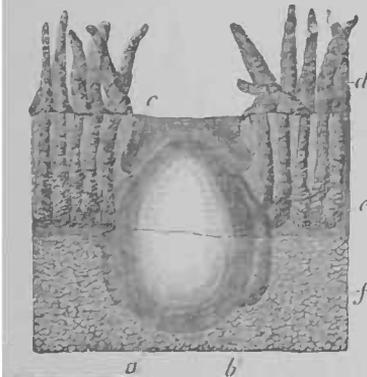
FIG. 111.   FIG. 112.
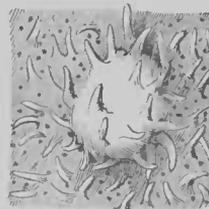
FIG. 111 —Side view of a portion of Intestinal Mucous Membrane of a Cat, showing Peyer's gland a; it is embedded in the submucous tissue f, the line of separation between which and the mucous membrane passes across the gland; b, one of the tubular follicles, the orifices of which form the zone of openings around the gland; c, the fossa in the mucous membrane; d, villi; e, follicles of Lieberkuhn. After BENDZ.

FIG. 112.—Solitary gland of small intestine. After BOEHM.

its free surface by being striated (Fig. 90). Internally, they are composed of a stroma of adenoid tissue, which contains the blood-

vessels, muscular fibres, lacteals, and also fibro-plastic cells and fat-globules (Fig. 113).

The lacteals usually appear as a single or double loop, and have no definable openings. They empty into the lacteals at the base of the villi. The unstriated muscular fibres are fibres

FIG. 113.
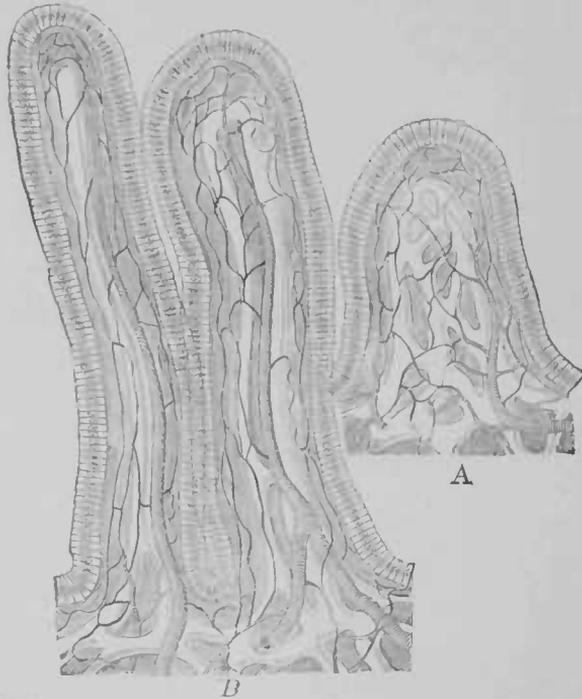
(Slightly altered from Teichmann.)   *A*, Villus of sheep; *B*, Villi of man.

Villi of intestine showing columnar epithelium covering them; also adenoid tissue, having in its meshes the dark vessels, which are portal capillaries, and a lacteal appearing as a white loop.

of the *muscularis mucosæ*, and are supposed to be active elements in emptying the lacteals. The longitudinal fibres, in contraction, serve to pull the villus down, and force the contents of the lacteals out, while valves in the larger vessels prevent a reflux of the fluid. The part which the villi take in the digestive process is to absorb the products of digestion. This function will be again referred to more in detail. The nerves are derived from the pneumogastric and sympathetic.]

Succus Entericus.

When, in a living animal, a portion of the small intestine is ligatured, so that the secretions coming down from above cannot enter its canal, while yet the blood-supply is maintained as usual, a small amount of secretion collects in its interior. This is spoken of as the *succus entericus,* and is supposed to be furnished by the glands of Lieberkühn. We have no exact knowledge, however, as to the extent to which such a secretion takes place under normal circumstances; and the statements with regard to its action are conflicting. Probably it has no direct action on either fats or proteids; but is amylolytic in some animals, though not in all.

A small quantity of fluid free from bile, gastric or pancreatic juice, and which may be considered as pure succus entericus, may also be obtained by the following method known as that of Thiry: The small intestine is divided in two places at some distance apart. By fine sutures the lower end of the upper section is united with the upper end of the lower section, thus, as it were, cutting out a whole piece of the small intestine from the alimentary tract. In successful cases, union between the cut surfaces takes place, and a shortened but otherwise satisfactory canal is reëstablished. Of the isolated piece the lower end is carefully closed by sutures, while the upper is brought to the wound in the abdominal wall and secured there. A fistula is thus formed leading into a short piece of intestine quite isolated from the rest of the alimentary canal.

Succus entericus has also been said to change cane- into grape-sugar, and by a fermentative action to convert cane sugar into lactic acid, and this again into butyric acid with the evolution of carbonic acid and free hydrogen.

Of the possible action of other secretions of the alimentary canal, as of the cæcum and large intestine, we shall speak when we come to consider the changes in the alimentary canal.

Concerning the secretion of Brunner's glands, our information is at present imperfect. The cells of the glands resemble the central cells of the gastric glands; and an extract of the gland is said to digest fibrin in an acid solution, but to have no distinct amylolytic action.

SEC. 2.—THE ACT OF SECRETION IN THE CASE OF THE DIGESTIVE JUICES AND THE NERVOUS MECHANISMS WHICH REGULATE IT.

The various juices whose properties we have just studied, though so different from each other, are all drawn ultimately from one common source—the blood—and they are poured into the alimentary canal, not in a continuous flow, but intermittently

as occasion may demand. The epithelium cells which supply them have their periods of rest and of activity, and the amount and quality of the fluids which these cells secrete are determined by the needs of the economy as the food passes along the canal. We have, therefore, to consider how the epithelium cell manufactures its special secretion out of the materials supplied to it by the blood, and how the cell is called into activity by the presence of food at some distance from itself, or by circumstances which do not bear directly on itself.   In dealing with these matters in connection with the digestive juices, we shall have to enter at some length into the physiology of secretion in general.

The question which presents itself first is : By what mechanism is the activity of the secreting cells brought into play ?

While fasting, a small quantity only of saliva is poured into the mouth ; the buccal cavity is just moist and nothing more. When food is taken, or when any sapid or stimulating substance, or, indeed, a body of any kind, is introduced into the mouth, a flow is induced which may be very copious. Indeed, the quantity secreted in ordinary life during twenty-four hours has been roughly calculated at as much as from one to two litres. An abundant secretion in the absence of food in the mouth may be called forth by an emotion, as when the mouth waters at the sight of food, or by a smell, or by events occurring in the stomach, as in some cases of nausea. Evidently in these cases some nervous mechanism is at work. In studying the action of this nervous mechanism, it will be of advantage to confine our attention at first to the submaxillary gland.

The submaxillary gland (Fig. 114) is supplied with nerves from two sources ; from the cervical sympathetic along the submaxillary arteries, and from the seventh or facial nerve by fibres, which, running in the chorda tympani, join the lingual branch of the fifth nerve, from which they diverge under the lower jaw, and run as a small nerve close beside the duct to the gland.

If a tube be placed in the duct, it is seen that when sapid substances are placed on the tongue, or the tongue is stimulated in any other way, or the lingual nerve is laid bare and stimulated with an interrupted current, a copious flow of saliva takes place. If the sympathetic be divided, stimulation of the tongue or lingual nerve still produces a flow. But if the small chorda nerve spoken of above be divided, stimulation of the tongue or lingual nerve produces no flow.

Evidently the flow of saliva is a nervous reflex action, the lingual nerve serving as the channel for the afferent and the small chorda nerve for the efferent impulses. If the trunk of the lingual be divided above the point where the chorda leaves it, as at *n. l'.*, Fig. 114, stimulation of the tongue produces, under ordi-

nary circumstances, no flow. This shows that the centre of the reflex action is higher up than the point of section; it lies, in fact, in the brain.

In the angle between the lingual and the chorda, where the latter leaves the former to pass to the gland, lies the small submaxillary gan-

FIG. 114.
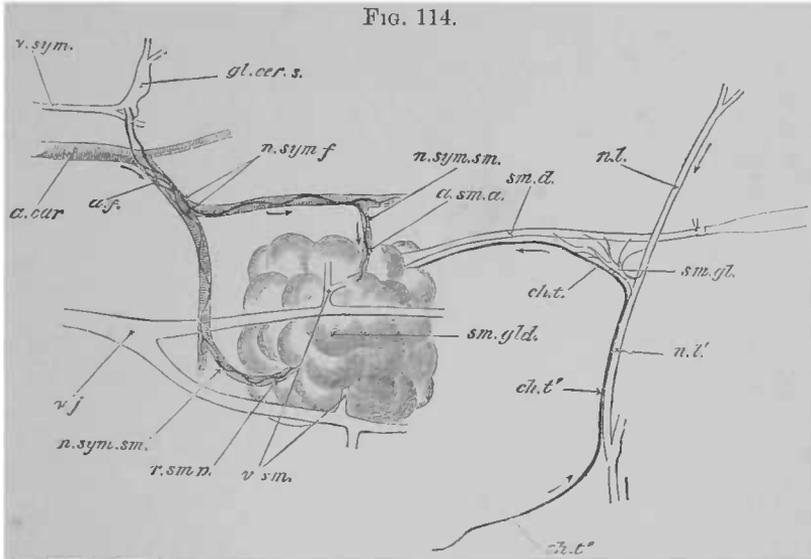
DIAGRAMMATIC REPRESENTATION OF THE SUBMAXILLARY GLAND OF THE DOG WITH ITS NERVES AND BLOODVESSELS. (This is not intended to illustrate the exact anatomical relations of the several structures.)

sm. gld. The submaxillary gland, into the duct (*sm. d.*) of which a canula has been tied. The sublingual gland and duct are not shown.

l, *n. l'.* The lingual branch nerve. *ch. t.*, *ch. t'.* The chorda tympani, proceeding from the facial nerve, becoming conjoined with the lingual at *n. l'.* and afterwards diverging and passing to the gland along the duct.

sm. gl. The submaxillary ganglion with its several roots. *n. l.* The lingual proceeding to the tongue.

a. car. The carotid artery, two branches of which, *a. sm. a.* and *r. sm. p.*, pass to the anterior and posterior parts of the gland. *v. sm.* the anterior and posterior veins from the gland, falling into *v. j* the jugular vein.

v. sym. The conjoined vagus and sympathetic trunks.

gl. cer. s. The supercervical ganglion, two branches of which forming a plexus (*a. f.*) over the facial artery, are distributed (*n. sym. sm.*) along the two glandular arteries to the anterior and posterior portions of the gland.

The arrows indicate the direction taken by the nervous impulses during reflex stimulation of the gland. They ascend to the brain by the lingual and descend by the chorda tympani.

glion (represented diagrammatically in Fig. 114, *sm. gl.*), from which branches pass to the lingual on the one hand and to the chorda on the other; branches may also be traced towards the ducts and glands and towards the tongue. It has been much debated whether this ganglion

can act as a centre of reflex action, but no conclusive evidence that it does so act has as yet been shown.

Stimulation of the glossopharyngeal is even more effectual than that of the lingual. Probably this, indeed, is the chief afferent nerve in ordinary secretion. Stimulation of the mucous membrane of the stomach (as by food introduced through a gastric fistula), or of the vagus, also, produces a flow of saliva, as indeed may stimulation of the sciatic, and probably of many other afferent nerves. All these cases are instances of reflex action, the cerebro-spinal system acting as a centre. We may further define the centre as a part of the medulla oblongata, apparently not far removed from the vaso-motor centre. When the brain is removed down to the medulla oblongata, that organ being left intact, a flow of saliva may still be obtained by adequate stimulation of various afferent nerves; when the medulla is destroyed, no such action is possible. And a flow of saliva may be produced by direct stimulation of the medulla itself. When a flow of saliva is excited by ideas, or by emotions, the nervous processes begin in the higher parts of the brain, and descend thence to the medulla before they give rise to distinctly efferent impulses; and it would appear that these higher parts of the brain are called into action when a flow of saliva is excited by distinct sensations of taste.

Considering then the flow of saliva as a reflex act the centre of which lies in the medulla oblongata, we may imagine the efferent impulses passing from that centre to the gland, either by the chorda tympani or by the sympathetic nerve. Although it would perhaps be rash to say that in this relation the sympathetic nerve never acts as an efferent channel, as a matter of fact we have no satisfactory experimental evidence that it does so; and we may therefore state that, practically, the chorda tympani is the sole efferent nerve. Section of that nerve, either where the fibres pass from the lingual nerve and the submaxillary ganglion to the gland, or where it runs in the same sheath as the lingual or in any part of its course from the main facial trunk to the lingual, puts an end, as far as we know, to the possibility of any flow being excited by stimuli applied to the sensory nerves or sentient surfaces of the mouth, or of other parts of the body.

The natural reflex act of secretion may be inhibited, like the reflex action of the vaso-motor nerves, at its centre. Thus when, as in the old rice ordeal, fear parches the mouth, it is probable that the afferent impulses caused by the presence of food in the mouth cease, through emotional inhibition of their reflex centre, to give rise to efferent impulses.

In life, then, the flow of saliva is brought about by the advent to the gland along the chorda tympani of efferent impulses,

started chiefly by reflex actions. The inquiry thus narrows itself to the question : In what manner do these efferent impulses cause the increase of flow ?

If in a dog a tube be introduced into Wharton's duct, and the chorda be divided, the flow, if any be going on, is from the lack of efferent impulses arrested. On passing an interrupted current through the peripheral portion of the chorda, a copious secretion at once takes place, and the saliva begins to rise rapidly in the tube ; a very short time after the application of the current the flow reaches a maximum which is maintained for some time, and then, if the current be long continued, gradually lessens. If the current be applied for a short time only, the secretion may last for some time after the current has been shut off. The saliva thus obtained is but slightly viscid, and contains few salivary corpuscles or protoplasmic lumps. If the gland itself be watched, while its activity is thus aroused, it will be seen that its arteries are dilated, and its capillaries filled, and that the blood flows rapidly through the veins in a full stream and of bright arterial hue, frequently with pulsating movements. If a vein of the gland be opened, this large increase of flow, and the lessening of the ordinary deoxygenation of the blood consequent upon the rapid stream, will be still more evident. It is clear that excitation of the chorda largely dilates the arteries ; the nerve acts energetically as a dilator nerve, probably from acting on some local vaso-motor centre in the gland.

Thus stimulation of the chorda brings about two events : a dilation of the bloodvessels of the gland, and a flow of saliva. The question at once arises, Is the latter simply the result of the former or is the flow caused by some direct action on the secreting cells, apart from the increased blood-supply ? In support of the former view we might argue that the activity of the epithelial secreting cell, like that of any other form of protoplasm, is dependent on blood-supply. When the small arteries of the gland dilate, while the pressure in the arteries on the side towards the heart is as we have seen in the last chapter correspondingly diminished, the pressure on the far side in the capillaries and veins is increased ; hence the capillaries become fuller, and more blood passes through them in a given time. From this we might infer that a larger amount of nutritive material would pass away from the capillaries into the surrounding lymph-spaces, and so into the epithelium cells, the result of which must be to quicken the processes going on in the cells, and to stir these up to greater activity. But even admitting all this it does not necessarily follow that the activity thus excited should take on the form of secretion. It is quite possible to conceive that the increased blood-supply should lead only to the accumulation in the cell of

the constituents of the saliva, or of the raw materials for their construction, and not to a discharge of the secretion. A man works better for being fed, but feeding does not make him work in the absence of any stimulus. The increased blood-supply therefore, while favorable to active secretion, need not necessarily bring it about. Moreover, the following facts are distinctly opposed to such a view. When a canula is tied into the duct and the chorda is energetically stimulated, the pressure acquired by the saliva accumulated in the canula and in the duct may exceed for the time being the arterial blood-pressure, even that of the carotid artery; that is to say, the pressure of fluid in the gland outside the bloodvessels is greater than that of the blood inside the bloodvessels. This must, whatever be the exact mode of transit of nutritive material through the vascular walls, tend to check that transit. Again, if the head of an animal be rapidly cut off, and the chorda immediately stimulated, a flow of saliva takes place far too copious to be accounted for by the emptying of the salivary channels through any supposed contraction of their walls. In this case secretion is excited in the absence of blood-supply. Lastly, if a small quantity of atropin be injected into the veins, stimulation of the chorda produces no secretion of saliva at all, though the dilation of the bloodvessels takes place as usual. These facts prove that the secretory activity is not simply the result of vascular changes, but may be called forth independently; they further lead us to suppose that the chorda contains two sets of fibres, one secreting fibres, acting directly on the epithelium cells only, and the other vaso-motor or dilating fibres, acting on the bloodvessels only, and further that atropin, while it has no effect on the latter, paralyzes the former just as it paralyzes the inhibitory fibres of the vagus. Hence when the chorda is stimulated, there pass down the nerve, in addition to impulses affecting the blood-supply, impulses affecting directly the protoplasm of the secreting cells, and calling it into action, just as similar impulses call into action the contractility of the protoplasm of a muscular fibre. Indeed the two things, secreting activity and contracting activity, are quite parallel. We know that when a muscle contracts, its bloodvessels dilate; and just as by atropin the secreting action of the gland may be isolated from the vascular dilation, so by urari muscular contraction may be removed, and leave dilation of the bloodvessels as the only effect of stimulating the muscular nerve. In both cases the greater flow of blood may be an adjuvant to, but is not the exciting cause of, the activity of the protoplasm.

Since the chorda acts thus directly on the secreting cells, we should expect to find an anatomical connection between the cells and the nerve; and some authors have maintained that the nerve-

fibres may be traced into the cells. But, save perhaps in the case of certain glands of invertebrates (so-called salivary glands of *Blatta*), the evidence is as yet not convincing.

When the cervical sympathetic is stimulated, the vascular effects are the exact contrary of those seen when the chorda is stimulated. The small arteries are constricted, and a small quantity of dark venous blood escapes by the vein. Sometimes, indeed, the flow through the gland is almost arrested. The sympathetic therefore acts as a constrictor nerve, and in this sense is antagonistic to the chorda. We have already referred to the probable existence of a local vaso-motor centre situated in the gland itself, in which indeed there are found ganglionic cells in abundance. The fact that section of the cervical sympathetic does not cause complete dilation of the vessels of the gland—the dilating effects of stimulation of the chorda being fully evident after previous section of the sympathetic—affords additional support to this view. We may accordingly suppose that, while the chorda tympani inhibits, the sympathetic exalts, the action of this local centre.

As concerns the flow of saliva brought about by stimulation of the sympathetic, in the case of the submaxillary gland of the dog the effects are very peculiar. A slight increase of flow is seen, but this soon passes off, and so much saliva as is secreted is remarkably viscid, of higher specific gravity, and richer in corpuscles and protoplasmic lumps, and is said to be more active on starch than the chorda saliva. This action of the sympathetic is said not to be affected by atropin.

In the submaxillary gland of the dog then the contrast between the effects of chorda stimulation and those of sympathetic stimulation are very marked : the former gives rise to vascular dilation with a copious flow of limpid saliva, the later to vascular constriction with a scanty flow of viscid saliva. And in other animals a similar contrast prevails, though with minor differences. Thus in the rabbit both chorda saliva and sympathetic saliva are limpid and free from mucus, and in the cat, chorda saliva is more viscid than sympathetic saliva ; but in both these cases, as in the dog, stimulation of the chorda causes a copious flow with dilated bloodvessels, and stimulation of the sympathetic a scanty flow with vascular constriction. We shall return again presently to these different actions of the two nerves; meanwhile we have seen enough of the history of the submaxillary gland to learn that secretion in this instance is a reflex action, the efferent impulses of which directly affect the secreting cells, and that the vascular phenomena may assist, but are not the direct cause of the flow. We have dwelt long on this gland because it has

been more fruitfully studied than any other. But the nervous mechanisms of the other secretions are in the main features similar.

Thus the secretion of the parotid gland, like that of the submaxillary, is governed by two sets of fibres: one of cerebrospinal origin, running along the auriculo-temporal branch of the fifth nerve but originating either in the glosso-pharyngeal or the facial, and the other of sympathetic origin coming from the cervical sympathetic. Stimulation of the cerebro-spinal fibres produces a copious flow of limpid saliva, free from mucus, the secretion reaching in the dog a pressure of 118 mm. mercury; stimulation of the cervical sympathetic gives rise in the rabbit to a secretion free from mucus but rich in organic matter and of greater amylolytic power than the cerebro-spinal secretion, but in the dog little or no secretion is produced, though we shall see later on, certain changes are brought about in the gland itself. In both animals the cerebro-spinal fibres are vaso-dilator and the sympathetic fibres vaso-constrictor in action. Stimulation of the central end of the glosso-pharyngeal produces by reflex action a secretion of the parotid, but that of the lingual is said to be without effect.

Gastric Juice.—Though a certain amount of gastric juice may sometimes be found in the stomachs of fasting animals, it may be stated generally that the stomach, like the salivary glands, remains inactive, yielding no secretion, so long as it is not stimulated by food or otherwise. The advent of food into the stomach, however, at once causes a copious flow of gastric juice; and the quantity secreted in the twenty-four hours is probably very considerable, but we have no trustworthy data for calculating the exact amount. So also when the gastric mucous membrane is stimulated mechanically, as with a feather, secretion is excited; but to a very small amount even when the whole interior surface of the stomach is thus repeatedly stimulated. The most efficient stimulus is the natural stimulus, viz., food; though dilute alkalies seem to have unusually powerful stimulating effects; thus the swallowing of saliva at once provokes a flow of gastric juice. During fasting the gastric membrane is of a pale gray color, somewhat dry, covered with a thin layer of mucus, and thrown into folds; during digestion it becomes red, flushed and tumid, the folds disappear, and minute drops of fluid appearing at the mouths of the glands, speedily run together into small streams. When the secretion is very active, the blood flows from the capillaries into the veins in a rapid stream without losing its bright arterial hue. The secretion of gastric juice is in fact accompanied by vascular dilation in the same way as in the secretion of saliva, but the vascular

mechanism has not yet been fully worked out, though there is evidence of the vagi nerves being concerned in the matter.

Seeing that, unlike the case of the salivary secretion, food is brought into the immediate neighborhood of the secreting cells, it is exceedingly probable that a great deal of the secretion is the result of the working of a local mechanism; and when a mechanical stimulus is applied to one spot of the gastric membrane the secretion is limited to the neighborhood of that spot, and is not excited in distant parts. This local mechanism may be nervous in nature, or the effect of the stimulus may, perhaps, be conveyed directly from cell to cell, from the mouth of the gland to its extreme base without the intervention of any nervous elements; but the vascular changes at least would seem to imply the presence of a nervous mechanism.

The importance of this local mechanism and the subordinate value of any connection between the gastric membrane and the central nervous system are further shown by the fact that a secretion of quite normal gastric juice will go on when both vagi, or when the sympathetic nerves going to the stomach are divided, or, indeed, when all the nervous connections of the stomach are severed. And all attempts to provoke or modify gastric secretion by the stimulation of the nerves going to it, have hitherto failed. On the other hand, in cases of gastric fistula, where by complete occlusion of the œsophagus stimulation by the descent of saliva has been avoided, the mere sight or smell of food has been seen to provoke a lively secretion of gastric juice. This must have been due to some nervous action; and the same may be said of the cases where emotions of grief or anger suddenly arrest the secretion or prevent the secretion which would otherwise have taken place as the result of the presence of food in the stomach. So that much has yet to be learnt in this matter.

The contrast presented between the scanty secretion resulting from mechanical stimulation and the copious flow which actual food induces, is interesting because it seems to show that the secretory activity of the cells is heightened by the absorption of certain products derived from the portions of food first digested. This is well illustrated by the following experiment of Heidenhain. This observer, adopting the method employed for the intestine (see p. 315), succeeded in isolating a portion of the fundus from the rest of the stomach; that is to say, he cut out a portion of the fundus, sewed together the cut edges of the main stomach, so as to form a smaller but otherwise complete organ, while by sutures he converted the excised piece of fundus into a small independent stomach opening on to the exterior by a fistulous orifice. When food was introduced into the main stomach secretion also took place in the isolated fundus. This at first

sight might seem the result of a nervous reflex act; but it was observed that the secondary secretion in the fundus was dependent on actual digestion taking place in the main stomach. If the material introduced into the main stomach were indigestible or digested with difficulty, so that little or no products of digestion were formed and absorbed into the blood—such, *ex. gr.*, as pieces of ligamentum nuchæ—very little secretion took place in the isolated fundus. We quote this now as bearing on the question of a possible nervous mechanism of gastric secretion, but we shall have to return to it under another aspect.

Bile.—When the acid contents of the stomach are poured over the orifice of the biliary duct, a gush of bile takes place. Indeed, stimulation of this region of the duodenum with a dilute acid at once calls forth a flow, whereas alkaline fluids so applied have little or no effect. This, probably, is a reflex action leading to the contraction of the muscular walls of the gall-bladder and ducts, accompanied by a relaxation of the sphincter of the orifice; it refers, therefore, to the discharge rather than to the secretion of bile.

When the secretion of the bile is studied by means of a biliary fistula (which, however, probably induces errors by the total withdrawal from the body of the bile which should naturally flow into the intestine), it is seen to rise rapidly after meals, reaching its maximum in from four to ten hours. There seems to be an immediate, sudden rise when food is taken, then a fall, followed subsequently by a more gradual rise up to the maximum, and ending in a final fall to the lowest point; but it must be remembered that the lowest point is not zero, since the secretion of the bile, unlike that of the saliva and gastric juice, is continuous, and even in a fasting animal does not cease. It may be that these variations are due to the action of the nervous system, but experiments have hitherto failed to demonstrate clearly the existence of any distinct nervous mechanism.

The pressure under which the bile is secreted is, in general, very low. When a water manometer is connected with the gall-bladder of a guinea-pig, the *ductus choledochus* being ligatured, the fluid may rise in the manometer to about 200 mm. (equivalent to about 16 mm. mercury), but not much beyond. This is, of course, much less than the arterial pressure in the same animal; but it must not be forgotten that the liver receives its chief blood-supply from a venous source, viz., from the portal vein; and it would appear from experiments on dogs that the pressure at which the bile is secreted exceeds that of the blood in the mesenteric veins going to form the portal vein. Hence, the limit of pressure, though so different from that of the salivary glands, resembles it in this

fundamental fact, that it exceeds the pressure of the blood in the capillaries of the organ. The same peculiar vascular supply of the liver renders it difficult to draw any comparison between its vascular condition during active secretion and that of the salivary glands, though during digestion the liver is swollen and increased in weight, apparently from an increase in the blood-supply.

The quantity of bile secreted in man in the twenty-four hours has been estimated to be exceedingly great, but the calculations are based on very imperfect data.

Pancreatic Juice.—In the dog the secretion of pancreatic juice after food has been taken, follows the curve given in Fig. 115.

FIG. 115.
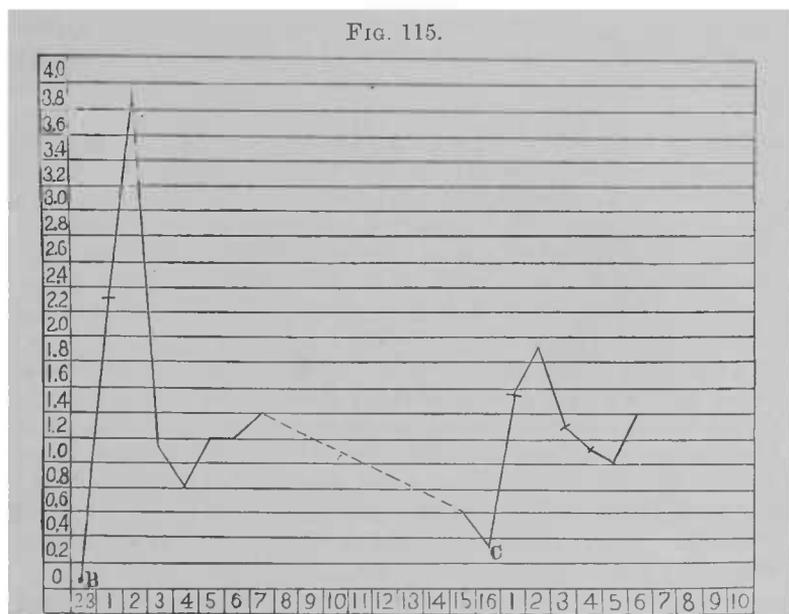
DIAGRAM ILLUSTRATING THE INFLUENCE OF FOOD ON THE SECRETION OF PANCREATIC JUICE.
(N. O. Bernstein.)

The abscissæ represent hours after taking food; the ordinates represent in c c. the amount of secretion in 10 minutes. A marked rise is seen at B immediately after food was taken, with a secondary rise between the 4th and 5th hours afterwards. Where the line is dotted the observations were interrupted. On food being again given at C, another rise is seen, followed in turn by a depression and a secondary rise at the 4th hour. A very similar curve would represent the secretion of bile.

There is a sudden maximum rise immediately after food has been taken. This, at all events, suggests very strongly some nervous action. Then follows a fall, after which there is, as in bile, a

secondary rise, the causation of which may, or may not, be nervous in nature. In the dog there may be, during fasting, a complete cessation of secretion. The quantity secreted in twenty-four hours by man has been calculated at 300 c.c. Like the salivary glands, the pancreas while secreting is flushed, through dilation of its bloodvessels.

The secretion, if present, may be increased, or, if absent, may be called forth by stimulation of the medulla oblongata, and when going on may be arrested by stimulation of the central end of the vagus through a reflex act, the efferent channels of which have not yet been made out; probably the arrest of the secretion which is said to be caused by nausea or vomiting is thus brought about by stimulation of the vagus endings. These facts show that the secretion is under the influence of the central nervous system; but we have no such satisfactory knowledge of the exact working of the nervous mechanism as in the case of the salivary glands.

Succus Entericus.—With regard to the secretion furnished by the intestine itself, our information is very limited. The secretion of the isolated intestine appears to be not a constant one, but to need for its production some stimulus (mechanical or other) which probably acts in a reflex manner. After section of the nerves going to a piece of intestine isolated after Thiry's method, a copious flow of a dilute intestinal juice is said to take place.

Thus, while the influence of the nervous system is in the case of the submaxillary gland tolerably clear, in the case of the other secretions we have yet much to learn, and we must rest rather on analogy with the submaxillary gland, than on any known facts. We cannot, however, go far wrong if we conclude that in all cases secretion is essentially due to a direct activity of the epithelium cells, and that variations in the blood-supply have a secondary effect only.

We may now pass on to the second problem, What is the exact nature of the activity which is thus called forth?

Towards the solution of this problem much progress has been made by the study of the microscopical changes in secreting glands during various stages of activity and rest. And these are, perhaps, in some respects best shown in the pancreas.

It is possible, by special precautions, to examine with even high powers of the microscope the pancreas of an animal such as the rabbit, while still alive with the circulation intact; and thus to watch the changes going on both when the animal has been deprived of food for some time, and the gland is, therefore, at rest, and when the animal has been recently fed, so that digestion

is going on, and the pancreas in consequence is engaged in pouring its secretion into the duodenum. In the former case—*i. e.*, when the pancreas is at rest and little or no secretion is being poured out, the following appearances may be recognized : The outlines of the individual cells forming au alveolus (Fig. 116, *A*) are very indistinct, and each cell is loaded with a number of small, highly refractive granules. These, however, are crowded towards the inner side of the cell abutting ou the lumen of the alveolus, leaving the outer part of the cell uext to the basement membrane clear and hyaline. We can, in fact, distinguish in each cell two zones—a smaller outer zone, free from granules, and a larger or broader inner zoue, thickly studded with granules.

Fig. 116.
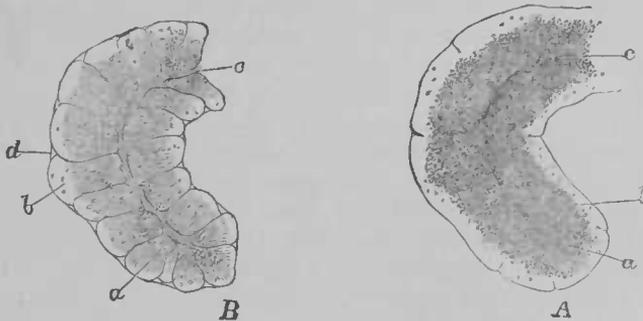
A PORTION OF THE PANCREAS OF THE RABBIT (KUHNE AND SHERIDAN LEA).
A at rest, *B* in a state of activity.

a the inner granular zone, which in *A* is larger and more closely studded with fine granules. than in *B*, in which the granules are fewer and coarser.

b the outer transparent zone, small in *A*, larger in *B*, and in the latter marked with faint striæ,

c the lumen, very obvious in *B*, but indistinct in *A*.

d an indentation at the junction of two cells, seen in *A*, but not occurring in *B*.

At the same time it may be remarked that the lumen of the alveolus is narrow aud very obscure ; the blood-supply, moreover, is scanty, the small arteries being constricted and the capillaries imperfectly filled with corpuscles.

If, however, the same pancreas be examined while it is in a state of activity, either from the presence of food in the stomach, or from the injection of some stimulating drug such as pilocarpin, a very different state of things is seen. The individual cells (Fig. 116, *B*) have become smaller and much more distinct in outline and the lumen of the alveolus is now wider and more conspicuous. In each cell the granules have become much fewer in number and as it were have retreated to the inner margin, so that the inner granular zone is much narrower aud

the outer transparent zone much broader than before; the latter too is frequently marked at its inner part by delicate striæ running into the inner zone. At the same time the bloodvessels are largely dilated and the stream of blood through the capillaries is full and rapid.

These things, the disappearance of granules during activity leading to a diminution of the inner granular zone and a widening of the outer transparent zone, and the appearance of new granules during rest leading to a restoration of the inner zone and its consequent encroachment on the outer zone, may be witnessed in the living pancreas of the rabbit, and the changes from the one condition to the other successively observed. And sections of the prepared and hardened gland of this or of any other animal tell nearly the same tale. Thus in the pancreas of a dog which has been fasting for about thirty hours, each secreting cell is found to consist of two zones: an inner zone, studded with fine granules, and a smaller outer zone, which is homogeneous or marked with delicate striæ, the nucleus being placed partly in the one and partly in the other zone. When however the pancreas of an animal in full digestion (about six hours after food) is examined, though the whole cell is smaller, the outer homogeneous zone is found to be relatively much wider, the granular inner zone being narrower, and in some cases actually disappearing. If the pancreas be examined at the end of digestion, when its activity has once more ceased, and it has entered into a state of rest, the outer zone is again found to be narrow, the granular inner zone occupying the greater part of the cell, which has once more become larger. Carmine stains the outer zone easily, the inner zone with difficulty. Hence when, as during activity, the outer zone is relatively large, the cell as a whole seems more deeply stained than when, as during rest, the outer zone is small. During activity the nucleus is large and round; during rest it often appears irregular, owing to its being in such a condition that it shrinks under the influence of the reagents employed.

Leaving aside for the present the changes in the nucleus, and the matter of staining, we may say that the results of the two methods are identical.

Before, however, we attempt to explain what these results mean, it will be well to pay attention for a while to another type of secreting gland, the so-called mucous glands. We have already seen that some salivary glands, such as the submaxillary of the dog, secrete a thick viscid saliva, the viscidity being due to the presence of the body *mucin* (see Appendix), the essential constituent of the so-called mucus; while other salivary glands, such as the parotid of most animals, secrete a thin limpid saliva free from mucin. Glands of the latter kind, from the nature of

their secretion, receive the name of "serous" glands. Glands, however, which give rise to a viscid mucin-holding secretion, always contain a certain number of cells of a distinct type. These cells are called "mucous cells," and the glands in which they are found are called "mucous glands." Sometimes the mucous cells are abundant forming a large part of many or most of the alveoli; sometimes they are scanty. Each "mucous" cell when examined in a fresh and natural condition is loaded throughout with somewhat large granules; but when treated with alcohol or other hardening reagent (Fig. 117, A) appears to consist of two parts: of a small quantity of what we may speak of as ordinary protoplasm, readily staining with carmine, etc., and gathered round the nucleus, which is placed towards the outside of the cell, generally close to the basement membrane; and of another different substance which occupies the greater part of the cell.

FIG. 117.

SECTION OF "MUCOUS" GLAND, A in a state of rest, B after it has been for some time actively secreting. (After LAVDOWSKY.)

a demilune cells; c leucocytes lying in the interalveolar spaces. The darker shading in both figures is intended to indicate the amount of staining.
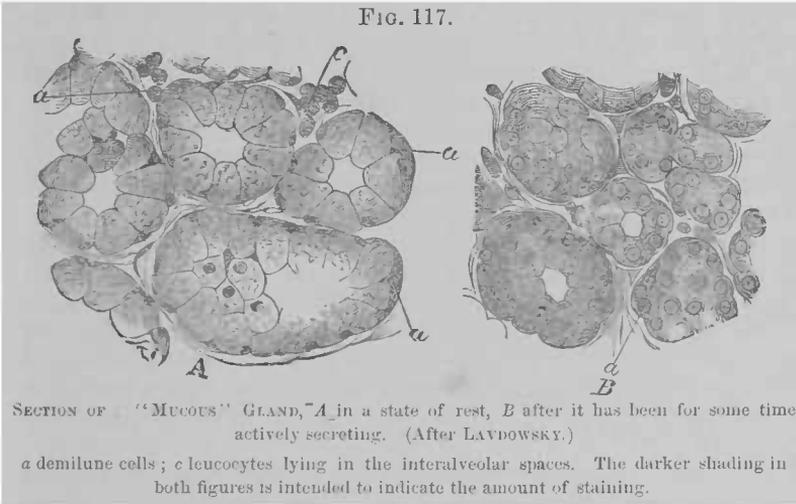
This latter substance is composed of a loose network of fine fibres, the spaces of which are occupied by a transparent material which does not stain readily with carmine; and upon examination is found to consist largely of a material which is readily transformed into mucin, and which may be spoken of as *mucinogen* or by abbreviation *mucigen*. So that the ordinary mucous cell of a mucous gland may be said to consist of a smaller portion of ordinary protoplasmic substance and of a larger portion of a mucigenous substance.

Such a condition of things exists however only in a mucous cell at rest. When the gland is actively secreting, or rather after the gland has for some time been actively secreting, as for

instance after the submaxillary gland of the dog has been sub-
jected to long and powerful stimulation of the chorda, a different
state of things presents itself when prepared sections of the
hardened gland are examined.   The alveolus is then found to be
made up of smaller cells (Fig. 117, *B*) almost wholly formed of
protoplasmic substance readily staining with carmine.   In ex-
treme cases hardly a trace is left of the mucigenous substance
spoken of above ; in cases of moderate activity cells may be
seen in which the mucigenous substance has diminished, with an
increase of the ordinary protoplasmic substance, but has not
entirely disappeared.

How are we to interpret these results? Obviously in this way :
The mucigenous basis is manufactured at the expense of the
ordinary protoplasm of the cell; the latter by its metabolism
produces the former and deposits it in the meshes of its own
framework, becoming as it were pregnant with mucigen.   This
during the resting phase of the gland may go on to such an
extent, that only a small quantity of protoplasm is left to carry
the large quantity of mucigen to which it has given rise; that
is to say, the growth of new protoplasm does not keep pace with
the manufacture of protoplasm into mucigen.   During activity
the mucigen is used up to provide the mucus of the saliva, being
probably converted into mucin and so discharged from the cell,
while at the same time the protoplasm takes a fresh start and
grows apace ; and thus a fresh supply of new, deeply staining
protoplasm takes the place of the mucigenous matrix which has
been lost.   We may remark incidentally that this rejuvenescence
of the protoplasm is marked, as in the corresponding phase of
the pancreas, by the nucleus becoming round and conspicuous,
whereas when the mucigen is abundant it is of such a nature as
to become irregular in outline when acted upon by hardening
reagents.

We have reason to think that in certain cases, where the
activity of the cell is long-continued and vehement, the whole
cell may disappear, and its place be taken by an entirely new
cell supplied by the so-called demilune cells lying on the outside
of the alveolus beneath the basement membrane.   But in ordinary
cases the same cell probably, for a while at all events, continues
to form and discharge successive quantities of mucin without
actually itself disappearing.

In any case we see that in the mucous cell what takes place
in secretion is as follows.   As the result of a period of rest there
accumulates in the cell a quantity of mucigen, which is a product
of the metabolism of the protoplasm of the cell.   During the
active phase, that is while the secretion is being poured forth,
the mucigen is converted into mucin and discharged from the

cell. A loss consequently accrues to the cell, but this is at once partly made up by the protoplasm being stirred to a more active growth. Subsequently during the succeeding rest the new protoplasm is transformed into new mucigen, the cell wholly regains its former dimensions and features and so the cycle is completed.

What relation do these changes in the mucous gland bear to those of the pancreas? To answer this question we must bring the reader back to a statement previously made, that in order to obtain an actively proteolytic aqueous pancreatic extract, the animal should be killed during full digestion. This statement now requires modification.

If the pancreas of an animal, even in full digestion, be treated, *while still warm from the body*, with glycerine, the glycerine extract, as judged of by its action on fibrin in the presence of sodium carbonate, is inert or nearly so as regards proteid bodies. If, however, the same pancreas be kept for twenty-four hours before being treated with glycerine, the glycerine extract readily digests fibrin and other proteids in the presence of an alkali. If the pancreas, while still warm, be rubbed up in a mortar for a few minutes with dilute acetic acid, and then treated with glycerine, the glycerine extract is strongly proteolytic. If the glycerine extract obtained without acid from the warm pancreas, and therefore inert, be diluted largely with water, and kept at 35° C. for some time, it becomes active. If treated with acidulated instead of distilled water, its activity is much sooner developed. If the inert glycerine extract of warm pancreas be precipitated with alcohol in excess, the precipitate, inert as a proteolytic ferment when fresh, becomes active when exposed for some time in an aqueous solution, rapidly so when treated with acidulated water. These facts show that a pancreas taken fresh from the body, even during full digestion, *contains but little ready-made ferment*, though there is present in it a body which, by some kind of decomposition, *gives birth to the ferment*. We may remark incidentally that though the presence of an alkali is essential to the proteolytic action of the actual ferment, the formation of the ferment out of its forerunner is favored by the presence of a small quantity of acid. To this body—this mother of the ferment which has not at present been satisfactorily isolated—the name of *zymogen* has been applied. But it is better to reserve the term zymogen as a generic name for all such bodies as not being themselves actual ferments, may by internal changes give rise to ferments, for all "mothers of ferment" in fact; and to give to the particular mother of the pancreatic proteolytic ferment, the name *trypsinogen*.

The pancreatic cell then contains trypsinogen; and now comes

the important observation that the amount of trypsinogen in a pancreas at any given time rises and sinks *pari passu* with the granular inner zone—*i. e.*, with the amount of granular substance in the cell. The wider the inner zone and the more abundant the granules the larger the amount, the narrower the zone and the fewer the granules the smaller the amount, of trypsinogen; and in the cases of old-established fistulæ, where the secretion is wholly inert on proteids, the inner granular zone is absent from the cells.

We have no corresponding satisfactory information concerning the history of any zymogen which may be supposed to belong to the amylolytic ferment of the pancreas, or to the ferment which acts upon fats. Nor, on the other hand, are we in a position to say that the granules are wholly composed of trypsinogen; but it seems clear that they contain trypsinogen, and that their abundance or scarcity affords a measure of the quantity of that substance present in the cell.

Hence, we may draw a parallel between the mucous cell and the pancreatic cell. Just as the protoplasm of the former by its metabolism manufactures mucigen, so the protoplasm of the latter by its metabolism manufactures trypsinogen, and just as the mucigen gives rise to mucin which escapes from the cell to form part of the actual secretion, so also the trypsinogen gives rise to trypsin, which similarly forms part of the pancreatic juice. Just as with the disappearance of the mucigen the protoplasm grows with renewed vigor, so in the pancreas with the disappearance of the granules from the inner zone, there is a rejuvenescence of the protoplasm, to be followed both in the one case and the other by a subsequent conversion of the protoplasm into a product—viz., mucigen and trypsinogen, respectively. In both cases the product of the protoplasmic metabolism is deposited in the inner parts of the cell, though the line of demarcation between the inner and outer zone is much more distinct in the pancreas than in the mucous gland. In the former abundance of granules is identical with a broad inner zone, scarcity of granules with a broad outer zone; and similarly the growth of the new protoplasm is most obvious as an increase of the outer zone. In the mucous cell, too, the mucigen appears on the inner side of the cell. This distinction, however, between an inner and outer zone is not an essential feature of the matter, though probably the growth of new protoplasm naturally tends to take place at a greater rate on the side of the cell most exposed to the blood-stream—*i. e.*, on the outer side towards the basement-membrane, and the deposition of zymogen or mucigen tends to be greatest on the other side nearer to the lumen, into which its products are about to be discharged.

When we come to study other glands, such as the serous salivary glands, the glands of the stomach, and the hepatic cells, we have evidence that in these also the same essential processes are going on. Certain special features, however, are in various instances met with, and, these becoming exaggerated by particular modes of preparation, are apt to obscure the normal series of events.

Thus, in the case of the glands of the stomach, if we were to trust exclusively to the indications given by sections of glands hardened in alcohol, we should be led to make the following statement. In an animal previous to taking a meal, the central or "chief" (as distinguished from the ovoid, "border," or "peptic") cells of the gastric glands are pale, finely granular, and do not stain readily with carmine and other dyes. During the early stages of gastric digestion, the same cells are found somewhat swollen, but turbid and more coarsely granular; they stain much more readily. At a later stage they become smaller and shrunken, but are even more turbid and granular than before, and stain still more deeply. This is true, not only of the central cells in the so-called peptic glands, but also of the cells of which the glands of the pyloric end of the stomach are built up. The ovoid or border cells appear swollen during digestion, and project more on the outside of the gland, but otherwise seem unchanged. This series of events is different from that which we have seen to take place in the pancreas, inasmuch as the cells appear to become more granular instead of less granular during activity. But we have reason to think that the granular character of the gastric cells thus seen during digestion is due to some special material precipitated by the alcohol, whereby changes really comparable to those of the pancreas are obscured. For we find that in the newt the cells, when examined in a living condition, are granular throughout when at rest, but during activity develop a clear outer zone, the granules becoming restricted to the inner zone. And in many mammals similar changes may be demonstrated by the use of osmic acid (Fig. 118). In some mammals no very obvious difference between rest and activity can be made out; and it is possible that in these a regeneration of granules takes place during activity as well as during rest, and that in proportion as granules are being used up, so that the amount of granules remains fairly constant.

Moreover, we have evidence of the existence in the gastric membrane of a zymogen, a mother of pepsin, a pepsinogen; though, owing to the facility with which apparently the conversion of pepsinogen into pepsin takes place, the matter is not so clear as in the analogous case of trypsinogen; and it would appear that the amount of pepsinogen and the abundance of visible

granules in fresh living cells run parallel to each other with considerable regularity.

In the case of the serous glands, also, the results are somewhat different according as use is made of preparations hardened in alcohol, or the gland is studied in a living state.   Thus, in the parotid of the rabbit, which is a serous gland, even when a most

FIG. 118.
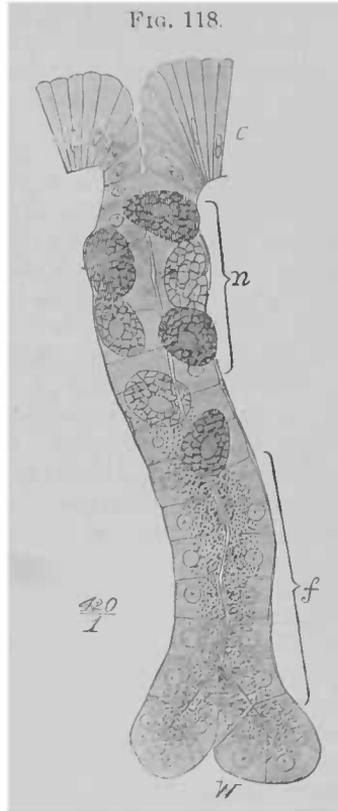
GASTRIC GLAND OF MAMMAL (MOLE) DURING ACTIVITY (LANGLEY).

c the mouth of the gland with its cylindrical cells.

n the neck containing conspicuous ovoid cells, with their coarse protoplasmic network.

f the body of the gland.   The granules are seen in the central cells to be limited to the inner portions of each cell.

copious secretion has been called forth by stimulation of the auriculo-temporal nerve, alcohol specimens show an almost complete absence of structural changes.   When, however, the cervical sympathetic is stimulated, either in the rabbit or the dog, very marked changes, quite similar to those witnessed in the

central cells of the gastric glands, may be seen in the parotid hardened by alcohol, even though, as occurs in the dog, no saliva whatever may be secreted. During rest, the cells of the parotid as seen in sections of the gland hardened in alcohol (Fig. 119, *A*) are pale, transparent, staining with difficulty, and the nuclei possess irregular outlines as if shrunken by the reagents employed. After stimulation of the sympathetic, the protoplasm of the cells becomes turbid (Fig. 119, *B*), and stains much more

FIG. 119.

SECRETION OF A "SEROUS" GLAND—THE PAROTID OF A RABBIT.
A at rest, *B*, after stimulation of the cervical sympathetic. After HEIDENHAIN.
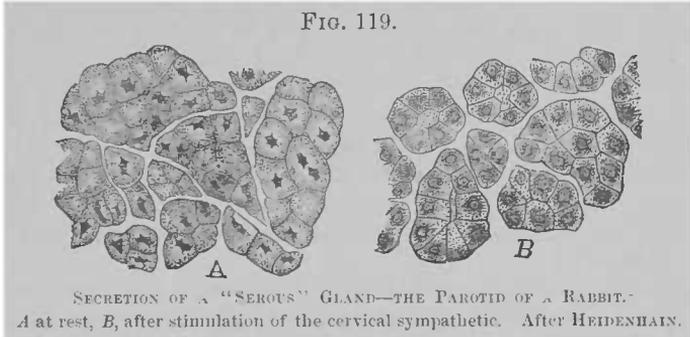
readily, while the nuclei are no longer irregular in outline, but round and large, with conspicuous nucleoli, the whole cell at the same time, at least after prolonged stimulation, becoming distinctly smaller. When, however, we study the gland in a living state, we find that the changes which take place during activity

FIG. 120.

CHANGES IN THE PAROTID DURING SECRETION (LANGLEY).

The figure, which is somewhat diagrammatic, represents the microscopic changes which may be observed in the living gland. *A* during rest. The obscure outlines of the cells are introduced to show the relative size of the cells, they could not be readily seen in the specimen itself. *B* after moderate stimulation. *C* after prolonged stimulation. The nuclei are diagrammatic, and introduced to show their appearance and position.

are quite comparable to those of the pancreas. During rest (Fig. 120, *A*), the cells are large, their outlines very indistinct—in fact, almost invisible—and the protoplasm of the cell is studded with granules. During activity (Fig. 120, *B*), the cells become

smaller, their outlines more distinct, and the granules disappear especially from the outer portions of each cell. After prolonged activity, as in Fig. 120, C, the cells are still smaller with their outlines still more distinct, and the granules have disappeared almost entirely, a few only being left at the extreme inner margin of each cell abutting upon the conspicuous almost gaping lumen of the alveolus. And upon special examination it is found that the nuclei are large and round. In fact we might almost take the parotid as thus studied, to be more truly typical of secretory changes than even the pancreas. For, as we have already stated, the demarcation of an inner and outer zone is not a necessary feature of the cell at rest. What is essential is that the proto-plasm manufactures granules, which for a while, that is during rest are deposited in the cell, and during activity these granules are used up, their disappearance being earliest and most marked at the outer portions of each cell, and progressing inwards towards the lumen, the whole cell becoming smaller, and as it were shrunken.

It would hardly be profitable to enter more fully into the dis-cussion of this matter, and especially of the differences, to which we have just called attention, as occurring in different glands; enough has been seen to justify us in the conclusion, which further study will be found to strengthen, that the act of secre-tion is not a mere filtration from the blood but a complicated business, which we may picture to ourselves somewhat as follows.

The protoplasm of the secreting cell lives upon its "internal medium," the lymph filling the lymph-spaces by which the alveolus is surrounded; this lymph being constantly renewed from the blood-stream. We have no reason to think that the main nutritive constituents of the lymph in the interstices of a gland are different from those in the interstices of a muscle; but are led to believe that the same substances are built up in the one case into muscular and in the other into glandular protoplasm by the specific activity of the already existing protoplasm which is different in the one case and the other. The cell substance which has thus built itself up out of the lymph materials sooner or later breaks down again: the constructive metabolism is inevi-tably followed by a destructive metabolism. In this downward path are probably many steps, two of which become conspicuous: the formation of some intermediate product or "mesostate," as we may call it, such as zymogen or mucigen, and the conversion of the zymogen into an actual ferment or of the mucigen into mucin—that is, of the mesostate into the final product, which is discharged as a constituent of the secretion.

In what we may consider the common or typical case where periods of rest alternate with periods of secretory activity, the

downward metabolism stops short at the formation of zymogen, which becomes deposited, commonly in the form of granules in the meshes of the protoplasm, the constructive metabolism or growth of the latter languishing as the storage increases. Then generally as the result of stimulation, changes take place in the cell by which the zymogen is converted into actual ferment, and this ejected from the cell. This is the process which we sometimes speak of as the act of secretion, and it obviously has many analogies with a muscular contraction. Coincident with the disturbances which thus give rise to the ejection of ferment, the constructive metabolism of the cell is excited to greater activity, and for awhile there is an accumulation of new protoplasm in great excess of zymogen. Soon, however, but slowly rather than suddenly, this new protoplasm again breaks down into zymogen, which in turn is stored up in the cell, and so the cycle is completed.

Such may be considered the more common mode of procedure ; and in such a case we are enabled, as in the pancreas or mucous gland, to watch the accumulation and disappearance of the zymogen or mucigen, because this is alternately in excess of or less than the actual protoplasm. But we can easily imagine a case in which all the various stages of the upward and downward metabolism keep pace with each other, in which for instance when any quantity of zymogen is converted into ferment which leaves the cell, just that quantity of zymogen is replaced by a destruction of protoplasm, and a new quantity of protoplasm appears just sufficient to replace the old which has been broken down. In such an instance of continuous changes it would be impossible, with our present means at least to trace out the series of events, though those at bottom would be identical with those where the changes were discontinuous. And indeed it is obvious that this same plan of secretion, if we may so call it, might be made to produce very varied results, by variations in the proportions and rates of the several steps.

Admitting, however, this view of what we may call the protoplasmic aspect of secretion, another feature has to be considered. The juice secreted by any gland consists not only of the specific ferments, trypsin, etc., as the case may be, found in it, but also of a large quantity of water, and of various saline or other soluble substances common to it and other juices. And the question arises, Is this water, or are these salts and soluble substances furnished by the same act as that which supplies the specific constituents?

To this we may reply, that the very water is discharged by the activity of the cell, and is not a mere filtration from the blood-vessels. For, as we have seen in the case of the salivary glands,

when atropin is given, not only do the specific constituents cease to be ejected in spite of the vessels becoming dilated, but the discharge of water is also arrested: no saliva at all leaves the gland. And what is true of the salivary glands probably holds good with the other glands. Assuming then that even the escape of water is the result of the activity of the cell, we cannot but feel an increased interest in the fact mentioned some time ago, that in the submaxillary gland of the dog, stimulation of the chorda tympani produces a copious flow of thin limpid saliva, and stimulation of the cervical sympathetic a scanty flow of thick viscid saliva. That is to say, stimulation of the chorda affects *chiefly* the discharge of water, which carries away with it various soluble matters, while stimulation of the sympathetic chiefly affects the conversion of mucigen into mucin. To this we may add the case of the parotid of the dog. In this stimulation of a cerebro-spinal nerve, the auriculo-temporal produces a copious flow of limpid saliva, while stimulation of sympathetic produces itself little or no secretion at all; but after previous stimulation of the sympathetic, the saliva which flows upon stimulation of the cerebro-spinal nerve is much richer in solid, and especially in organic, matter. And we have already seen that while the microscopic changes after cerebro-spinal stimulation are inappreciable, those following upon sympathetic stimulation are very conspicuous. The latter give rise to certain constituents; while the former, so to speak, wash them away into the duct.

These and other facts, on which we need not now dwell, have led to the conception that the act of secretion consists of two parts, both distinct efforts of the cell, which in one case may coincide, in another may take place apart or in different proportions. On the other hand, there is the discharge of water carrying with it common soluble substances; on the other, the escape of specific substances resulting from the profound metabolism of the cell protoplasm. And it has been supposed that two kinds of nerve-fibres exist, one governing the former process and preponderating in the chorda tympani, for instance, the other governing the latter and preponderating in the branches of the cervical sympathetic. Further hypotheses have been put forward to explain the modus operandi of the discharge of water, such as the existence of substances in the cell which absorb water from the blood or lymph on the one side and give it up on the other side into the lumen of the alveolus. But these matters are not yet ripe for any distinct assertion, and though we have thought it right to bring the matter before our readers, we must not pursue the discussion any further. Whether there be two sets of fibres or no, whether the two processes be absolutely distinct or merely variations of the same fundamental changes, the proposition on

which we have so long dwelt—that the flow of juice from a secreting gland is essentially the outcome of the activity of the secreting cell—remains equally true.

Before we leave the mechanism of secretion, there are one or more accessory points which deserve attention.

In treating just now of the gastric glands, we spoke as if pepsin were the only important constituent of gastric juice, whereas, as we have previously seen, the acid is equally essential. The formation of the free acid of the gastric juice is very obscure, and many ingenious but unsatisfactory views have been put forward to explain it. It seems natural to suppose that it arises in some way from the decomposition of sodium chloride drawn from the blood; and this is supported by the fact that when the secretion of gastric juice is actively going on, the amount of chlorides leaving the blood by the kidney is proportionately diminished; but nothing definite can at present be stated as to the mechanism of that decomposition, though an organic acid such as lactic, which as we have seen appears in the juice, might under certain conditions succeed in decomposing chlorides. And even admitting that the sodium chloride of the body at large is the ultimate source of the chlorine element of the acid, it appears more likely that that element should be set free in the stomach by the decomposition of some highly complex and unstable chlorine compound previously generated, than that it should arise by the direct splitting-up of so stable a body as sodium chloride, at the time when the acid is secreted.

In the frog, while pepsin free from acid is secreted by the glands in the lower portion of the œsophagus, an acid juice is afforded by glands in the stomach itself, which have accordingly been called *oxyntic* (ὀξύνειν, to sharpen, acidulate) glands; but these oxyntic glands appear also to secrete pepsin. In the mammal, the isolated pylorus secretes an alkaline juice; in fact the appearance of an acid juice is limited to those portions of the stomach in which the glands contain both " chief" or " central," and "ovoid" or "border" cells. Now there can be no doubt that the chief cells do secrete pepsin. During life the granules visible in the living chief cells abound or are scanty according as pepsin is about to be or has been secreted, and after death they contain pepsin (or pepsinogen), and that in proportion to their richness in granules. No such correspondence can be seen in the " border " or "ovoid " cells. Hence it has been inferred that the border cells secrete acid; but the argument is one of exclusion only, there being no direct proofs of these cells actually manufacturing the acid.

The rennet ferment appears to be formed by the same cells which manufacture the pepsin—that is, by the chief cells of the

fundus generally, and to some extent by the cells of the pyloric glands. We may add that we have evidence of the existence of a zymogen of the rennet ferment analogous to the zymogen of pepsin or trypsin.

The mucus which is present as a thin layer over the surface of the fasting stomach, and which, especially in herbivorous animals, is increased during digestion, comes from the mucous cells which line the mouths of the several glands and cover the intervening surfaces.

We previously called attention to the fact that in the case of the stomach the absorption of the products of digestion largely increased the activity of the secreting cells. This has led to the idea that one effect of food is to " charge " the gastric cells with pepsinogen, and that certain articles of food might be considered as especially peptogenous—i. e., conducive to the formation of pepsin. Such a view is tempting, but needs as yet to be more fully supported by facts.

Seeing the great solvent power of both gastric and pancreatic juice, the question is naturally suggested, Why does not the stomach digest itself? After death, the stomach is frequently found partially digested—viz., in cases when death has taken place suddenly on a full stomach. In an ordinary death, the membrane ceases to secrete before the circulation is at an end. That there is no special virtue in living things which prevents their being digested is shown by the fact, that the legs of a frog or the ear of a rabbit introduced into a stomach through a fistula are readily digested. It has been suggested that the blood-current keeps up an alkalinity sufficient to neutralize the acidity of the juice in the region of the glands themselves; but this will not explain why the pancreatic juice, which is active in an alkaline medium, does not digest the proteids of the pancreas itself, or why the digestive cells of the bloodless actinozoon or hydrozoon do not digest themselves. We might add, it does not explain why the amœba, while dissolving the protoplasm of the swallowed diatom, does not dissolve its own protoplasm. We cannot answer this question at all at present, any more than the similar one, why the delicate protoplasm of the amœba resists during life all osmosis, while a few moments after it is dead, osmotic effects become abundantly evident.

The secretion of bile needs a few additional words. The analogy of the other glands, and what we already know of the microscopic changes in the hepatic cells, lead us to believe that the secretion of even such a complex fluid as the bile is in the main the result of the direct metabolic activity of the protoplasm of the hepatic cells. And this view is supported by the fact that after extirpation of the liver, no accumulation of the biliary con-

stituents is observed to take place during the few hours of life remaining to the animal after the operation. Still the great complexity of the secretion introduces several very important considerations. In the first place, the liver, unlike the other digestive glands, has a double supply of blood; and vain attempts have been made to settle by direct experiment the question whether the hepatic artery or the vena portæ is the more closely concerned in the production of bile. Ligature of the hepatic artery has sometimes had no effect on the secretion, sometimes has interfered with it. Sudden ligatuie of the vena portæ at once stops the flow of bile; but gradual obliteration may be effected without either causing death or even interfering with the secretion, anastomotic branches forming a collateral circulation, and thus maintaining an efficient flow of blood through the liver. The problem, which is probably a barren one, cannot be settled in this way.

In the second place, the hepatic cells not only secrete bile, but, as we shall see later on, take an active part in other operations of even greater importance. The consideration of the question in what way these several functions of the hepatic cells are related to each other must be deferred for the present.

In the third place, even if we maintain that the chief constituents of the bile are manufactured in the hepatic cells, and not simply drained off from the blood, we are not thereby precluded from admitting that the hepatic cells may avail themselves of certain half-made materials, the arrival of which in the blood may, so to speak, lighten their labors; or that they may even boldly seize upon and pass off as their own handiwork any wholly manufactured constituents which may be offered to them. Thus we have already seen reasons for thinking that the bile-pigments are not made *de novo* in the hepatic cells, but spring from hæmoglobin, the change in the liver being one of comparatively simple transformation. So, also, it is quite possible, though not proved, that much if not all of the cholesterin of bile is merely withdrawn by the liver from the body at large. And even with the central components of bile, the bile salts, we know that in the case of taurocholic acid, taurin is normally present in certain tissues, and that in the case of glycocholic acid, glycin, if not a normal constituent of any tissue, is present in the body, since the body can convert benzoic into hippuric acid, as we shall see in a succeeding section; so that the formation of these bodies by the hepatic cells may be limited to the production of cholalic acid and its conjugation with one or other of the above amido-acids. Moreover, as a matter of fact, we find that the flow of bile from a biliary fistula is much increased by the injection of bile into the small intestine. This experiment renders it possible that

some of the bile which in natural digestion is poured into the intestine is reabsorbed, and carried back to the liver to do duty over again.

In medical practice, distinction is drawn between jaundice by suppression of the secreting functions of the liver and jaundice by retention, brought about by an obstruction existing in some part of the biliary passages. The gravity of the symptoms in the first class of cases shows that an arrest or a too great diminution of the normal functions of the hepatic cells is at least accompanied by the presence in the blood of substances injurious to life; but how far the presence of those substances is due to a failure of the manufacture of bile and the accumulation in the system of the materials for the formation of bile, or to a failure of other functions of the hepatic cells, must be regarded as at present undetermined. The presence of the bile-pigment in this form of jaundice would seem to indicate that the formation of the pigment—*i. e.*, the transformation of hæmoglobin into bilirubin, in contrast to the formation of bile acids, requires but little labor on the part of the cell, and may be carried on even when the nutrition of the cell is highly deranged.

Sec. 3.—The Muscular Mechanisms of Digestion.

From its entrance into the mouth until such remnant of it as is undigested leaves the body, the food is continually subjected to movements having for their object the trituration of the food as in mastication, or its more complete mixture with the digestive juices, or its forward progress through the alimentary canal. These various movements may briefly be considered in detail.

Mastication.—Of this it need only be said that in man it consists chiefly of an up and down movement of the lower jaw, combined, in the grinding action of the molar teeth, with a certain amount of lateral and fore-and-aft movement. The lower jaw is raised by means of the temporal, masseter, and internal pterygoid muscles. The slighter effort of depression brings into action chiefly the digastric muscle, though the mylohyoid and geniohyoid probably share in the matter. Contraction of the external pterygoids pulls forward the condyles, and thrusts the lower teeth in front of the upper. Contraction of the pterygoids on one side will also throw the teeth on to the opposite side. The lower horizontally placed fibres of the temporal serve to retract the jaw.

During mastication, the food is moved to and fro, and rolled

about by the movements of the tongue. These are effected by the muscles of that organ governed by the hypoglossal nerve.

The act of mastication is a voluntary one, guided, as are so many voluntary acts, not only by muscular sense but also by contact sensations. The motor fibres of the fifth cranial nerve convey motor impulses from the brain to the muscles; but paralysis of the sensory fibres of the same nerve renders mastication difficult by depriving the will of the aid of the usual sensations.

Deglutition.—The food when sufficiently masticated is, by the movements of the tongue, gathered up into a bolus on the middle of the upper surface of that organ. The front of the tongue being raised—partly by its intrinsic muscles, and partly by the styloglossus—the bolus is thrust back between the tongue and the palate through the anterior pillars of the fauces or isthmus faucium. Immediately before it arrives there, the soft palate is raised by the levator palati, and so brought to touch the posterior wall of the pharynx, which, by the contraction of the upper margin of the superior constrictor of the pharynx, bulges somewhat forward. The elevation of the soft palate causes a distinct rise of pressure in the nasal chambers; this can be shown by introducing a water manometer into one nostril, and closing the other just previous to swallowing. By the contraction of the palato-pharyngeal muscles which lie in the posterior pillars of the fauces, the curved edges of those pillars are made straight, and thus tend to meet in the middle line, the small gap between them being filled up by the uvula. Through these manœuvres, the entrance into the posterior nares is blocked, while the soft palate forms a sloping roof, guiding the bolus down the pharynx. By the contraction of the stylo-pharyngeus and palato-pharyngeus, the funnel-shaped bag of the pharynx is brought up to meet the descending morsel, very much as a glove may be drawn up over the finger.

Meanwhile, in the larynx, as shown by the laryngoscope, the arytenoid cartilages and vocal cords are approximated; the latter being also raised so that they come very near to the false vocal cords; the cushion at the base of the epiglottis covers the rima glottidis, while the epiglottis itself is depressed over the larynx. The thyroid cartilage is now, by the action of the laryngeal muscles, suddenly raised up behind the hyoid bone, and thus assists the epiglottis to cover the glottis. This movement of the thyroid can easily be felt on the outside. Thus, both the entrance into the posterior nares and that into the larynx being closed, the impulse given to the bolus by the tongue can have no other effect than to propel it beneath the sloping soft palate, over

the incline formed by the root of the tongue and the epiglottis. The palato-glossi or constrictores isthmi faucium, which lie in the anterior pillars of the fauces, by contracting, close the door behind the food which has passed them.

When the bolus of food is large, it is received by the middle and lower constrictors of the pharynx, which, contracting in sequence from above downwards, thrust it into the œsophagus, along which it is driven by a similar series of successive contractions, which we shall speak of immediately as peristaltic action. This comparatively slow descent of the food from the pharynx into the stomach may be readily seen if animals with long necks, such as horses and dogs, be watched while swallowing. Recent observations, however, seem to show that when the morsel is not large, and especially when the substance swallowed is liquid, the movement of the back part of the tongue is sufficient not merely to introduce the food into the grasp of the constrictors of the pharynx, but even to propel it rapidly—to shoot it in fact —along the lax œsophagus before the muscles of that organ have time to contract. In such a mode of swallowing, the middle and lower constrictors take little or no part in driving the food onward, though they and the œsophagus appear to contract from above downwards after the food has passed by them, as if to complete the act and to insure that nothing has been left behind. Deglutition in this fashion still remains possible after the constrictors have become paralyzed by section of their motor nerves.

Deglutition, therefore, though a continuous act, may be regarded as divided into three stages. The first stage is the thrusting of the food through the isthmus faucium; this may be either of long or short duration. The second stage is the passage through the upper part of the pharynx. Here the food traverses a region common both to the food and to respiration, and in consequence the movement is as rapid as possible. The third stage is the descent through the grasp of the constrictors. Here the food has passed the respiratory orifice, and in consequence its passage may again become comparatively slow, or, as we have seen, may continue to be rapid.

The first stage in this complicated process is undoubtedly a voluntary action. The raising of the soft palate and the approximation of the posterior pillars may also be, at times, voluntary, since they have been seen, in a case where the pharynx was laid bare by an operation, to take place before the food had touched these parts; but the movement may take place without any exercise of the will or presence of consciousness. And, indeed, the second stage taken as a whole, though some of the earlier component movements are, as it were, on the borderland between the voluntary and involuntary kingdoms, must be

regarded as a reflex act.   The third and last stage, whatever be the exact form which it takes, is undoubtedly reflex ; the will has no power whatever over it, and can neither originate, stop, nor modify it.

Deglutition, in fact, as a whole, is a reflex act ; it cannot take place unless some stimulus be applied to the mucous membrane of the fauces.   When we voluntarily bring about swallowing movements with the mouth empty, we supply the necessary stimulus by forcing with the tongue a small quantity of saliva into the fauces, or by touching the fauces with the tongue itself.

In the reflex act of deglutition the afferent impulses originated in the fauces are carried up chiefly by the glosso-pharyngeal, but also by branches of the fifth, and by the pharyngeal branches of the superior laryngeal division of the vagus.   The efferent impulses descend the hypoglossal to the muscles of the tongue, and pass down the glosso-pharyngeal, the vagus through the pharyngeal plexus, the fifth, and the facial, to the muscles of the fauces and pharynx ; their exact paths being as yet not fully known, and probably varying in different animals.   The laryngeal muscles are governed by the laryngeal branches of the vagus.

The centre of the reflex act lies in the medulla oblongata. Deglutition can be excited, by tickling the fauces, in an animal rendered unconscious by removal of the brain, provided the medulla be left.   If the medulla be destroyed, deglutition is impossible.   The centre for deglutition lies higher up than that of respiration, so that the former act is frequently impaired or rendered impossible while the latter remains untouched.   It is probable that, as is the case in so many other reflex acts, the whole movement can be called forth by stimuli affecting the centre directly, and not acting on the usual afferent nerves.

Movements of the Œsophagus.—As we have already said, in certain cases at all events, the food is carried down from the pharynx to the stomach in a comparatively slow manner, by the action of the muscular coat of the œsophagus itself.   Contractions of the circular fibres occur in succession from above downwards, driving the food before them, very much as a fluid may be driven along a tube by squeezing it.   The movement is probably assisted by a similarly progressive contraction of the longitudinal muscular coat ; but the exact manner in which this acts is uncertain.   Such a progressive movement, of which we have already spoken on p. 133, and which is much more pronounced in the small intestine than in other parts of the alimentary canal, is spoken of as "peristaltic action."   These peristaltic movements of the œsophagus may, like those of the intestine, be seen after

removal of the organ from the body; and, indeed, may continue to appear upon stimulation, for an unusual length of time. Nevertheless, in the intact body, the movements of the œsophagus seem to be much more closely dependent on the central nervous system than do those of the intestines; the contractions are not, as in the latter case, transmitted from section to section of the tube, but afferent impulses started in the pharynx and passing to the medulla oblongata, give rise to reflex efferent impulses which descend along nervous tracts to successive portions of the organ. If the œsophagus be cut across some way down, or if a portion of the middle region be excised, stimulation of the pharynx will produce a peristaltic contraction, which, travelling downwards, will not stop at the section, but will be continued on into the lower disconnected portion by means of the central nervous system. And it is stated that ordinary peristaltic contractions of the lower part of the œsophagus can be readily excited by stimulation of the pharynx, but not by stimuli applied to its own mucous membrane. In the reflex act which thus brings about the peristaltic contraction of the œsophagus, the afferent nerves are those of the pharynx, viz., the superior laryngeal nerve, branches of the fifth, and in some animals at least branches of the glossopharyngeal, but chiefly the first. The centre lies in the medulla oblongata, being a part of the general deglutition centre; and the efferent impulses pass along fibres of the vagus, reaching the upper part of the œsophagus by the recurrent laryngeal nerves, and the lower part through the plexuses over the root of the lungs and the stomach, to which the vagus gives origin. Section of the trunk of the vagus renders difficult the passage of food along the œsophagus, and stimulation of the peripheral stump causes œsophageal contractions. The force of this movement in the œsophagus is considerable; thus Mosso found that in the dog, a ball pulling by means of a pulley against a weight of 250 grammes was readily carried down from the pharynx to the stomach.

The junction of the œsophagus with the stomach remains in a more or less permanent condition of tonic or obscurely rhythmic contraction, more particularly when the stomach is full of food, and thus serves as a sphincter to prevent the return of food from the stomach into the œsophagus. During the passage of the food from the œsophagus into the stomach, this sphincter becomes relaxed, probably by a mechanism which will be described in treating of vomiting.

Movements of the Stomach.—These are at bottom peristaltic in nature, though largely modified by the peculiar arrangement of the gastric muscular fibres. When food first enters the

stomach, the movements are feeble and slight, but as digestion goes on, they become more and more vigorous, giving rise to a sort of churning within the stomach, the food travelling from the cardiac orifice along the greater curvature to the pylorus, and returning by the lesser curvature, while at the same time subsidiary currents tend to carry the food which has been passing close to the mucous membrane toward the middle of the stomach, and *vice versa*. At the pyloric end strong circular contractions are set up, by which portions of food, more especially the dissolved parts, but also small solid pieces, are carried through the relaxed sphincter into the duodenum. As digestion proceeds, more and more material leaves the stomach, which is thus gradually emptied, the last portions which are carried through being those matters which are least digestible, and foreign bodies which happen to have been swallowed. The presence of food, then, leads to the development of obscurely peristaltic rhythmic movements, the stomach when empty being contracted, but quiescent; but evidently it is not the mere mechanical repletion of the organ which is the cause of the movements, since the stomach is fullest at the beginning when the movements are slight, and becomes emptier as they grow more forcible. The one thing which does increase *pari passu* with the movements is the acidity, which is at a minimum when the (generally alkaline) food has been swallowed, and increases steadily onwards. It has not, however, been definitely shown that the increasing acidity is the efficient stimulus giving rise to the movements.

The nervous mechanism of the gastric movements is at present very obscure. The stomach receives its nervous supply from the vagi and also from the solar plexus, with which the splanchnics are connected. When the vagi are divided, a spasmodic constriction of the cardiac orifice takes place; in other words, the tonic action of the sphincter is increased, and food is thus prevented, for a time at least, from leaving the œsophagus. In addition, the natural movements of the stomach itself cease, or become uncertain and irregular, even if food be present. Incomplete movements may be induced by stimulation of the peripheral stumps of the vagi, when the stomach is full, but not so readily if it be empty. The effects of section or stimulation of the splanchnics or of the branches from the solar plexus are uncertain. Nor do we know the exact mechanism by which the pyloric sphincter is used to strain off gradually the more digested portions of the food. The movements of even a full stomach are said to cease during sleep.

Movements of the Small Intestine.—Though peristaltic movements occur along the whole length of the alimentary canal, from

the œsophagus to the rectum, they are more pronounced in the small intestine than elsewhere.   When the intestines are watched, after opening the abdomen, circular contractions—that is, contractions of the circular coat—may be seen travelling lengthways along the intestine, and often upwards as well as downwards. Similarly, longitudinal contractions—that is, contractions of the longitudinal coat, may also be seen to travel lengthways.   The circular coat being much thicker and stouter than the longitudinal coat, is the more important of the two, and it is by the contractions of the circular coat that in the normal state of things the contents of the intestine are driven along toward the ilio-cæcal valve.   The contractions of the longitudinal coat appear to be chiefly of use in producing peculiar oscillating movements of the pendant loops in which the intestine is arranged.   The rhythmic occurrence of these circular and to and fro movements, together with the passive movements caused by the entrance of the fluid contents into or their exit from the various loops, brings about the peculiar writhing of the intestines which has given rise to the phrase, peristaltic action.

The movements, as we have said, take place from above downwards, and a wave beginning at the pylorus may be traced a long way down.   But contractions may, and in all probability occasionally do, begin at various points along the length of the intestine.   In the living body the intestines have periods of rest, alternating with periods of activity, the occurrence of the periods depending on various circumstances.

With regard to the causation of the peristaltic movements of the intestine, this much may be affirmed, that they may occur, as in a piece of intestine cut out from the body, wholly independently of the central nervous system; and the only nervous elements which can be regarded as essential to their development are the ganglia of Auerbach or those of Meissner in the intestinal walls.   Though the movements can readily be excited by stimuli, applied either to the outside, or, more especially, to the inside of the intestine, they are probably at bottom automatic.   The presence of food, especially of food in motion, may at times act as a stimulus, and may in all cases be a condition affecting the nature and extent of the movement; but cannot be regarded as the real cause of the action.   When any body is introduced into the intestine, a contraction at first occurs, but soon passes off as the intestine becomes accustomed to the presence of the body. There is no reason why the intestine should not become equally accustomed to the presence of food; and, as a matter of fact, peristaltic movements are often absent when the intestines are full.   The presence of food bears about the same relation to the movements of the intestine, that the presence of blood bears to

the beat of the heart. Both are favoring but not indispensable conditions; in both cases the action can go on without them. We may add, that just as the tension of a muscle increases up to a certain extent the amount of its contraction, and a full heart beats more strongly than an empty one, so distention of the intestine largely increases peristaltic action. Hence, in cases of obstruction of the bowels, the movements become distressing by their violence.

Among the chief circumstances affecting peristaltic action may be mentioned in the first place the condition of the blood. A lack of oxygen or an excess of carbonic acid in the blood excites powerful movements. This is well seen in asphyxia, and the powerful post-mortem peristaltic movements witnessed on opening a recently killed animal, as well as those which frequently occur when in the living body the blood-stream is cut off by compression of the aorta, are probably due to the deficiency of oxygen or the accumulation of carbonic acid in the blood and tissues of the intestinal walls. Conversely, saturation of the blood with oxygen, as in the peculiar condition known as apnœa (see chapter on Respiration), tends to check peristaltic movements.

In the second place, peristaltic action is largely influenced by nervous influences passing along the splanchnic and vagus nerves. The movements will go on after section of both these nerves; but as a general rule, while stimulation of the splanchnic tends to check, that of the vagus tends to excite them; but much has probably yet to be learnt about the exact manner in which these nerves act. It is probably through the vagus that peristaltic movements can be effected in an indirect manner, as in that increase of the movements of the intestine in consequence of emotions, which has given rise to the phrase, "my bowels yearned."

When the vagus is stimulated, peristaltic contraction is seen to begin at the pylorus of the stomach, and so to descend along the intestine. When, however, the duodenum is mechanically stimulated, both a peristaltic and an antiperistaltic wave—that is, a wave of contraction passing upwards instead of downwards, may be observed, the former passing downward, and ceasing at the ileo-cæcal valve if not before, the latter passing up and ceasing at the pylyrus. And when in the exposed intestines a wave, as occasionally happens, begins spontaneously in the duodenum, it may sometimes be seen to pass both upwards and downwards. It is worthy of notice, that stimulation of the small intestine is said not to cause movement either in the stomach or large intestine, and stimulation of the large intestine or of the stomach causes no movement of the small intestine, the ilio-cæcal valve and the pylorus barring the progress of the waves.

Certain drugs, such as nicotin, induce strong peristaltic action; the modus operandi of these and of the more specific purgative drugs is at present uncertain.

Movements of the Large Intestine.—These are fundamentally the same as those of the small intestine, but distinct in so far as the latter cease at the ileo-cæcal valve, at which spot the former normally begin.   They are said, moreover, not to be inhibited by stimulation of the splanchnics.

The feces in their passage through the colon are lodged in the sacculi during the pauses between the peristaltic waves.   Arrived at the sigmoid flexure, they are supported by the bladder and the sacrum, so that they do not press on the sphincter ani.

Defecation.—This is a mixed act, being superficially the result of an effort of the will, and yet carried out by means of an involuntary mechanism.   Part of the voluntary effort consists in producing a pressure-effect, by means of the abdominal muscles. These are contracted forcibly as in expiration, but the glottis being closed, and the escape of air from the lungs prevented, the whole force of the pressure is brought to bear on the abdomen itself, and so drives the contents of the descending colon onward into the rectum.   The sigmoid flexure is by its position sheltered from this pressure; a body introduced per anum into the empty rectum is not affected by even forcible contractions of the abdominal walls.

The anus is guarded by the sphincter ani, which is habitually in a state of normal tonic contraction, capable of being increased or diminished by a stimulus applied, either internally or externally, to the anus.   The tonic contraction is in part at least due to the action of a nervous centre situated in the lumbar spinal cord.   If the nervous connection of the sphincter with the spinal cord be broken, relaxation takes place.   If the spinal cord be divided in the dorsal region, the sphincter, after the depressing effect of the operation, which may last several days, has passed off, still maintains its tonicity, showing that the centre is not placed higher up than the lumbar region of the cord.   The increased or diminished contraction following on local stimulation is probably due to reflex augmentation or inhibition of the action of this centre.   The centre is also subject to influences proceeding from higher regions of the cord, and from the brain.   By the action of the will, by emotions, or by other nervous events, the lumbar sphincter centre may be inhibited, and thus the sphincter itself relaxed ; or augmented, and thus the sphincter tightened.   A second item, therefore, of the voluntary process in defecation is the inhibition of the lumbar sphincter centre, and

consequent relaxation of the sphincter muscle. Since the lumbar centre is wholly efficient when separated from the brain, the paralysis of the sphincter which occurs in certain cerebral diseases is probably due to inhibition of this centre, and not to paralysis of any cerebral centre.

Thus, a voluntary contraction of the abdominal walls, accompanied by a relaxation of the sphincter, might press the contents of the descending colon into the rectum and out of the anus. Since, however, as we have seen, the pressure of the abdominal walls is warded off the sigmoid flexure, such a mode of defecation would always end in leaving the sigmoid flexure full. Hence the necessity for these more or less voluntary acts being accompanied by an entirely involuntary augmentation of the peristaltic action of the large intestine and sigmoid flexure. Or rather, to describe matters in their proper order, defecation takes place in the following manner : The sigmoid flexure and large intestine becoming more and more full, stronger and stronger peristaltic action is excited in their walls. By this means the feces are driven against the sphincter. Through a voluntary act, or sometimes, at least, by a simple reflex action, the lumbar sphincter centre is inhibited and the sphincter relaxed. At the same time the contraction of the abdominal muscles presses firmly on the descending colon, and thus the contents of the rectum are ejected.

It must, however, be remembered that, while in appealing to our own consciousness, the contraction of the abdominal walls and the relaxation of the sphincter seem purely voluntary efforts, the whole act of defecation, including both of these seemingly so voluntary components, may take place in the absence of consciousness, and, indeed, in the case of the dog at least, after the complete severance of the lumbar from the dorsal cord. In such cases the whole act must be purely reflex, excited by the presence of feces in the rectum.

Vomiting.—In a conscious individual this act is preceded by feelings of nausea, during which a copious flow of saliva into the mouth takes place. This being swallowed, carries down with it a certain quantity of air, the presence of which in the stomach, by assisting in the opening of the cardiac sphincter, subsequently facilitates the discharge of the gastric contents. The nausea is generally succeeded at first by ineffectual retching in which a deep inspiratory effort is made, so that the diaphragm is thrust down as low as possible against the stomach, the lower ribs being at the same time forcibly drawn in ; since during this inspiratory effort the glottis is kept closed, no air can enter into the lungs ; but some is drawn into the pharynx, and thence probably de-

scends by a swallowing action into the stomach. In actual vomiting this inspiratory effort is succeeded by a sudden violent expiratory contraction of the abdominal walls, the glottis still being closed, so that the whole force of the effort is spent, as in defecation, in pressure on the abdominal contents. The stomach is therefore forcibly compressed from without. At the same time, or rather immediately before the expiratory effort, by a contraction of its longitudinal fibres the œsophagus is shortened and the cardiac orifice of the stomach brought close under the diaphragm, while apparently by a contraction of the fibres which radiate from the end of the œsophagus over the stomach, the cardiac orifice, which is normally closed, is somewhat suddenly dilated. This dilation opens a way for the contents of the stomach, which, pressed upon by the contraction of the abdomen, and to a certain but probably only to a slight extent by the contraction of the gastric walls, are driven forcibly up the œsophagus, their passage along that channel being possibly assisted by the contraction of the longitudinal muscles. The mouth being widely open, and the neck stretched to afford as straight a course as possible, the vomit is ejected from the body. At this moment there is an additional expiratory effort which serves to prevent the vomit passing into the larynx. In most cases, too, the posterior pillars of the fauces are approximated, in order to close the nasal passage against the ascending stream. This, however, in severe vomiting is frequently ineffectual.

Thus, in vomiting there are two distinct acts: the dilation of the cardiac orifice and the extrinsic pressure of the abdominal walls in an expiratory effort. Without the former the latter, even when distressingly vigorous, is ineffectual. Without the latter, as in urari poisoning, the intrinsic movements of the stomach itself are rarely sufficient to do more than eject gas, and, it may be, a very small quantity of food or fluid. Pyrosis or waterbrash is probably brought about by this intrinsic action of the stomach.

During vomiting, the pylorus is generally closed, so that but little material escapes into the duodenum. When the gall-bladder is full, a copious flow of bile into the duodenum accompanies the act of vomiting. Part of this may find its way into the stomach, as in bilious vomiting, the pylorus then having evidently been opened.

The nervous mechanism of vomiting is complicated and in many aspects obscure. The efferent impulses which cause the expiratory effort must come from the respiratory centre in the medulla; with these we shall deal in speaking of respiration. The dilation of the cardiac orifice is caused, in part at least, by efferent impulses descending the vagi, since when these are cut

real vomiting with discharge of the gastric contents is difficult, through want of readiness in the dilation. The sympathetic abdominal nerves coming from the cœliac ganglia and the splanchnic nerves seem to have no share in the matter. The efferent impulses which cause the flow of saliva in the introductory nausea descend the facial along the chorda tympani branch. These various impulses may best be considered as starting from a vomiting centre in the medulla, having close relations with the respiratory centre. This centre may be excited, may be thrown into action, in a reflex manner, by stimuli applied to peripheral nerves, as when vomiting is induced by tickling the fauces, or by irritation of the gastric membrane, or by obstruction due to ligature, hernia, etc., of the intestine. That the vomiting in the last instance is due to nervous action, and not to any regurgitation of the intestinal contents, is shown by the fact that it will take place when the intestine is perfectly empty and may be prevented by section of the mesenteric nerves. The vomiting attending renal and biliary calculi is apparently also reflex in origin. The centre however may be affected directly, as probably in the cases of some poisons, and in some instances of vomiting from disease of the medulla oblongata. Lastly, it may be thrown into action by impulses reaching it from parts of the brain higher up than itself, as in cases of vomiting, produced by smells, tastes, and emotions, and by the memory of past occasions, and in some cases of vomiting due to cerebral disease.

Many emetics, such as tartar emetic, appear to act directly on the centre, since, introduced into the blood, they will produce vomiting even when a bladder is substituted for the stomach. Others again, such as mustard and water, act in a reflex manner by irritation of the gastric mucous membrane. With others, again, which cause vomiting by developing a nauseous taste, the reflex action involves parts of the brain higher than the centre itself.

Sec. 4.—The Changes Which the Food Undergoes in the Alimentary Canal.

Having studied the properties of the digestive juices, and the various mechanisms by means of which the food is brought under their influence, we have now to consider what, as matters of fact, are the actual changes which the food does undergo in passing along the alimentary canal, what are the steps by which the food is converted into feces.

In the mouth the presence of the food, assisted by the movements of the jaw, causes, as we have seen, a flow of saliva. By

mastication, and by the addition of mucous saliva, the food is broken into small pieces, moistened, and gathered into a convenient bolus for deglutition. In man some of the starch is, even during the short stay of the food in the mouth, converted into sugar ; for if boiled starch free from sugar be even momentarily held in the mouth, and then ejected into water (kept boiling to destroy the ferment), it will be found to contain a decided amount of sugar. In many animals no such change takes place. The viscid saliva of the dog serves almost solely to assist in deglutition ; and even the longer stay which food makes in the mouth of the horse is insufficient to produce any marked conversion of the starch it may contain. During the rapid transit through the œsophagus no appreciable change takes place.

In the stomach, the arrival of the food, the reaction of which is either naturally alkaline, or is made alkaline, or at least is reduced in acidity, by the addition of saliva, causes a flow of gastric juice. This, already commencing while the food is as yet in the mouth, increases as the food accumulates in the stomach, and as, by the churning gastric movements, unchanged particles are continually being brought into contact with the mucous membrane. Moreover, the absorption of the earlier digested portions gives rise to a further increase of secretion, and especially of pepsin. The percentage of pepsin in the gastric juice (in the dog) varies considerably, actually sinking during the earlier stages, but rising rapidly afterwards, and attaining a maximum at about the fourth or fifth hour. The secretion of acid appears to continue at a fairly constant rate ; and consequently, unless neutralized by fresh alkaline food, the reaction of the gastric contents becomes more and more distinctly acid as digestion proceeds. It would appear that in man, sometimes at least, the contents of the stomach do not at first contain any free acid, and during this period the conversion of starch into sugar can still go on. When the contents become acid, the conversion is arrested, and indeed the amylolytic ferment probably destroyed. The fats themselves probably remain in great measure unchanged ; though it would appear that in the dog at least a certain amount of fat can be digested—that is, emulsionized, or even partly split up into fatty acids, by the action of the gastric juice, and absorbed. Moreover, even in man, through the conversion of proteids into peptone, not only are the more distinctly proteid articles of food, such as meat, broken up and dissolved, but the proteid framework, in which the starch and fats are frequently embedded, is loosened, the starch-granules are set free, and the fats, melted for the most part by the heat of the stomach, tend to run together in large drops, which in turn are more or

less apt to be broken up into an imperfect emulsion. The collagenous tissues are dissolved ; and hence the natural bundles of meat and vegetables fall asunder ; the muscular fibre splits up into disks, and the protoplasm is dissolved from the vegetable cells. Milk is at once curdled by the rennet ferment, and the clotted casein subsequently dissolved. Since peptone and the other products of artificial digestion with gastric juice have been found in the contents of the stomach, we have every reason to believe that natural digestion in the stomach agrees with the results of laboratory experiments described in a previous section. While these changes are proceeding, the thick, turbid, grayish liquid or chyme, formed by the imperfectly dissolved food, is, from time to time, ejected through the pylorus, accompanied by even large morsels of solid less-digested matter. This may occur within a few minutes of food having been taken ; but larger escape from the stomach probably does not, in man, begin till from one to two, and lasts from four to five hours, after the meal, becoming more rapid towards the end, and such pieces as most resist the gastric juice being the last to leave the stomach.

The time taken up in gastric digestion probably varies not only with different articles of food, but also with varying conditions of the stomach and of the body at large. In different animals, it varies very considerably, being from twelve to twenty-four hours in the dog, while the stomachs of rabbits are never empty, but always remain largely filled with food.

In a dog fed on an exclusively meat diet, nearly the whole of the digestion is carried out by the stomach, very little work apparently being left for the intestines. In man, especially on a mixed diet, the case in all probability is different, a considerable portion of the proteids, as well as the greater part of the fats and carbohydrates, passing but little changed through the pylorus. But our information on this matter is imperfect, being chiefly drawn from the study of cases of gastric or duodenal fistula, in which, probably, the order of things is not normal, or being in large measure deductions from experiments on dogs, whose economy in this respect must be largely different from our own.

In the presence of healthy gastric juice, and in the absence of any nervous interference, the question of the digestibility of any food is determined chiefly by mechanical conditions. The more finely divided the material, and the less the proteid constituents are sheltered by not easily soluble envelopes, such as those of cellulose, the more rapid the solution. So, also, pieces of hard-boiled egg, which have to be gradually dissolved from the outside, are less easily digested than the more friable muscular fibre, the repeated transverse cleavage of which increases the surface

exposed to the juice. Unboiled white of egg, again, unless thoroughly beaten up and mixed with air, is less digestible than the same boiled. The unboiled white forms a viscid clotted mass, of low diffusibility, into which the juice permeates with the greatest difficulty. And so with the other instances. Beyond this mechanical aspect of digestibility, it is to be remembered that different substances may differently affect the gastric membrane, promoting or checking the secretion of the juice. Hence, a substance, the mass of which is readily dissolved by gastric juice, and which offers no mechanical obstacles to digestion, may yet prove indigestible by so affecting the gastric membrane through some special constituent (or possibly in other ways) as to inhibit the secretion of the juice.

That substances can be absorbed from the cavity of the stomach into the circulation is proved by the fact that food when introduced disappears very largely from the stomach of an animal, the pylorus of which has been ligatured. But we cannot speak with certainty as to what extent in ordinary life gastric absorption takes place, or by what mechanism it is carried out. The presumption is, that peptone and the diffusible sugars pass by osmosis direct into the capillaries, and so into the gastric veins. In a dog fed on meat, the quantity of peptone present at any one time in the stomach has been found fairly constant. From this, it may fairly be inferred that the peptone is absorbed in proportion as it is formed.

In the act of swallowing, no inconsiderable quantity of air is carried down into the stomach, entangled in the saliva, or in the food. This is returned in eructations. When the gas of eructation or that obtained directly from the stomach is examined, it is found to consist chiefly of nitrogen and carbonic acid, the oxygen of the atmospheric air having been largely absorbed. In most cases the carbonic acid is derived by simple diffusion from the blood, or from the tissues of the stomach, which similarly take up the oxygen. In many cases of flatulency, however, it may arise from a fermentative decomposition of the sugar which has been taken as such in food, or which has been produced from the starch, the gas being either formed in the stomach or passing upwards from the intestine through the pylorus.

The enormous quantity of gas which is discharged through the mouth in cases of hysterical flatulency, even on a perfectly empty stomach, and which seems to consist largely of carbonic acid, presents difficulties in the way of explanation ; it is possible that it may be simply diffused from the blood.

In the small intestine, the semi-digested acid food, or chyme, as it passes over the biliary orifice, causes gushes of bile, and at

the same time, as we have seen (p. 325), the pancreatic juice, which flowed freely into the intestine at the taking of the meal, is secreted again with renewed vigor, when the gastric digestion is completed. These two alkaline fluids tend to neutralize the acidity of the chyme, but the contents of the duodenum do not become distinctly alkaline until some distance from the pylorus is reached. Even in the lower part of the ileum the chyme may be acid; possibly, however, in such cases it has been reacidified in consequence of acid fermentations taking place in the intestinal contents. The reaction of these contents appears to vary, in fact, according to the nature of the food, the changes which it undergoes, and other circumstances. Moreover, it is probably not the same in all animals. In a dog fed on starch and fat, the contents of the intestine may remain acid throughout.

The conversion of starch into sugar, which, as we have seen, is probably arrested in the stomach, is resumed with great activity and indeed completed by the pancreatic juice, possibly assisted by the succus entericus; portions, however, of still undigested starch may be found in the large intestine and even at times in the feces.

The pancreatic juice, as we have seen, emulsifies fats, and also splits them into their respective fatty acids and glycerine. The fatty acids thus set free become converted by means of the alkaline contents of the intestine into soaps, but to what extent saponification thus takes place is not exactly known. Undoubtedly soaps have to a small extent been found both in portal blood and in the thoracic duct after a meal, but there is no proof that any large quantity of fat is introduced in this form into the circulation. On the other hand, the presence of neutral fats, both in portal blood, and especially in the lacteals, is a conspicuous result of the digestion of fatty matters, and in all probability saponification in the intestine is a subsidiary process, intended rather to facilitate the emulsion of neutral fats than to introduce soaps as such into the blood. For the presence of soluble soaps favors the emulsion of neutral fats. Thus a rancid fat—*i. e.*, a fat containing a certain amount of free fatty acid, forms an emulsion with an alkaline fluid more readily than does a neutral fat. A drop of rancid oil let fall on the surface of an alkaline fluid, such as a solution of sodium carbonate of suitable strength, rapidly forms a broad ring of emulsion, and that even without the least agitation. As saponification takes place at the junction of the oil and alkaline fluid currents are set up, by which globules of oil are detached from the main drop and driven out in a centrifugal direction. The intensity of the currents and the consequent amount of emulsion depend on the concentration of the alkaline medium and on the solubility of the soaps which are

formed; hence some fats, such as cod-liver oil, are much more
easily emulsionized in this way than others. Now, the bile and
pancreatic juice supply just such conditions as the above for
emulsionizing fats; they both together afford an alkaline me-
dium, the pancreatic juice gives rise to an adequate amount
of free fatty acid, and the bile in addition brings into solution
the soaps as they are formed. So that we may speak of the
emulsion of fats in the small intestine as being carried on by
the bile and pancreatic juice acting in conjunction, and as a
matter of fact the bile and pancreatic juice do largely emulsify
the contents of the small intestine, so that the grayish turbid
chyme is changed into a creamy looking fluid, which has been
sometimes called chyle. It is advisable, however, to reserve
this name for the contents of the lacteals.

This mutual help of bile and pancreatic juice in producing an
emulsion, explains to a certain extent the controversy which long
existed between those who maintained that the bile and those
who maintained that the pancreatic juice was necessary for the
digestion and absorption of fatty food. That the pancreatic
juice does produce in the intestine such a change as favors the
tranference of neutral fats from the intestine into the lacteals,
is shown by the fact that in diseases affecting the pancreas, much
fatty food frequently passes through the intestine undigested,
and great wasting ensues; but it cannot be maintained that the
pancreatic juice is the sole agent in this matter, since in animals
in which the pancreatic ducts have been successfully ligatured
chyle is still found in the lacteals. On the other hand, that the
bile is of use in the digestion of fat is shown by the prevalence
of fatty stools in cases of obstruction of the bile-ducts, and though
the operation of ligaturing the bile-ducts, and leading all the
bile externally through a fistula of the gall-bladder, is open to
objection, since it so exhausts the animal as indirectly to affect
digestion, still the results of Bidder and Schmidt, in which the
resorption of fat was distinctly lessened (the quantity of fat in
the lacteals falling from 3.2 to 0.02 per cent.) by the ligature and
fistula, obviously point to the same conclusion. That in man
the succus entericus possesses a wholly insufficient emulsifying
power is shown by the observation of Busch, in the case where
the duodenum opened on the surface by a fistula in such a way
that the lower part of the intestine could be kept free from the
contents of the upper part containing the bile and pancreatic
juice and matters proceeding from the stomach. Fats introduced
into the lower part, where they could not be acted upon either
by the bile or by the pancreatic juice, were but slightly digested.
Without denying the possible assistance of the succus entericus,
or even of gastric juice, we may conclude that the digestion of

fat is in the main carried out by the conjoint action of bile and pancreatic juice.

We have seen that the addition of bile to a digesting mixture gives rise to a precipitate consisting of parapeptone, and bile salts with some pepsin, but that on the further addition of bile this precipitate is redissolved. In the upper part of the duodenum the inner surface, if examined while digestion is going on, is found to be lined by a colored granular material, which is probably a precipitate thus formed; but the purpose of its formation does not seem clear. It is more important to remember that not only is bile antagonistic to peptic digestion, but apparently pepsin is destroyed by trypsin in an alkaline medium, so that with the flow of bile and pancreatic juice into the duodenum the processes which have been going on in the stomach come to an end. In fact it would seem that the juices of the various districts of the alimentary canal are mutually destructive; thus, while pepsin in an acid solution destroys the active constituents of saliva, and of pancreatic juice (probably also those of the succus entericus), it is in its turn antagonized or destroyed by the bile and the other alkaline juices of the intestine. Hence pancreatic juice introduced through the mouth must lose its powers in the stomach and can only be of use as an alkaline medium containing certain proteid matters. On the other hand if, as we have reason to believe, the contents of the stomach as they issue from the pylorus still contain a large quantity of undigested proteids, these must be digested by the pancreatic juice (with or without the assistance of the succus entericus), the action of which seems to be assisted or at least not hindered by bile. To what stage the pancreatic digestion is carried, whether peptone is chiefly formed, and when formed at once absorbed, or whether the pancreatic juice in the body, as out of the body, carries on its work in the more destructive form, whereby the proteid material subjected to it is broken down largely into leucin and tyrosin, is at present not exactly known. Leucin and tyrosin have been found in the intestinal contents, and may therefore be formed during normal digestion, but whether a large quantity or a small quantity of the proteid material of food is thus hurried into a crystalline form cannot be definitely stated. The extent to which the action is carried is probably different in different animals, and varies also according to the nature of the meal and the condition of the body. Possibly when a large and unnecessary quantity of proteid material is taken at a meal together with other substances, no inconsiderable amount of the proteids undergo this profound change, and, as we shall see, rapidly leave the body as urea, without having been used by the tissues, their contribution to the energy of the body being limited to the heat given out during their formation. To

this apparently wasteful use of proteids we shall return in speaking of what is called the "luxus consumption" of food.

Possibly also, in the intestines as in the laboratory, this pancreatic digestion of proteids in excess is accompanied by a considerable development of bacteria and other organized bodies, which create trouble by inducing fermentative changes in the accompanying saccharine constituents of the chyme. That fermentative changes may occur in the small intestine is indicative by the facts that the gas present there may contain free hydrogen, and that chyme after removal from the intestine continues at the temperature of the body to produce carbonic acid and hydrogen in equal volumes. This suggests the possibility of the sugar of the intestinal contents undergoing the butyric acid fermentation (during which, as is well known, carbonic anhydride and hydrogen are evolved) and thus, so to speak, put on its way to become fat; and we shall see hereafter that sugar is somewhere in the body converted into fat. Moreover it is probable that by other fermentative changes a considerable quantity of sugar is converted into lactic acid, since this acid is found in increasing quantities as the food descends the intestine.

Thus during its transit through the small intestine by the action of the bile and pancreatic juice, assisted possibly to some extent by the succus entericus, the proteids are largely dissolved and converted into peptone and other products, the starch is changed into sugar, the sugar possibly being in part further converted into lactic acid, and the fats are largely emulsified, and to some extent saponified. These products, as they are formed, pass into either the lacteals or the portal bloodvessels, so that the contents of the small intestine, by the time they reach the ileocaecal valve, are largely but by no means wholly deprived of their nutritious constituents. As far as water is concerned, the secretion into the small intestine is about equal to the absorption from it, so that the intestinal contents at the end of the ileum, though much more broken up, are about as fluid as in the duodenum.

In the large intestine the contents become once more distinctly acid. This, however, is not caused by any acid secretion from the mucous membrane; the reaction of the intestinal walls in the large as in the small intestine is alkaline. It must, therefore, arise from acid fermentations going on in the contents themselves; and that fermentations do go on is shown by the appearance of marsh gas as well as hydrogen in this portion of the alimentary canal. The character and amount of fermentation probably depend largely on the nature of the food and probably also vary in different animals.

Of the particular changes which take place in the large intestine, we have no definite knowledge; but it is exceedingly probable that in the voluminous cæcum of the herbivora, a large amount of digestion of a peculiar kind goes on. We know that in herbivora a considerable quantity of cellulose disappears in passing through the alimentary canal, and even in man some is probably digested. It seems probable that this cellulose digestion is carried on in the large intestine, though we know nothing of the nature of the agency by which it is effected, and possibly the conversion may take place elsewhere as well; indeed, recent evidence goes to show that in ruminants the change takes place in part in the stomach, and that it is effected by the saliva. The other digestive changes are probably of a fermentative kind.

Be this as it may, whether digestion, properly so called, is all but complete at the ileo-cæcal valve, or whether important changes still await the chyme in the large intestine, one great characteristic of the work done in the colon is absorption. By the abstraction of all the soluble constituents, and especially by the withdrawal of water, the liquid chyme becomes, as it approaches the rectum, converted into the firm solid feces, and the color shifts from the bright orange, which the gray chyme gradually assumes after admixture with bile, into a darker and dirtier brown.

In the feces there are found, in the first place, the indigestible and undigested constituents of the meal: shreds of elastic tissue, hairs and other corneous elements, much cellulose and chlorophyll from vegetable, and some connective tissue from animal food, fragments of disintegrated muscular fibre, fat-cells, and not unfrequently undigested starch-corpuscles. The amount of each must, of course, vary very largely, according to the nature of the food, and the digestive powers, temporary or permanent, of the individual. In the second place, to these must be added substances, not introduced as food, but arising as part of, or as products of, the digestive secretions. The feces contain a ferment similar to pepsin, and an amylolytic ferment similar to that of saliva or pancreatic juice. They also contain mucus in variable amount, sometimes albumin, cholesterin, butyric, and other fatty acids, lime and magnesia soaps, *excretin* (a non-nitrogenous crystalline body, containing sulphur, obtained by Marcet), coloring matters, and salts, especially those of magnesia. Cholalic acid (and dyslysin) are found in very small quantities only, thus indicating that the bile salts have been, in part at least, destroyed (they may have been in part reabsorbed, see p. 342), the less stable taurocholic acid (of the dog) disappearing more readily than the glycocholic acid (of the cow). The fact that the feces

become "clay-colored" when the bile is cut off from the intestine shows that the bile-pigment is at least the mother of the fecal pigment; and a special pigment, which has been isolated and called stercobilin, is said to be identical with the substance called urobilin, which may be formed from bilirubin.[1]   We have already seen that during artificial pancreatic digestion, a distinctly fecal odor due to the presence of indol is generated; and the fact that the presence of bacteria, or other similar organisms, is essential to the production of this body, does not preclude the possibility of it (or of the allied body *skatol*, having an evil fecal odor, formed after prolonged putrefaction of the pancreas and present in human excrement) being the chief cause of the natural odor of feces, for undoubtedly bacteria may exist throughout the whole length of the intestinal canal.   At the same time it is quite possible that specific odoriferous substances may be secreted directly from the intestinal wall, especially from that of the large intestine.

SEC. 5.—ABSORPTION OF THE PRODUCTS OF DIGESTION.

We have seen that absorption does, or at least may, take place from the stomach,   We have also stated that a large absorption, especially of water, occurs along the whole large intestine.   We may add that absorption from the large intestine after injection *per anum* or through a fistula has been observed not only in the case of soluble peptone and sugar, but also in that of starch, white of egg, and casein, though the exact changes undergone by the latter previous to absorption are as yet unknown.

Nevertheless the largest and most important part of the digested material passes away from the canal, during the transit of food along the small or large intestine, partly into the lacteals, partly into the portal vessels.   The portal vessels are simply parts of the general vascular system, but the lacteals, into which we may at once say the greater part of the fat passes, need special attention.

The Lymphatics.

Characters of Chyle.—In a fasting animal the contents of the thoracic duct are clear and transparent; shortly after a meal they become milky and opaque, the change being entirely due to a difference in the quality and quantity of the fluid brought to the duct by the lacteals, that fluid also being, as seen by inspection of the mesentery, transparent during fasting, and becoming

[1] See Appendix.

milky and opaque after a meal, especially after one containing much fat. The contents of the thoracic duct, therefore, after a meal may be taken as illustrative of the nature of the chyle present in the lacteals, though strictly speaking the chyle of the thoracic duct is mixed with lymph coming from the intestines and from the rest of the body. During fasting the contents of the lacteals agree in their general character with lymph obtained from other structures.

The contents of the thoracic duct may be obtained by laying bare the junction of the subclavian and jugular veins and introducing a canula into the duct as it enters into the venous system at that point. The operation is not unattended with difficulties.

Chyle obtained from the thoracic duct, after a meal, is a white milky-looking fluid, which after its escape coagulates, forming a not very firm clot. The nature of the coagulation seems to be exactly the same as that of blood. The surface of the clot after exposure to air becomes pink, even though no blood be artificially mixed with the chyle during the operation; the color is due to immature red corpuscles proper to the chyle. Examined microscopically, the coagulated chyle consists of fibrin, a large number of white corpuscles, a small number of developing red corpuscles, an abundance of oil-globules of various sizes but all small, and a quantity of fatty granules, too minute to be recognized under the microscope as fatty in nature, forming the so-called "molecular basis." Each oil-globule is invested with an albuminous envelope; this may be dissolved by the aid of alkalies, whereupon the globules run together. The fibrin and white corpuscles are very scanty (and the red corpuscles entirely absent) in lymph or chyle taken from peripheral vessels; but they increase in quantity as the lymph passes through the lymphatic glands.

The composition of chyle varies considerably not only in different animals but in the same animal at different times. The average percentage of solids may perhaps be put down as about 9, that of proteid material as about 4 or 5, and that of fat as about 3 or 4 (though the latter may sometimes rise as high as 14), the remainder being extractives and salts. The fats occur chiefly in the form of neutral fats, though some soaps or fatty acids are present. Some amount of lecithin, and cholesterin in considerable quantity, are also frequently present.

The proteids consist chiefly of serum-albumin, with a globulin, probably paraglobulin, and a variable but small quantity of fibrin. Among the extractives have been found sugar, urea, and leucin; since these are found in lymph as well as chyle, they cannot be regarded as derived exclusively from the intestinal

contents. The ash is remarkable for the abundance of sodium chloride and the scantiness of phosphates. Iron is present in greater quantity than can be accounted for by the presence of red corpuscles.

The nature of the fat is supposed to vary with that of the food, but this has not been conclusively shown.

The lymph taken from the duct during fasting differs chiefly from that taken after a meal, in the much smaller quantity of fat, the microscope showing besides the white corpuscles only very few oil-globules, and in the almost entire absence of the molecular basis. Lymph in fact is, broadly speaking, blood *minus* its red corpuscles, and chyle is lymph *plus* a very large quantity of minutely divided neutral fat.

It has been calculated that a quantity equal to that of the whole blood may pass through the thoracic duct in twenty-four hours, and of this it is supposed that about half comes from food through the lacteals and the remainder from the body at large; but these calculations are based on uncertain data.

Entrance of the Chyle into the Lacteals.—The lacteal begins as a club-shaped (or bifurcate) lymphatic space lying in the centre of the villus, and connected with the smaller lymphatic spaces of the adenoid tissue around it; it opens below into the submucous lymphatic plexus from which the lacteal vessels spring. The adenoid tissue of the surrounding crypts of Lieberkühn is by its lymphatic spaces connected with the same lymphatic plexus. That the finely divided fat does pass from the intestine, through the epithelial envelope of the villus, into the adenoid tissue, and so into the lacteal chamber, is certain, but much discussion has arisen as to the exact mechanism of the transit. Most observers agree that after a meal the epithelium cells of the villus are loaded with fat and that this fat is derived from the intestinal contents, Since the striation of the hyaline border of the cells is not due to pores, as was once thought, the particles must have entered into the cells very much as foreign particles enter the body of an amœba. The epithelium may thus be said to eat the fat, and subsequently to pass it on into the lymphatic spaces of the adenoid tissue of the villus and so into the central lymphatic chamber. There would thus be a stream of fatty particles through the cell from without inwards, a stream in the causation of which the cell took an active part. In fact, under this view, absorption by the cell might be regarded as a sort of inverted secretion, the cell taking much material from the chyme and secreting it, with little or no change, into the villus. Other observers, however, believe that the fat passes not through but between the epithelium-cells, being taken by the

interepithelial processes of the peculiar epithelioid cells, described as forming a continuous protoplasmic reticulum, connecting the surface of the villus with the central chamber. Along this reticulum the fat is supposed to travel, the epithelium-cells themselves having no active share in absorption.

The passage is probably assisted by the movements of the intestine, though even in the contractions of strong peristaltic movements the pressure within the intestine is never very great. Of more obvious use is the contraction of the villus itself. The longitudinal muscular fibre-cells, in contracting, pull down the villus on itself; the contents of the lacteal chamber are thus forced into the underlying lymphatic plexus. When the fibre-cells relax, the empty lacteal chamber is expanded; the chyle cannot flow back from the lymphatic channels by reason of the valves present in them, and in consequence the lacteal chamber is filled from the substance of the villus, and thus the entrance into the villus of material from the intestine is facilitated. The villus in fact acts as a kind of muscular suction-pump.

Movements of the Chyle.—Having reached the lymphatic channels the onward progress of the chyle is determined by a variety of circumstances. Putting aside the pumping action of the villi, the same events which cause the movement of the lymph generally also further the flow of the chyle; and these are briefly as follows. In the first place, the wide-spread presence of valves in the lymphatic vessels causes every pressure exerted on the tissues in which they lie to assist in the propulsion forward of the lymph. Hence all muscular movements increase the flow. If a canula be inserted in one of the larger lymphatic trunks of the limb of a dog, the discharge of lymph from the canula will be more distinctly increased by movements, even passive movements, of the limb than by anything else. In addition to the valves along the course of the vessels, the embouchement of the thoracic duct into the venous system is guarded by a valve, so that every escape of lymph or chyle from the duct into the veins becomes itself a help to the flow. In the second place, we have already seen that the blood-pressure in the capillaries and minute vessels is considerably greater than that in the large veins, such as the jugular; in fact, this difference of pressure is the cause of the flow of blood from the capillaries to the heart. Now the lymph in the lymphatic spaces outside the capillaries and minute vessels undoubtedly stands at a lower pressure than the blood inside the capillaries; otherwise the transudation from the blood into the tissues would be checked; but the difference is probably not great. So that the lymph in the lymphatic spaces of the tissues may still be considered as standing at a

higher pressure than the blood in the venous trunks, for instance in the jugular vein. That is to say, the lymphatic vessels, as a whole, form a system of channels leading from a region of higher pressure, viz., the lymphatic spaces of the tissues, to a region of lower pressure, viz., the interior of the jugular and subclavian veins. This difference of pressure will, as in the case of the bloodvessels, cause the lymph to flow onward in a continuous stream. Further, this flow, caused by the lowness of the mean venous pressure at the subclavian, will be assisted at every respiratory movement, since at every inspiration the pressure in the venous trunks becomes negative, and thus lymph will be sucked in from the thoracic duct, while the increase of pressure in the great veins during expiration is warded off from the duct by the valve at its opening. In the third place, the flow may possibly be increased by rhythmical contractions of the muscular walls of the lymphatics themselves; but this is doubtful, since it is not clear whether the rhythmic variations which have been observed in the lacteals of the mesentery of the guinea-pig are active or simply passive—*i. e.*, caused by the rhythmic peristaltic action of the intestine, each contraction of the intestine filling the lymph-channels more fully. Lastly, it is quite open for us to suppose that just as osmosis may give rise to increased pressure on one side of a diffusion septum, so the diffusion of substances from the intestines into the lacteals, or from the tissues into the lymphatics, may be itself one of the causes of the flow of lymph. We have at least, under all circumstances, one or other of these causes at work promoting a continual flow from the lymphatic roots to the great veins. We have no very satisfactory evidence that the flow of lymph is in any way directly governed by the nervous system. We cannot prove any direct connection between the nervous system and absorption, though the phenomena of disease render such a connection at least probable.

That the nervous system does exert an influence on absorption is shown by the following experiment, though probably in this case the influence is an indirect one, carried out through the mediation of the vascular system. Of two frogs placed under the influence of urari so as to do away with muscular movements and the action of the lymph hearts, the brain and spinal cord are destroyed in the one, but in the other are left intact. Both animals are suspended by the lower jaw; chloride of sodium solution (0.75 per cent.) is poured into the dorsal lymphatic sacs of both; and in both the aorta is cut across. In the one where the nervous system is intact, absorption from the lymphatic sac takes place copiously, and the heart pumps out large quantities of fluid by the aorta. In the other, absorption does not occur; the heart, though beating, remains empty, and the skin becomes

dry. The experiment probably shows the influence of the nervous system in maintaining the tonicity of the bloodvessels and keeping up the connection of the heart with the peripheral vessels, rather than any direct connection between absorption proper and the nervous system. When the nervous system is destroyed, dilation of the splanchnic vascular area causes all the blood to remain stagnant in the portal vessels, and probably these as well as other veins are rendered unusually lax, so that the blood is largely retained in the venous system, and very little reaches the heart; and with the enfeebled circulation, the absorption from the lymphatic sac is slight. So long as the nervous system is still intact, this stagnation does not occur; the blood reaches the heart as usual, and with the more vigorous circulation, absorption from the lymphatic sac goes on rapidly. As the blood is pumped away, its place is renewed by the lymph, supplied by the fluid in the sac, and thus the heart may be made for a long time to pump away the fluid poured into the sac.

Lymph Hearts.—In frogs and some other animals, the centripetal flow of lymph from the limbs is assisted by rhythmically pulsating muscular lymph hearts, which present many curious analogies with the blood heart. In the frog, in which they have been chiefly studied, their action, as we have already stated (p. 141), is in a measure dependent on the spinal cord. The posterior lymph hearts belonging to the hind limbs are connected by means of the delicate tenth pair of spinal nerves, with a region of the cord opposite the sixth or seventh vertebra, in such a way that section of the nerve or destruction of the particular region of the cord suspends or destroys their activity. The anterior pair are similarly connected with a region of the spinal cord opposite the third vertebra. Each pair, therefore, seems to have a "centre" in the spinal cord; but it is probable, though observers are not wholly agreed, that the hearts, after destruction of their spinal centre, ultimately resume their rhythmic beats, so that the dependence of their activity on the spinal centre, like the similar dependence of the blood heart on the ganglia of the sinus venosus, is not an absolute one. Like the blood heart, the lymph hearts may be inhibited, and that in a reflex manner, the inhibition centre being, moreover, in the medulla oblongata. If a frog be carefully observed, the activity of the lymph hearts will be found to vary largely, and these variations appear to be in part due to nervous influences; so that in this way the movement of lymph, and hence the processes of absorption, are in this animal directly dependent on the nervous system.

The course taken by the several products of digestion.

Digestion being, broadly speaking, the conversion of non-diffusible proteids and starch into highly diffusible peptone and sugar, and the emulsifying, or division into minute particles, of various fats, it is natural to suppose that the diffusible peptone and sugar pass by osmosis into the portal vessels and so directly into the blood, and that the emulsified fats pass into the lacteals and so indirectly into the blood. That a large part of the fat which enters the body from the intestine does pass through the lacteals, there can be no doubt; and there can be but little doubt that a considerable quantity of peptone and sugar does pass into the portal blood (Fig. 121). But the question as to how far the fat in its difficult passage into the lacteal is accompanied by soluble peptone, or by less diffusible forms of proteids arising as subsidiary products of proteolytic digestion, or by carbohydrate products, deserves attention.

It cannot be a matter of indifference which course is taken by the particular digestive products. For if they pass by the lacteals they fall into the general blood-current after having undergone only such changes as they may experience in the lymphatic system; while, if they pass into the portal vein, they are subjected to the powerful influences of the liver before they find their way to the right side of the heart. What those influences are, we shall study in a future chapter.

Fats.—As we have seen, a special mechanism is provided for the passage of fats into the lacteals. On the other hand, it is difficult to suppose that solid particles of fat can pass into the interior of the blood capillaries. So that we are led *à priori* to the view that the whole of the fat takes the course of the lacteals. But we cannot say that this is definitely proved. On the contrary, a large deficit is observed when the quantity of fat disappearing after a meal from the alimentary canal is compared with that flowing out through a canula placed in the end of the thoracic duct; and if it be true, as is stated, that the blood of the portal vein contains during digestion more fat than the general venous blood, some of this deficit may be explained by the fat passing into the blood capillaries, difficult as that passage may appear. The portal blood, moreover, during digestion contains a small but appreciable quantity of soaps. It may be, however, that the deficit observed is due to some of the fat disappearing in some way—in the glands, for instance—from the interior of the vessels in its transit.

The fat thus entering the blood either directly or indirectly is rapidly got rid of in some way or other, for from experiments on

dogs it would appear that the percentage of fat in the blood after a meal rich in fat, does not, after the lapse of twenty hours from the swallowing of the food, differ materially whether the

[FIG. 121.
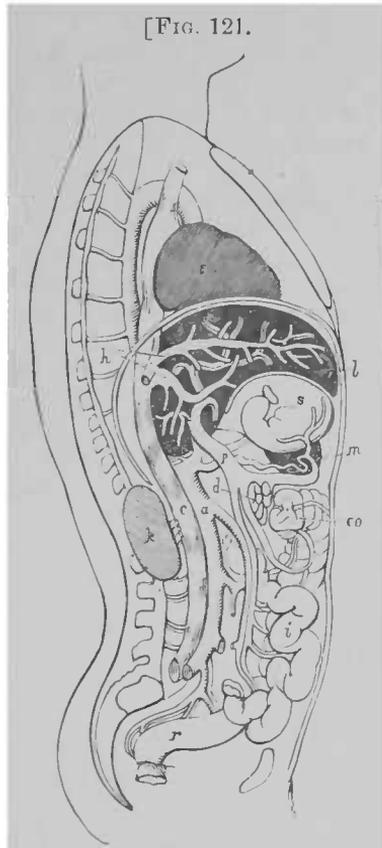
DIAGRAM SHOWING THE LARGER VESSELS CONCERNED IN THE SO-CALLED PORTAL CIRCULATION OR SYSTEM. After MARSHALL.

The trunk, or body, is supposed to be divided down the middle line, so as to show the cavity of the thorax or chest above the arched diaphragm, and that of the abdomen below it. In the abdomen, l, is the liver; s, the stomach; d, a section of the duodenum and pancreas; i, the small intestine; co, a part of the colon; r, the rectum; m, the lower end of the spleen, and k, the right kidney. The blood of all these parts is supplied through arteries which are branches of the abdominal aorta, marked a. From the rectum r, and the kidney k, the blood is returned by veins, which end in the great ascending vein, named the ascending vena cava, marked c, which conveys the venous blood directly through the diaphragm, and into the right side of the heart, o. But the blood from the stomach s, spleen m, duodenum and pancreas d, small intestine i, and large intestine co (excepting the rectum r), is collected by venous branches which end in a large venous trunk named the vena portæ or portal vein, p, by which this venous blood is conveyed to and distributed by branches through the liver. From this organ it is collected by other veins, which unite to form hepatic veins, h, which then join the ascending vena cava c, and so reach the right side of the heart.]

fat has been during the whole time shut off from the blood by
being allowed to flow out of a canula placed in the thoracic duct,
or has been allowed to pass into the venous system in the usual
way.

Proteids.—The question as to the course taken by the digested
proteids is complicated by the insufficiency of our knowledge
concerning the exact stages to which the digestion of proteids is
naturally carried in the alimentary canal.   If we take it for
granted that the proteids taken as food are reduced to the con
dition of soluble and diffusible peptone, it seems easy to suppose
that the proteids of food pass by diffusion as peptone into the
blood-capillaries which, as is well known, are placed in the villus
between the epithelium and the lacteal chamber; though even
on this view it is open for us to imagine that all the peptone
which passes through the epithelium is not intercepted by the
blood-capillaries, but that some reaches and passes away by the
more centrally placed lacteal.   It is difficult to imagine how
proteids in any other form than that of diffusible peptone can
pass through the walls of the blood-capillaries; though, perhaps,
the difficulty is not insurmountable, seeing that our conceptions
of nutrition are based on the assumption that the natural pro-
teids of the blood-plasma pass from the interior of the vessels into
the extravascular elements of the tissues; and we might imagine
that an accumulation of proteids in the same extravascular spaces
might cause a reversal of the proteid current, and thus lead to
proteids other than peptone passing through the vascular walls.
On the other hand, it is at least open for us to ask the question,
If solid particles of fat can pass from the interior of the alimen-
tary canal into the lacteals, why should not various forms of
proteids pass in the same way into the lacteals, either in solution
or even as solid particles?

It would thus seem possible for some of the proteids to pass
into the lacteals and so into the system in a less digested form
than peptone; and it is further possible that the proteids thus
entering into the system in different forms may play different
parts in the nutritive labors of the economy.

But in all these considerations the fact must be borne in mind
that the intestinal walls undoubtedly possess a selective power of
absorption, which overrides the laws of diffusion and solubility.
This is shown, for instance, by an observation made on a dog, in
which such fairly soluble and diffusible salts as sodium tauro-
cholate and glycocholate were found not to be absorbed by the
duodenum and upper jejunum, even at a time when fat was being
rapidly absorbed in those regions, but to disappear in the ileum
or lower jejunum, the glycocholate apparently being absorbed by

both the ileum and lower jejunum, while the taurocholate passed away in the ileum alone.

We cannot judge, therefore, of the course taken by the proteids, or of the form in which they are absorbed, by deductions based on solubility and diffusion. The problems we are discussing can only be satisfactorily settled by direct experiment. And here we meet with difficulties. If all proteids are converted into peptone, and so pass into the lacteals or into the blood-capillaries, we might expect to find a quantity of peptone in the chyle or in portal blood, or in both, after a proteid meal. Now, all observers are agreed that peptone is absent from chyle, or at least that its presence cannot by satisfactorily proved, in spite of the possibility of its entering into the lacteals, together with the fat. And while some have succeeded in finding peptone in the blood after food, but not during fasting, many have failed to demonstrate the presence of peptone in the blood either of the portal vein, or of the vessels at large, even after a meal containing large quantities of proteids. Of course, the quantity of peptone passing into the portal blood at any moment might be small, and yet a considerable quantity might so pass during the hours of digestion. We may suppose, moreover, that that which does pass is immediately converted, possibly by some ferment action, into one or other of the natural proteids of the blood, or otherwise disposed of; and, indeed, peptone injected carefully into a vein disappears from the blood, though little or even none passes out by the kidney. And the view that peptone is so changed, possibly in the very act of absorption, is supported not only by the fact that peptone may be found in the walls of the intestine, even when it appears to be absent from the blood, but also and especially by the following observation. If an artificial circulation of blood be kept up in the mesenteric arteries supplying a loop of intestine removed from the body, the loop may be kept alive for some considerable time. During this survival a considerable quantity of peptone placed in the cavity of the loop, will disappear—i. e., will be absorbed, but cannot be recovered from the blood which is being used for the artificial circulation, and which escapes from the veins after traversing the intestinal capillaries. The disappearance is not due to any action of the blood itself, for peptones introduced into the blood before it is driven through the mesenteric arteries in the experiment may be recovered from the blood as it escapes from the mesenteric veins. It would seem as if the peptone were changed before it actually gets into the capillaries.

But the argument that the absence of peptone from the blood is no proof that peptones are not absorbed into the blood, may also be applied to the chyle. We have, however, an indirect

proof that peptones do not pass into the chyle. We shall see hereafter that the quantity of urea passing by the kidney may, with certain precautions, be taken as a measure of the quantity of proteid material taken into the body. Now, when a canula is placed in the thoracic duct of a dog, so that all the chyle passes away, and is lost to the blood, the amount of urea leaving the body by the kidney does not materially differ from the amount which, with the same food, is passed when all the chyle flows into the blood. Did any large quantity of peptone (or proteid) pass by the chyle, we should expect to find the urea much diminished. Hence, except on the very improbable view that proteids absorbed into the lacteals of the villi escape from the lymphatic system before they reach the thoracic duct, we must accept the view which seems to follow legitimately from the results of artificial digestion—that proteid food is converted into peptone, and so passes from the alimentary canal into the blood. And we know that artificially formed peptone is available for nutrition; for dogs fed on peptone and non-nitrogenous food, may actually put on flesh and gain in weight.

Sugar.—With regard to the path taken by the sugar, careful inquiries show that the percentage of sugar, both in chyle and in general blood, is fairly constant, being to no marked extent increased by even amylaceous meals; but that a meal of sugar or starch does temporarily increase the quantity of sugar in the portal blood. From this we may infer that such portions of the sugar of the intestinal contents as are absorbed as sugar pass exclusively by the portal vein. But it must be remembered that at present we have no accurate information as to how large a proportion of the sugar resulting from a meal passes in this way unchanged until it reaches the liver, and how much undergoes the lactic acid or analogous fermentation. Nor do we know as yet how much of the starch taken as food is removed from the alimentary canal in the form not of sugar but of dextrin.

When a solution of sugar is injected into an empty isolated loop of intestine, a large quantity disappears without the contents of the loop becoming acid. In such a case, it may fairly be inferred that the sugar is directly absorbed without undergoing any change. And where sugar is introduced in large quantities into the alimentary canal, the percentage of sugar in the blood may be temporarily increased; to such an extent, indeed, that sugar may appear in the urine. But neither of these facts prove that the sugar of an ordinary meal, passing as it does along the intestine with the other portions of the food, and products of digestion, and appearing as it does, in most cases, in comparatively small quantities at a time, owing to the more or less gradual con-

version of the starch of the meal, is similarly absorbed unchanged; while in order that the marked acidity of the contents of the lower intestine should be kept up, a considerable quantity of sugar must suffer lactic acid fermentation, if the acidity be due as stated to lactic acid.

To sum up, the evidence is distinctly in favor of the fats passing largely by the chyle, and of the proteids and sugar passing largely by the portal vein; but there still remains much doubt as to the course and fate of a not inconsiderable portion of the fat, and the question as to the exact form in which proteids and carbohydrates leave the alimentary canal, cannot be answered in a perfectly definite manner.

Absorption by Diffusion.—It is evident, from the discussion just concluded, that simple diffusion is far from explaining the whole transit of the digested food from the intestine into the blood. Nevertheless, it must not be supposed that the great and general property of diffusion does not make itself felt in the process of absorption, however much it may, in the case of various substances, be subordinated and held in check by more potent influences. Thus the passage of water from the alimentary cavity into the blood, or from the blood into the alimentary cavity, and the behavior of various inorganic salts, when taken as food or medicine, illustrate very clearly the influence of osmosis. When the intestine contains a large quantity of watery matter, the surplus water passes by diffusion into the blood, just as it passes through the membrane of a dialyzer, with blood or serous fluid on the one side, and water on the other. When an albuminous fluid of the specific gravity of blood-serum is exposed in a dialyzer to water, about 200 parts of water pass through the membrane of the dialyzer from the water into the albuminous fluid for every one part of the albumin which passes from the fluid into the water. Moreover, in the living body, the blood in the mesenteric capillary, thus diluted by diffusion from the intestinal contents, is continually being replaced by fresh blood concentrated by its passage through the skin, lung, or kidney. By the help of the circulation an almost unlimited quantity of water can be absorbed from the alimentary canal.

It is a matter of common experience that such inorganic and organic salts as are readily diffusible, pass with great rapidity into the blood (and thus into the urine) when taken by the mouth; and the rapidity with which they are absorbed is in large measure proportionate to their diffusibility. Of course, coincident with this passage of the salt from the intestine into the blood, there is a proportionate current of water in the contrary direction from the blood into the intestine: but this, though opposed

to, is, under ordinary circumstances, too small to diminish to any serious extent the passage of water from the intestine into the blood, of which we spoke just now, as caused by the osmotic influence of the albuminous constituents of the blood.   But, under certain circumstances, the former may overcome the latter. Thus, when a concentrated solution of a highly diffusible salt, such as magnesium sulphate, is introduced into the alimentary canal, the flow of water from the blood into the intestine accompanying the osmotic transit of the salt from the intestine into the blood, is so great as largely to exceed the current in the contrary direction ; and the intestine becomes filled with water at the expense of the blood.   This is probably the cause of the purgative action of large doses of many saline substances.   And even the purgative action of more dilute solutions may be explained in the same way, since in the case of some salts at least the transit of water as compared with the transit of the salt is relatively more rapid with very dilute solutions than with more concentrated solutions.   Salts such as these, which, when introduced into the intestine, produce diarrhœa, bring about a contrary condition when injected directly into the blood ; and magnesium sulphate, with its higher endosmotic equivalent, is more purgative in its action than sodium chloride with its lower equivalent.

CHAPTER II

THE TISSUES AND MECHANISMS OF RESPIRATION.

[Physiological Anatomy of the Trachea and Lungs.

THE trachea is a membrano-cartilaginous cylindrical tube, somewhat flattened posteriorly. It is about four and a half inches long, about three-fourths of an inch in diameter, and is composed of an external fibrous and an internal mucous coat. The fibrous coat consists of several layers which are composed of elastic and non elastic fibrous tissue, a circular and longitudinal layer of unstriated muscular tissue, and about twenty imperfect cartilaginous rings, which are placed parallel with each other and partially encircle the tube. The rings are imperfect posteriorly, where the tube is completed by a fibro-muscular membrane. The mucous coat consists of a basement membrane which is covered by a layer of ciliated columnar epithelium. On the surface of this membrane can be seen numerous orifices, which are the apertures of the ducts leading from the tracheal mucous glands. These glands are of the racemose and follicular varieties, and are most abundant in the posterior portions of the trachea.

The lungs are bilateral organs, situated within the thoracic cavity. When the chest is opened, they are seen to occupy but a portion of the space, or, in other words, are collapsed. This is not the case in the unopened chest, where the lungs are partially expanded and in contact with the chest-walls.

The lungs are divided into lobes, which are subdivided into lobules, and are composed of a *parenchyma,* and a *serous* and *subserous coat.* The serous coat is a continuation of the intrathoracic lining, and forms the pulmonary or visceral layer of the pleura. The subserous coat is composed of an areolar tissue containing a very large amount of elastic fibres. This coat envelops the lungs and sends numerous prolongations or trabeculæ into the pulmonary substance. The *parenchyma* of the lungs is made up of the lobules, which are bound together by a fibroelastic tissue, which also forms a nidus for the ramifications of the bloodvessels, lymphatics, and nerves. This fibro-elastic tissue plays an important part in expiration ; in inspiration the fibres

are put on the stretch, and in their return to their normal condition, contract, and thus assist in expelling the air.

The trachea is connected above with the larynx; below, it divides into two branches, which are the *right* and *left* bronchial tubes. The right is larger, shorter, and placed more horizontal than the left. The reason of the larger size of the right is obviously due to the greater capacity of the right lung. These primary bronchial tubes undergo subdivision through numerous gradations of smaller tubes until the ultimate divisions, or *alveolar passages*, are reached. The coats of the bronchial tubes become more delicate in structure as the tubes are diminished in size. The layer of cartilaginous rings, which is seen in the trachea, is continued in the larger bronchi, but the rings soon become

FIG. 122.
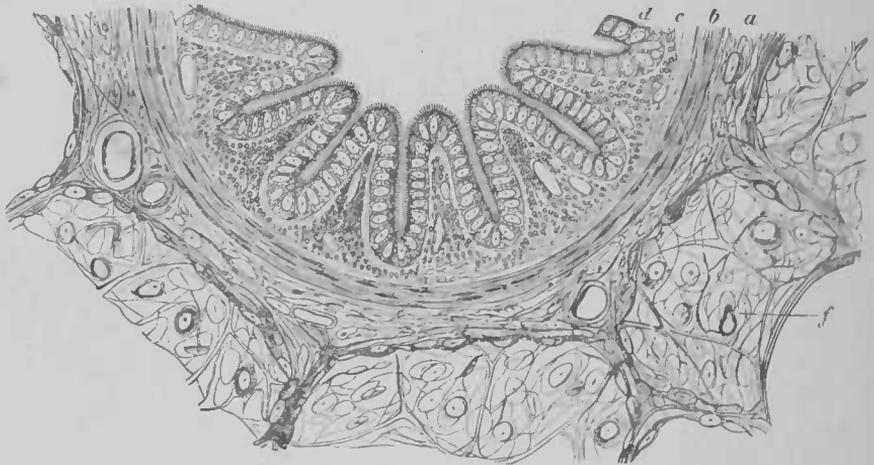
Part of a Transverse Section of a Bronchial Tube from the Pig   Magnified 240 diam. *a*, external fibrous layer; *b*, muscular layer; *c*, internal fibrous layer; *d*, epithelial layer; *f*, one of the surrounding alveoli.

replaced by irregular cartilaginous plates, which themselves disappear when the size of the bronchi have reached a diameter of about 2 mm. The mucous glands disappear consentaneously with the disappearance of the cartilaginous plates. The muscular fibres are in the form of a continuous transverse layer. The fibrous and muscular tissues are continued into the smallest bronchi.

The mucous membrane is also continuous with that of the trachea, and is lined with ciliated columnar epithelium.

The smallest bronchi terminate in subdivisions, called the *alveolar passages*. (Figs. 123 and 124.) Each of these passages

subdivides through several gradations, and ultimately terminates
in cæcal processes, which gradually become expanded towards
their cæcal extremities, and present an appearance similar to that
of the expanded part of a funnel; hence they have been called
the *infundibula.* The interior of each infundibulum is marked
by fifteen or twenty incomplete cells, which are termed *alveoli* or
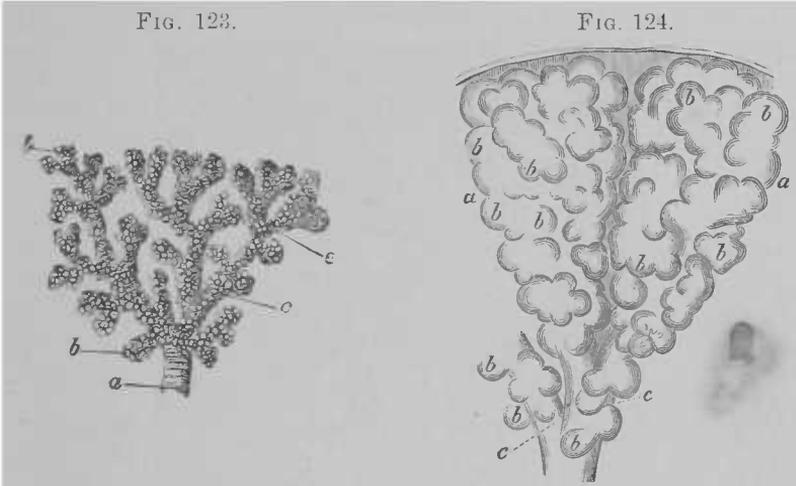
FIG. 123.—System of Alveolar Passages and Infundibula from the Margin of the Lung of
a Monkey (Cercopethecus) injected with mercury. Magnified 10 diam. *a*, Terminal bronchial
twig; *b b*, infundibula; *c c*, alveolar passages.

FIG. 124.—Two small groups of air-cells, or *infundibula. a a*, with air-cells; *b b*, and the
alveolar passages; *c*, with which the air-cells communicate. From newborn child.
After KOLLIKER.

air-cells. These cells average about 0.25 mm. in diameter. Their
walls consist of a delicate basement membrane, which is lined by
a layer of pavement epithelium. This membrane forms by its
reduplications the incomplete septa between the air-cells. The
space in the interior of an infundibulum is termed an *intercellular
passage.*

Each lobule or infundibulum is composed of an ultimate
alveolar passage, with its terminal alveoli, and of nerves, blood-
vessels, and lymphatics; all of which are bound together by
fibro-elastic tissue.

The capillaries (Fig. 125) form a plexus between the cells,
which is remarkable for its density. The diameters of the inter-
capillary spaces are often less than the diameters of the vessels.
These capillaries are so arranged in the intercellular tissue that
both sides of the vessels are in contact with the walls of con-
tiguous cells.

The cartilaginous rings of the trachea and larger bronchi keep them continually open. The smaller bronchi, in which these cartilages are absent, are capable of considerable expansion and contraction by virtue of their elastic and muscular tissues. The nerves of the lungs are derived from the pneumogastric and sympathetic. Blood is conveyed through the pulmonary artery

Fig. 125.
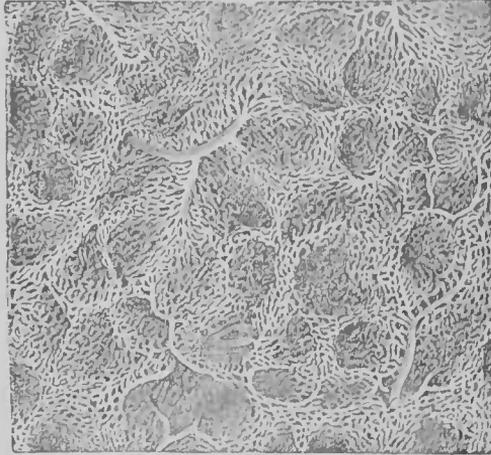
Capillary Network of the Pulmonary Bloodvessels in the Human Lung.

to the lungs, where it is arterialized, and then returned through the pulmonary veins to the heart. The lungs receive blood for their nutrition, principally through the bronchial arteries.]

We have already seen (Introduction, p. 27) that one particular item of the body's income—viz., oxygen—is peculiarly associated with one particular item of the body's waste—viz., carbonic acid —the means which are applied for the introduction of the former being also used for the getting rid of the latter. Both are gases, and, in consequence, the ingress of the one as well as the egress of the other is far more dependent on the simple physical process of diffusion than on any active vital processes carried on by means of tissues. Oxygen passes from the air into the blood mainly by diffusion, and mainly by diffusion also from the blood into the tissues; in the same way, carbonic acid passes mainly by diffusion from the tissues into the blood, and from the blood into the air. Whereas, as we have seen, in the secretion of the digestive juices the epithelium-cell plays an all-important part, in respiration the entrance of oxygen from the lungs into the blood, and from the blood into the tissue, and the passage of car-

bonic acid in the contrary direction, are effected, if at all, in a wholly subordinate manner, by the behavior of the pulmonary, or of the capillary epithelium. What we have to deal with in respiration, then, is not so much the vital activities of any particular tissue, as the various mechanisms by which a rapid interchange between the air and the blood is effected, the means by which the blood is enabled to carry oxygen and carbonic acid to and from the tissues, and the manner in which the several tissues take oxygen from and give carbonic acid up to the blood. We have reasons for thinking that oxygen can be taken into the blood, not only from the lungs, but also from the skin, and, as we have seen, occasionally from the alimentary canal also; and carbonic acid certainly passes away from the skin, and through the various secretions, as well as by the lungs. Still the lungs are so eminently the channel of the interchange of gases between the body and the air, that in dealing at the present with respiration, we shall confine ourselves entirely to pulmonary respiration, leaving the consideration of the subsidiary respiratory processes till we come to study the secretions of which they respectively form part.

Sec. 1.—The Mechanics of Pulmonary Respiration.

The lungs are placed, in a semi-distended state, in the air-tight thorax, the cavity of which they, together with the heart, great bloodvessels and other organs, completely fill. By the contraction of certain muscles the cavity of the thorax is enlarged; in consequence the pressure of the air within the lungs becomes less than that of the air outside the body, and this difference of pressure causes a rush of air through the trachea into the lungs until an equilibrium of pressure is established between the air inside and that outside the lungs. This constitutes inspiration. Upon the relaxation of the inspiratory muscles (the muscles whose contraction has brought the thoracic expansion), the elasticity of the lungs and chest-walls, aided perhaps to some extent by the contraction of certain muscles, causes the chest to return to its original size; in consequence of this the pressure within the lungs now becomes greater than that outside, and thus air rushes out of the trachea until equilibrium is once more established. This constitutes expiration; the inspiratory and expiratory act together forming a respiration. The fresh air introduced into the upper part of the pulmonary passages by the inspiratory movement contains more oxygen and less carbonic acid than the old air previously present in the lungs. By diffusion the new or *tidal* air, as it is frequently called, gives up its oxygen to, and takes carbonic acid from, the old or *stationary* air, as it has been

called, and thus when it leaves the chest in expiration has been the means of both introducing oxygen into the chest and of removing carbonic acid from it. In this way, by the ebb and flow of the tidal air, and by diffusion between it and the stationary air, the air in the lungs is being constantly renewed through the alternate expansion and contraction of the chest.

In ordinary respiration, the expansion of the chest never reaches its maximum; by more forcible muscular contraction, by what is called labored inspiration, an additional thoracic expansion can be brought about, leading to the inrush of a certain additional quantity of air before equilibrium is established. This additional quantity is often spoken of as *complemental* air. In the same way, in ordinary respiration, the contraction of the chest never reaches its maximum. By calling into use additional muscles, by a labored expiration, an additional quantity of air, the so-called *reserve* or *supplemental* air, may be driven out. But even after the most forcible expiration, a considerable quantity of air, the *residual* air, still remains in the lungs. The natural condition of the lungs in the chest is, in fact, one of partial distention. The elastic pulmonary tissue is always to a certain extent on the stretch; it is always, so to speak, striving to pull asunder the pulmonary from the parietal pleura; but this it cannot do, because the air can have no access to the pleural cavity. When, however, the chest ceases to be air-tight; when, by a puncture of the chest-wall or diaphragm, air is introduced into the pleural chamber, the elasticity of the lungs pulls the pulmonary away from the parietal pleura, and the lungs collapse, driving out by the windpipe a considerable quantity of the residual air. Even then, however, the lungs are not completely emptied, some air still remaining in the air-cells and passages. It need hardly be added that when the pleura is punctured, and air can gain *free* admittance from the exterior into the pleural chamber, the effect of the respiratory movements is simply to drive air in and out of that chamber, instead of in and out of the lung. There is in consequence no renewal of the air within the lungs under those circumstances.

In man, the pressure exerted by the elasticity of the lungs alone amounts to about 5 mm. of mercury. This is estimated by tying a manometer into the windpipe of a dead subject and observing the rise of mercury which takes place when the chest-walls are punctured. If the chest be forcibly distended beforehand, a much larger rise of the mercury is observed, amounting, in the case of a distention corresponding to a very forcible inspiration, to 30 mm. In the living body this mechanical elastic force of the lungs is assisted by the contraction of the plain muscular fibres of the bronchi; the pressure, however,

which can be exerted by these probably does not exceed 1 or 2 mm.

When a manometer is introduced into a lateral opening of the windpipe of an animal, the mercury will fall, indicating a negative pressure as it is called, during inspiration, and rise, indicating a positive pressure, during expiration, both fall and rise being slight, and varying according to the freedom with which the air passes in and out of the chest. When a manometer is fitted with air-tight closure into the mouth, or better, in order to avoid the suction-action of the mouth, into one nostril, the other nostril and the mouth being closed, and efforts of inspiration and expiration are made, the mercury falls or undergoes negative pressure with inspiration, and rises or undergoes positive pressure during expiration. It has been found in this way that the negative pressure of a strong inspiratory effort may vary from 30 to 74 mm., and the positive pressure of a strong expiration from 62 to 100 mm.

The total amount of air which can be given out by the most forcible expiration following upon a most forcible inspiration— that is, the sum of the complemental, tidal, and reserve airs, has been called "the vital capacity;" "extreme differential capacity" is a better phrase. It may be measured by a modification of a gas-meter called a *spirometer;* and, though it varies largely, the average may be put down at 3000–4000 cc. (200 to 250 cubic inches).

Of the whole measure of vital capacity, about 500 c.c. (30 c. inch) may be put down as the average amount of tidal air, the remainder being nearly equally divided between the complemental and reserve airs. The quantity left in the lungs after the deepest expiration amounts to about 1400–2000 c.c.

Since the respiratory movements are so easily affected by various circumstances, the simple fact of attention being directed to the breathing being sufficient to cause modifications both of the rate and depth of the respiration, it becomes very difficult to fix the volume of an average breath. Thus various authors have given figures varying from 53 c.c. to 792 c.c. The statement made above is that given by Vierordt as the mean of observations varying from 177 to 699 c.c.

The Rhythm of Respiration.—If the movements of the column of tidal air, or the movements of expansion and contraction, or the fall and rise of the diaphragm, be registered, curves are obtained, which, while differing in detail, exhibit the same general features, and more or less resemble the curve shown in Fig. 126.

The movements of the column of air may be recorded by introducing a T-piece into the trachea, one cross-piece being left open or connected with a piece of India-rubber tubing open at the end, and the other con-

nected with a Marey's tambour, or with a receiver which in turn is con-
nected with a tambour, Fig. 55, p. 186, and Fig. 127.   The movements of
the column of air in the trachea are transmitted to the tambour, the con-
sequent expansions and contractions of which are transmitted to the
recording drum by means of a lever resting on it   The movements of
the chest-walls may be recorded by means of the recording stethometer of
Burdon-Sanderson.   This consists of a rectangular framework constructed
of two rigid parallel bars joined at right angles to a cross-piece.   The free

FIG 126.

TRACING OF THORACIC RESPIRATORY MOVEMENTS OBTAINED BY MEANS OF MAREY'S
PNEUMATOGRAPH.   To be read from left to right.

A whole respiratory phase is comprised between a and a; inspiration, during which the
lever descends, extending from a to b, and expiration from b to a.   The undulations at c are
caused by the heart's beat.
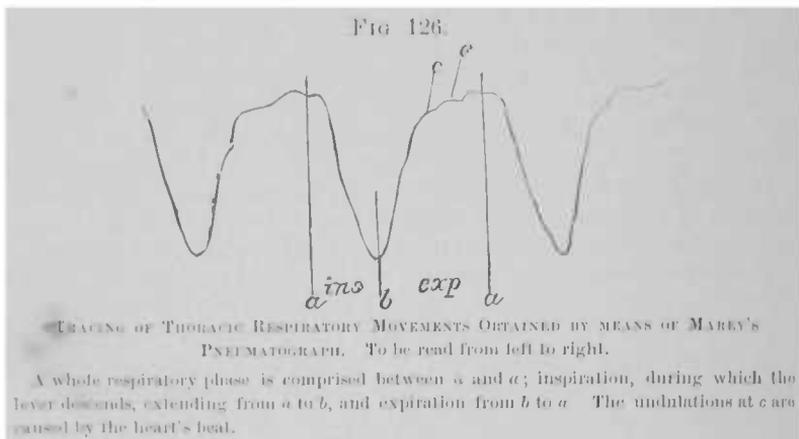
ends of the bars, the distance between which can be regulated at pleasure,
are armed, the one with a tambour, the other simply with an ivory button.
The tambour also bears on the metal plate of its membrane (Figs. 55
and 127, m') a small ivory button (in place of the lever shown in Figs
55 and 127).   When it is desired to record the changes occurring in any
diameter of the chest, e. g., an antero-posterior diameter from a point
in the sternum to a point in the back, the instrument is made to encircle
the chest somewhat after the fashion of a pair of calipers, the ivory
button at one free end being placed on the spine of a vertebra behind
and the tambour at the other on the sternum in front in the line of the
diameter which is being studied.   The distance between the free ends of
the instrument being carefully adjusted so that the button of the tambour
presses slightly on the sternum, any variations in the length of the
diameter in question will, since the framework of the tambour is immo-
bile, give rise to variations of pressure within the tambour.   These varia-
tions of the "receiving" tambour, as it is called, are conveyed by a
flexible tube containing air to a second or "recording" tambour similar
to that shown in Figs. 55 and 127, the lever of which records the varia-
tions on a travelling surface.   For the purpose of measuring the extent
of the movements the instrument must be experimentally graduated.
In Marey's pneumatograph, a long elastic chamber is used as a pectoral
girdle.   When the chest expands, the girdle is elongated, and the air
within it rarefied, and the lever of the tambour connected with it de-
pressed; and conversely, when the chest contracts, the lever is elevated.
The pneumatograph of Fick is somewhat similar.   The movements of
the diaphragm may be registered by means of a needle, which is thrust
through the sternum so as to rest on the diaphragm; the head of the
needle being connected with a lever   Various modifications of these
several methods have been adopted by different observers.

Fig. 127.
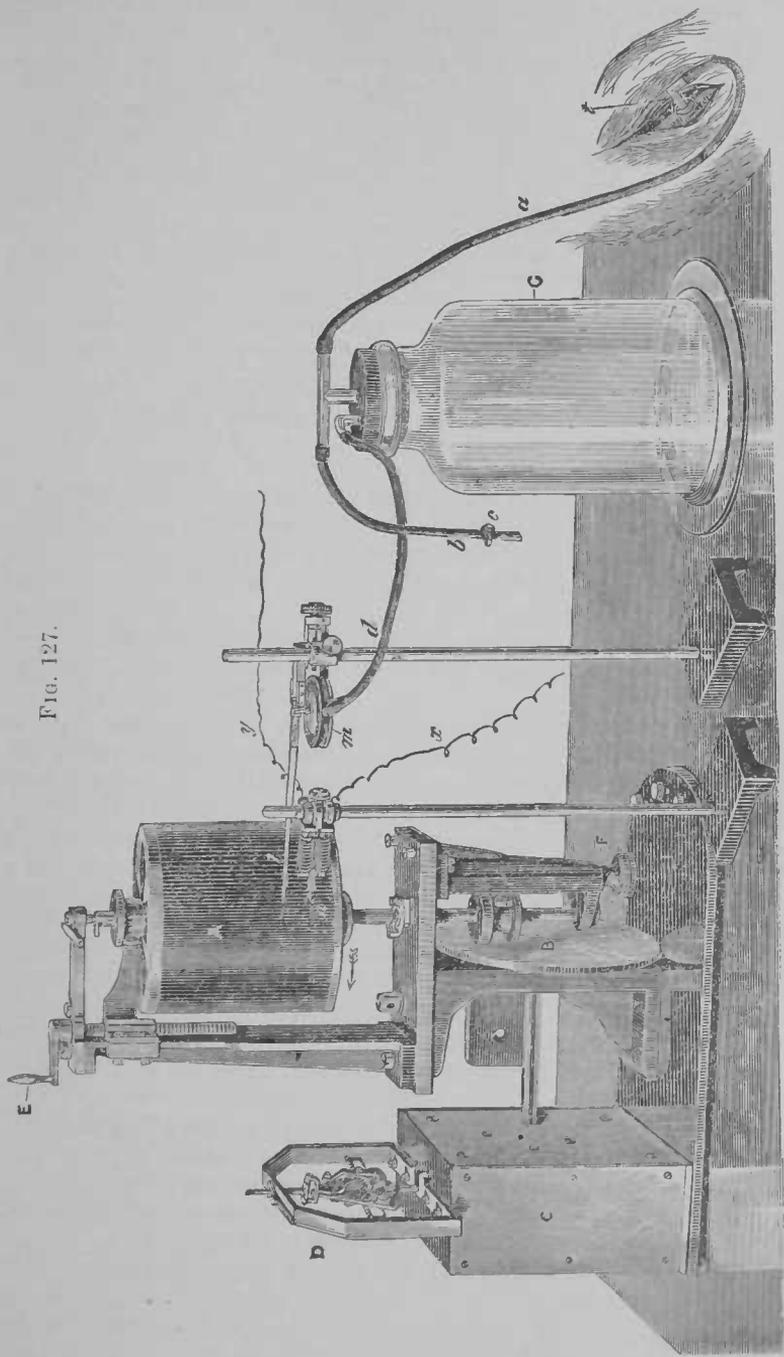
APPARATUS FOR TAKING TRACINGS OF THE MOVEMENTS OF THE COLUMN OF AIR IN
RESPIRATION.

The recording apparatus shown is the ordinary cylinder recording apparatus. The cylinder A covered with smoked paper is by means of the friction-plate B, put into revolution by the spring clockwork in C, regulated by Foucault's regulator D. By means of the screw E, the cylinder can be raised or lowered, and by means of the screw F, its speed may be increased or diminished.

The tracheotomy tube t, fixed in the trachea of an animal is connected by India-rubber tubing a, with a glass T-piece inserted into the large jar G. From the other end of the T-piece proceeds a second piece of tubing b, the end of which can be either closed or partially obstructed at pleasure by means of the screw clamp c. From the jar proceeds a third piece of tubing d, connected with a Marey's tambour m (see Fig. 35, p. 186), the lever of which, l, writes on the recording surface. When the tube b is open the animal breathes freely through this, and the movements in the air of G, and consequently in the tambour, are slight. On closing the clamp c, the animal breathes only the air contained in the jar, and the movements of the lever of the tambour become consequently much more marked.

Below the lever is seen a small time-marker n, connected with an electro-magnet, the current through which coming from battery by the wires e and g, is made and broken by a clockwork or metronome

As is shown in Fig. 126, inspiration begins somewhat suddenly and advances rapidly, being followed immediately by expiration which is carried out at first rapidly, but afterwards more and more slowly. Such pauses as are seen occur between the end of expiration and the beginning of inspiration. In normal breathing, hardly any such pause exists, but in cases where the respiration becomes infrequent, pauses of considerable length may be observed.

In what may be considered as normal breathing, the respiratory act is repeated about seventeen times a minute; and the duration of the inspiration as compared with that of the expiration (and such pause as may exist) is about as ten to twelve.

The rate of the respiratory rhythm varies very largely, and in this as in the volume of each breath it is very difficult to fix a satisfactory average, the figures given varying from twenty to thirteen a minute. It varies according to age and sex. It is influenced by the position of the body, being quicker in standing than in lying, and in lying than in sitting. Muscular exertion and emotional conditions affect it deeply. In fact, almost every event which occurs in the body may influence it. We shall have to consider in detail hereafter the manner in which this influence is brought to bear.

When the ordinary respiratory movements prove insufficient to effect the necessary changes in the blood, their rhythm and character become changed. Normal respiration gives place to labored respiration, and this in turn to dyspnœa, which, unless some restorative event occurs, terminates in asphyxia. These abnormal conditions we shall study more fully hereafter.

The Respiratory Movements.

When the movements of the chest during normal breathing are watched, it is seen that during respiration an enlargement takes place in the antero-posterior diameter, the sternum being thrown forwards, and at the same time moving upward. The lateral width of the chest is also increased. The vertical increase of the cavity is not so obvious from the outside, though when the movements of the diaphragm are watched by means of an inserted needle, the upper surface of that organ is seen to descend at each inspiration, the anterior walls of the abdomen bulging out at the same time. In the female human subject, the movement of the upper part of the chest is very conspicuous, the breast rising and falling with every respiration ; in the male, however, the movements are almost entirely confined to the lower part of the chest. In labored respiration all parts of the chest are alternately expanded and contracted, the breast rising and falling as well in the male as in the female. We have now to consider these several movements in greater detail, and to study the means by which they are carried out.

Inspiration.—There are two chief means by which the chest is enlarged in normal inspiration, viz., the descent of the diaphragm and the elevation of the ribs. The former causes that movement in the lower part of the chest and abdomen so characteristic of male breathing, which is called diaphragmatic; the latter causes the movement of the upper chest characteristic of female breathing, which is called costal. These two main factors are assisted by less important and subsidiary events.

The descent of the diaphragm is effected by means of the contraction of its muscular fibres. When at rest the diaphragm presents a convex surface to the thorax ; when contracted it becomes much flatter, and in consequence the level of the chest-floor is lowered, the vertical diameter of the chest being proportionately enlarged. In descending, the diaphragm presses on the abdominal viscera, and so causes a projection of the flaccid abdominal walls. From its attachments to the sternum and the false ribs, the diaphragm, while contracting, naturally tends to pull the sternum and the upper false ribs downwards and inwards, and the lower false ribs upwards and inwards, towards the lumbar spine. In normal breathing, this tendency produces little effect, being counteracted by the accompanying general costal elevation, and by certain special muscles to be mentioned presently. In forced inspiration however, and especially where there is any obstruction to the entrance of air into the lungs, the lower ribs may be so much drawn in by the contraction of

the diaphragm, that the girth of the trunk at this point is
obviously diminished.

The elevation of the ribs is a much more complex matter than
the descent of the diaphragm. If we examine any one rib, such
as the fifth, we find that while it moves freely on its vertebral
articulation, it inclines when in the position of rest in an oblique
direction from the spine to the sternum ; hence it is obvious that
when the rib is raised, its sternal attachment must not only be
carried upward, but also thrown forwards (Fig. 128).   The rib

[Fig. 128.]
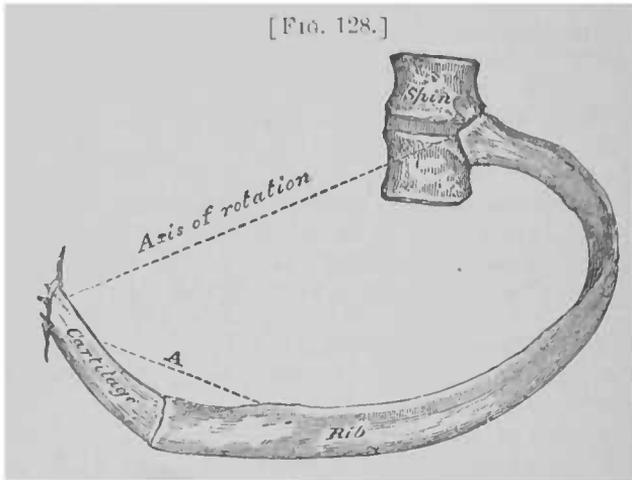
may, in fact, be regarded as a radius, moving on the vertebral
articulation as a centre, and causing the sternal attachment to
describe an arc of a circle in the vertical plane of the body ; as
the rib is carried upwards from an oblique to a more horizontal
position, the sternal attachment must of necessity be carried
further away in front of the spine. Since all the ribs have a
downward slanting direction, they must all tend, when raised
towards the horizontal position, to thrust the sternum forward,
some more than others according to their slope and length.   The
elasticity of the sternum and costal cartilages, together with the
articulation of the sternum to the clavicle above, permits the front
surface of the chest to be thus thrust forwards as well as upwards,
when the ribs are raised.   By this action the antero-posterior
diameter of the chest is enlarged.

Since the ribs form arches which increase in their sweep as one
proceeds from the first downwards as far at least as the seventh,
it is evident that when a lower rib such as the fifth is elevated
so as to occupy or to approach towards the position of the one
above it, the chest at that level will become wider from side to

side, in proportion as the fifth arch is wider than the fourth. Thus the elevation of the rib increases not only the antero-posterior but also the transverse diameter of the chest. Further, on account of the resistance of the sternum, the angles between the ribs and their cartilages are, in the elevation of the ribs, somewhat opened out, and thus also the transverse as well as the antero-posterior diameter, somewhat increased. In several ways, then, the elevation of the ribs enlarges the dimensions of the chest.

The ribs are raised by the contraction of certain muscles. Of these the external intercostals are the most important. Even in the case of two isolated ribs such as the fifth and sixth, the contraction of the external intercostal muscle of the intervening space raises the two ribs, thus bringing them towards the position in which the fibres of the muscle have the shortest length, viz., the horizontal one. This elevating action is further favored by the fact that the first rib is less movable than the second, and so affords a comparatively fixed base for the action of the muscles between the two, the second in turn supporting the third and so on, while the scaleni muscles in addition serve to render fixed, or to raise, the first two ribs. So that in normal respiration, the act begins probably by a contraction of the scaleni. The first two ribs being thus fixed, the contraction of the series of external intercostal muscles acts to the greatest advantage.

While the elevating—*i. e.*, inspiratory—action of the external intercostals is admitted by all authors, the function of the internal intercostals has been much disputed. Haller may be regarded as the leader of those who regard the internal intercostals as inspiratory, while Hamberger was the first who successfully advocated the perhaps more commonly adopted view that while those parts of them which lie between the sternal cartilages act like the external intercostals as elevators—*i. e.*, as inspiratory in function, those parts which lie between the osseous ribs act as depressors—*i. e.*, as expiratory in function.

In the well-known model invented by Bernoulli and adopted by Hamberger, consisting of two rigid bars, representing the ribs, moving vertically by means of their articulations with an upright representing the spine and connected at their free ends by a piece representing the sternum, it is undoubtedly true that stretched elastic bands attached to the bars (Fig. 129) in such a way as to represent respectively the external and internal intercostals, viz., sloping in the one case downwards and forwards and in the other downwards and backwards, do, on being left free to contract, in the former case elevate and in the latter depress the ribs. Such a model however does not fairly represent the natural conditions of the ribs, which are not straight and rigid, but peculiarly curved and of varying elasticity, capable more-

over of rotation on their own axes, and having their movements
determined by the characters of their vertebral articulations.
The mechanical conditions in fact of these muscles are so com-
plex, that a deduction of their actions from simple mechanical
principles, or from the direction of the fibres, must be exceedingly
difficult and dangerous. Actual experiments on the cat and dog
tend to show that in these animals the contraction of the internal

[Fig. 129.

a and b represent cross-bars, articulating on the vertical bar c; x y and w z are two rubber
bands, which represent respectively the external and internal intercostal muscles. Diagram
A represents the muscles in a state of rest. If, now, the band x and y was free to contract, it
is obvious that in order to attain its shortest length, it would assume a position as in diagram
C. If, now, the band w and z was free to move, the converse would take place of what was
seen when x and y became shortened. Thus, in diagram B, the cross-bars are depressed.

The bands x and y represent the external intercostal muscles, which, by contraction, elevate
the ribs. The bands w and z represent the internal intercostals, which, by contracting, de-
press the ribs.]

intercostals, along their whole length, takes place, in point of
time, alternately with that of the diaphragm, and thus afford an
argument in favor of these muscles being expiratory in function.

Next in importance to the external intercostals come the leva-
tores costarum, which, though small muscles, are able, from the
nearness of their costal insertions to the fulcrum, to produce
considerable movement of the sternal ends of the ribs. The
external intercostals and the levatores costarum with the scaleni
may fairly be said to be the elevators of the ribs—*i. e.*, the chief
muscles of costal inspiration in normal breathing.

Additional space in the transverse diameter is afforded probably
by the rotation of the ribs on an antero-posterior axis; but this
movement is quite subsidiary and unimportant. When the chest
is at rest, the ribs are somewhat inclined with their lower borders
directed inwards as well as downwards. When they are drawn
up by the action of the intercostal muscles, their lower borders

are everted. Thus their flat sides are presented to the thoracic cavity, which is thereby slightly increased in width.

Labored Inspiration.—When respiration becomes labored, other muscles are brought into play. The scaleni are strongly contracted, so as to raise or at least give a very fixed support to the first 'and second ribs. In the same way the *serratus posticus superior*, which descends from the fixed spine in the lower cervical and upper dorsal regions to the second, third, fourth, and fifth ribs, by its contractions raises those ribs. In labored breathing a function of the lower false ribs, not very noticeable in easy breathing, comes into play. They are depressed, retracted, and fixed, thereby giving increased support to the diaphragm, and directing the whole energies of that muscle to the vertical enlargement of the chest. In this way the *serratus posticus inferior*, which passes upward from the lumbar aponeurosis to the last four ribs, by depressing and fixing those ribs becomes an adjuvant inspiratory muscle. The *quadratus lumborum* and lower portions of the *sacro-lumbalis* may have a similar function.

All these muscles may come into action even in breathing, which, deeper than usual, can hardly, perhaps, be called labored. When, however, the need for greater inspiratory efforts becomes urgent, all the muscles which can, from any fixed point, act in enlarging the chest, come into play. Thus, the arms and shoulder being fixed, the *serratus magnus* passing from the scapula to the middle of the first eight or nine ribs, the *pectoralis minor* passing from the coracoid to the front parts of the third, fourth, and fifth ribs, the *pectoralis major* passing from the humerus to the costal cartilages, from the second to the sixth, and that portion of the *latissimus dorsi* which passes from the humerus to the last three ribs, all serve to elevate the ribs, and thus to enlarge the chest. The sterno-mastoid and other muscles passing from the neck to the sternum, are also called into action. In fact, every muscle which by its contraction can either elevate the ribs or contribute to the fixed support of muscles which do elevate the ribs, such as the trapezius, levator anguli scapulæ and rhomboidei by fixing the scapula, may, in the inspiratory efforts which accompany dyspnœa, be brought into play.

Expiration.—In normal easy breathing, expiration is in the main a simple effect of elastic reaction. By the inspiratory effort the elastic tissue of the lungs is put on the stretch; so long as the inspiratory muscles continue contracting, the tissue remains stretched, but directly those muscles relax, the elasticity of the lungs comes into play, and drives out a portion of the air contained in them. Similarly the elastic sternum and costal carti-

lages are by the elevation of the ribs put on the stretch—they are driven into a position which is unnatural to them. When the intercostal and other elevator muscles cease to contract, the elasticity of the sternum and costal cartilages causes them to return to their previous position, thus depressing the ribs, and diminishing the dimensions of the chest. When the diaphragm descends, in pushing down the abdominal viscera, it puts the abdominal walls on the stretch—and hence, when at the end of inspiration the diaphragm relaxes, the abdominal walls return to their place, and by pressing on the abdominal viscera, push the diaphragm up again into its position of rest. Expiration then is, in the main, simple elastic reaction; but there is probably some, though possibly in most cases, a very slight expenditure of muscular energy to bring the chest more rapidly to its former condition. This is, as we have seen, supposed by many to be afforded by the internal intercostals acting as depressors of the ribs. If these do not act in this way, we may suppose that the elastic return of the abdominal walls is accompanied and assisted by a contraction of the abdominal muscles. The triangularis sterni, the effect of whose contraction is to pull down the costal cartilages, may also be regarded as an expiratory muscle.

When expiration becomes labored, the abdominal muscles become important expiratory agents. By pressing on the contents of the abdomen, they thrust them, and, therefore, the diaphragm also up towards the chest, the vertical diameter of which is thereby lessened, while by pulling down the sternum, and the middle and lower ribs they lessen also the cavity of the chest in its antero-posterior and transverse diameters. They are, in fact, the chief expiratory muscles, though they are doubtless assisted by the serratus posticus inferior and portions of the sacro-lumbalis, since when the diaphragm is not contracting, the depression of the lower ribs—which the contraction of these muscles causes—serves only to narrow the chest. As expiration becomes more and more forced, every muscle in the body which can either by contracting depress the ribs, or press on the abdominal viscera, or afford fixed support to the muscles having those actions, is called into play.

Facial and Laryngeal Respiration.—The thoracic respiratory movements are accompanied by associated respiratory movements of other parts of the body, more particularly of the face and of the glottis.

In normal, healthy respiration, the current of air which passes in and out of the lungs, travels, not through the mouth but through the nose, chiefly through the lower nasal meatus. The ingoing air, by exposure to the vascular mucous membrane of the

narrow and winding nasal passages, is more efficiently warmed than it would be if it passed through the mouth; and at the same time the mouth is thereby protected from the desiccating effect of the continual inroad of comparatively dry air.

During each inspiratory effort the nostrils are expanded probably by the action of the dilatores naris, and thus the entrance of air facilitated. The return to their previous condition during expiration is effected by the elasticity of the nasal cartilages, assisted, perhaps, by the compressores naris. This movement of the nostrils, perceptible in many people, even during tranquil breathing, becomes very obvious in labored respiration.

When the mouth is closed, the soft palate which is held somewhat tense, is swayed by the respiratory current, but entirely in a passive manner, and it is not until the larynx is reached by the ingoing air that any active movements are met with. When the larynx is examined with the laryngoscope, it is frequently seen that, while during inspiration the glottis is widely open, with each expiration the arytenoid cartilages approach each other so as to narrow the glottis, the cartilages of Santorini projecting inwards at the same time. Thus, synchronous with the respiratory expansion and contraction of the chest, and the respiratory elevation and depression of the alæ nasi, there is a rhythmic widening and narrowing of the glottis. Like the movements of the nostril, this respiratory action of the glottis is much more evident in labored than in tranquil breathing. Indeed, in the latter case it is frequently absent. The manner in which this rhythmic opening and narrowing are effected will be described when we come to study the production of the voice. Whether there exists a rhythmic contraction and expansion of the trachea and bronchial passages effected by means of the plain muscular tissue of those organs and synchronous with the respiratory movements of the chest, is uncertain.

Sec. 2.—Changes of the Air in Respiration.

During its stay in the lungs, or rather during its stay in the bronchial passages, the tidal air (by means of diffusion chiefly) effects exchanges with the stationary air; in consequence, the expired air differs from inspired air in several important particulars.

1. The temperature of expired air is variable, but under ordinary circumstances is higher than that of the inspired air. At an average temperature of the atmosphere, for instance at about 20° C., the temperature of expired air is, in the mouth, 33.9°; in the nose, 35.3°. When the external temperature is low, that

of the expired air sinks somewhat, but not to any great extent; thus, at —6.3° C., it is 29.8° C. When the external temperature is high, the expired air may become cooler than the inspired; thus, at 41.9° it was found by Valentin to be 38.1°. The exact temperature, in fact, depends on the relative temperatures of the blood and inspired air, and on the depth and rate of breathing.

2. The expired air is loaded with aqueous vapor. The point of saturation of any gas—that is, the utmost quantity of water which any given volume of gas can take up as aqueous vapor—varies with the temperature, being higher with the higher temperature. For its own temperature, expired air is, according to most observers, saturated with aqueous vapor.

3. When the total quantity of tidal air given out at any expiration is compared with that taken in at the corresponding inspiration, it is found that, both being dried and measured at the same pressure, the expired air is less in volume than the inspired air, the difference amounting to about $\frac{1}{40}$th or $\frac{1}{50}$th of the volume of the latter. Hence, when an animal is made to breathe in a confined space, the atmosphere is absolutely diminished, as was observed so long ago as 1674 by Mayow. The approximate equivalence in volume between inspired and expired air arises from the fact that the volume of any given quantity of carbonic acid is equal to the volume of the oxygen consumed to produce it; the slight falling short of the expired air is due to the circumstance that all the oxygen inspired does not reappear in the carbonic acid expired, some having formed other combinations.

4. The expired air contains about four or five per cent. less oxygen, and about four per cent. more carbonic acid than the inspired air, the quantity of nitrogen suffering but little change. Thus

	Oxygen.	Nitrogen.	Carbonic Acid.
Inspired air contains	20.81	79.15	0.04
Expired air contains	16.033	79.587	4.380

The quantity of nitrogen in the expired air is sometimes found to be slightly greater, as in the table above, but sometimes less, than that of the inspired air.

In a single breath the air is richer in carbonic acid (and poorer in oxygen) at the end than at the beginning. Hence the longer the breath is held, the greater the pause between inspiration and expiration, the higher the percentage of carbonic acid in the expired air. Thus, by increasing the interval between two expirations to 100 seconds, the percentage may be raised to 7.5. When the rate of breathing remains the same, by increasing the depth of the breathing the percentage of carbonic acid in each breath is lowered, but the total quantity of carbonic acid

expired in a given time is increased. Similarly, when the depth of breath remains the same, by quickening the rate the percentage of carbonic acid in each breath is lowered, but the quantity expired in a given time is increased.

Taking, as we have done, at 500 c.c. the amount of tidal air passing in and out of the chest of an average man, such a person will expire about 22 c.c. of carbonic acid at each breath; this, reckoning the rate of breathing at 17 a minute, would give over 500 litres of carbonic acid for the day's production. By actual experiment, however, Pettenkofer and Voit, of whose researches we shall have to speak hereafter, determined the total daily excretion of carbonic acid in an average man to be 800 grms.— i. e., rather more than 400 litres (406), containing 218.1 grms. carbon, and 581.9 grms. oxygen, the oxygen actually consumed at the same time being about 700 grms. This amount represents the gases given out and taken in, not by the lungs only, but by the whole body; but the amount of carbonic acid given out by the skin is, as we shall see, very slight (10 grms., or even less), so that 800 grms. may be taken as the average production of carbonic acid by an average man. The quantity, however, both of oxygen consumed and of carbonic acid given out, is subject to very wide variations; thus, in Pettenkofer and Voit's observations, the daily quantity of carbonic acid varied from 686 to 1285 grms., and that of the oxygen from 594 to 1072 grms. These variations and their causes will be discussed when we come to deal with the problems of nutrition.

5. Besides carbonic acid, expired air contains various impurities, many of an unknown nature, and all in small amounts. Traces of ammonia have been detected in expired air, even in that taken directly from the trachea, in which case its presence could not be due to decomposing food lingering in the mouth. When the expired air is condensed by being conveyed into a cooled receiver, the aqueous product is found to contain organic matter, and rapidly to putrefy. The organic substances thus shown to be present in the expired air are the cause in part of the odor of breath. It is probable that many of them are of a poisonous nature; for an atmosphere containing simply one per cent. of carbonic acid (with a corresponding diminution of oxygen) has very little effect on the animal economy; whereas, an atmosphere in which the carbonic acid has been raised to one per cent. by breathing, is highly injurious. In fact, air rendered so far impure by breathing that the carbonic acid amounts to 0.08 per cent is distinctly unwholesome; not so much on account of the carbonic acid, as of the accompanying impurities. Since these impurities are of unknown nature, and cannot be estimated, the easily determined carbonic acid is usually taken as the meas-

urc of their presence. We have seen that the average man loads, at each breath, 500 c.c. of air with carbonic acid to the extent of four per cent. He will accordingly at each breath load two litres to the extent of one per cent.; and in one hour, if he breathe seventeen times a minute, will load rather more than 2000 litres to the same extent. At the very least, then, a man ought to be supplied with this quantity of air hourly; and if the air is to be kept fairly wholesome—that is, with the carbonic acid reduced considerably below 0.1 per cent.—he should have even more than ten times as much.

Sec. 3.—The Respiratory Changes in the Blood.

While the air in passing in and out of the lungs is thus robbed of a portion of its oxygen, and loaded with a certain quantity of carbonic acid, the blood as it streams along the pulmonary capillaries undergoes important correlative changes. As it leaves the right ventricle it is venous blood of a dark purple or maroon color; when it falls into the left auricle, it is arterial blood of a bright scarlet hue. In passing through the capillaries of the body from the left to the right side of the heart, it is again changed from the arterial to the venous condition. We have to inquire, What are the essential differences between arterial and venous blood, by what means is the venous blood changed into arterial in the lungs, and the arterial into venous in the rest of the body, and what relations do these changes in the blood bear to the changes in the air which we have already studied?

The facts, that venous blood at once becomes arterial on being exposed to or shaken up with air or oxygen, and that arterial blood becomes venous when kept for some little time in a closed vessel, or when submitted to a current of some indifferent gas, such as nitrogen or hydrogen, prepare us for the statement that the fundamental difference between venous and arterial blood is in the relative proportion of the oxygen and carbonic acid gases contained in each. From both, a certain quantity of gas can be extracted by means which do not otherwise materially alter the constitution of the blood; and this gas when obtained from arterial blood is found to contain more oxygen and less carbonic acid than that obtained from venous blood. This is the real differential character of the two bloods; all other differences are either, as we shall see to be the case with the color, dependent on this, or are unimportant and fluctuating.

If the quantity of gas which can be extracted by the mercurial air-pump from 100 vols. of blood be measured at 0° C., and a pressure of 760 mm., it is found to amount, in round numbers, to 60 vols.

FIG. 130.
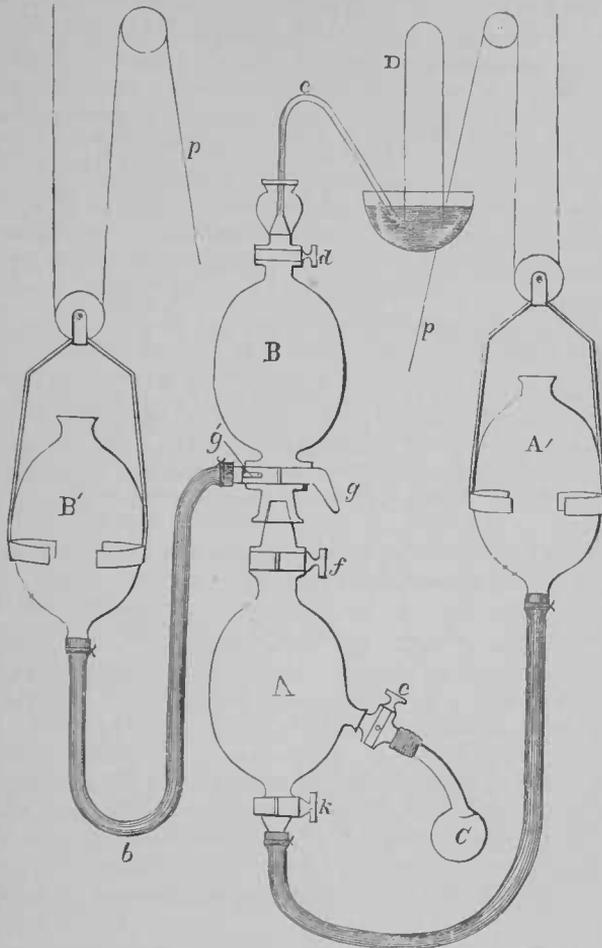
DIAGRAMMATIC ILLUSTRATION OF LUDWIG'S MERCURIAL GAS-PUMP.

A and B are two glass globes, connected by strong India-rubber tubes, a and b, with two similar glass globes A' and B'. A is further connected by means of the stopcock c, with the receiver C containing the blood (or other fluid) to be analyzed, and B by means of the stopcock d and tube e with the receiver D for receiving the gases. A and B are also connected with each other by means of the stopcocks f and g, the latter being so arranged that B also communicates with B' by the passage g'. A' and B' being full of mercury, and the cocks k, f, g, and d being open, but c and g' closed, on raising A' by means of the pulley p, the mercury of A' fills A, driving out the air contained in it, into B, and so out through e. When the mercury has risen above g, f is closed, and g' being opened, B' is in turn raised till B is completely filled with mercury, all the air previously in it being driven out through e. Upon closing d and lowering B', the whole of the mercury in B falls in B', and a vacuum consequently is established in B. On closing g' but opening g, f, and k, and lowering A', a vacuum is similarly established in A and in the junction between A and B. If the cock c be now opened the gases of the blood in C escape into the vacuum of A and B. By raising A', after the closure of c and opening of d, the gases so set free are driven from A into B, and by the raising of B' from B, through e into the receiver D, standing over mercury.

The vacuum produced by the ordinary mechanical air-pump is insuffi-
cient to extract all the gas from blood Hence it becomes necessary to use
either a large Torricellian vacuum or a Sprengel's pump. In the former
(Fig. 130) case two large globes of glass, one fixed and the other movable,
are connected by a flexible tube; the fixed globe is made to communicate
by means of air-tight stopcocks alternately with a receiver containing
the blood, and with a receiver to collect the gas. When the movable
globe filled with mercury is raised above the fixed one, the mercury from
the former runs into and completely fills the latter, the air previously
present being driven out. After adjusting the cocks, the movable globe
is then depressed thirty inches below the fixed one, in which the conse-
quent fall of the mercury produces an almost complete vacuum. By
turning the proper cock this vacuum is put into connection with the re-
ceiver containing the blood, which thereupon becomes proportionately
exhausted. By again adjusting the cocks and once more elevating the
movable globe, the gas thus extracted is driven out of the fixed globe
into a receiver. The vacuum is then once more established and the
operation repeated as long as gas continues to be given off from the blood.
This form of pump, introduced by Ludwig, or a modification of it, with
drying apparatus, employed by Pflüger, or a similar form introduced by
French observers, is the one which has been hitherto most extensively
used, but a Sprengel's pump is preferred by some.

The average composition of this gas in the two kinds of blood
is, stated in round numbers, as follows:

From 190 volumes		may be obtained	
	Of oxygen,	Of carbonic acid,	Of nitrogen,
Of arterial blood,	20 vols.	40 vols.	1 to 2 vols.
Of venous blood,	8 to 12 vols.	46 vols.	1 to 2 vols.

All measured at 760 mm. and 0° C.

That is to say, venous blood, as compared with arterial blood,
contains from 8 to 12 per cent. less oxygen and 6 per cent. more
carbonic acid. But the gases of venous blood are much more
variable than those of arterial blood.

It will be convenient to consider the relations of each of these
gases separately.

The Relations of Oxygen in the Blood.

When a liquid such as water is exposed to an atmosphere
containing a gas, such as oxygen, some of the oxygen will be
dissolved in the water—that is to say, will be absorbed from the
atmosphere. The quantity which is so absorbed will depend on
the quantity of oxygen which is in the atmosphere above—that
is to say, on the pressure of the oxygen; the greater the pressure
of the oxygen, the larger the amount which will be absorbed. If
on the other hand water, already containing a good deal of
oxygen dissolved in it, be exposed to an atmosphere containing
little or no oxygen, the oxygen will escape from the water into

the atmosphere. The oxygen, in fact, which is dissolved in the water is in a state of tension, the degree of tension depending on the quantity dissolved; and when water containing oxygen dissolved in it is exposed to any atmosphere, the result—that is, whether the oxygen escapes from the water into the atmosphere, or passes from the atmosphere into the water—depends on whether the tension of the oxygen in the water is greater or less than the pressure of the oxygen in the atmosphere. Hence, when water is exposed to oxygen, the oxygen either escapes or is absorbed until equilibrium is established between the pressure of the oxygen in the atmosphere above and the tension of the oxygen in the water below. This result is, as far as mere absorption and escape are concerned, quite independent of what other gases are present in the water or in the atmosphere. Suppose a half-litre of water were lying at the bottom of a two-litre flask, and that the atmosphere in the flask above the water was one-third oxygen; it would make no difference, as far as the absorption of oxygen by the water was concerned, whether the remaining two-thirds of the atmosphere was carbonic acid, or nitrogen, or hydrogen, or whether the space above the water was a vacuum filled to one-third with pure oxygen. Hence, it is said that the absorption of any gas depends on the *partial pressure* of that gas in the atmosphere to which the liquid is exposed. This is true not only of oxygen and water, but of all gases and liquids which do not enter into chemical combination with each other. Different liquids will, of course, absorb different gases with differing readiness; but, with the same gas and the same liquid, the amount absorbed will depend directly on the partial pressure of the gas. It should be added that the process is much influenced by temperature. Hence, to state the matter generally, the absorption of any gas by any liquid, will depend on the nature of the gas, the nature of the liquid, the pressure of the gas, and the temperature at which both stand.

Now, it might be supposed, and indeed was once supposed, that the oxygen in the blood was simply dissolved by the blood. If this were so, then the amount of oxygen present in any given quantity of blood exposed to any given atmosphere, ought to rise and fall steadily and regularly as the partial pressure of oxygen in that atmosphere is increased or diminished. But this is found not to be the case. If we expose blood containing little or no oxygen to a succession of atmospheres containing increasing quantities of oxygen, we find that, at first, there is a very rapid absorption of the available oxygen, and then this somewhat suddenly ceases or becomes very small; and if, on the other hand, we submit arterial blood to successively diminishing pressures, we find that for a long time very little is given off, and

then suddenly the escape becomes very rapid. The absorption
of oxygen by blood does not follow the general law of absorption
according to pressure. The phenomena, on the other hand, sug-
gest the idea that the oxygen in the blood is in some particular
combination with a substance or some substances present in the
blood, the combination being of such a kind that dissociation
readily occurs at certain pressures and certain temperatures.
What is that substance or what are those substances?

If serum, free from red corpuscles, be used in such absorption
experiments, it is found that as compared with the entire blood,
very little oxygen is absorbed, about as much as would be ab-
sorbed by the same quantity of water; but such as is absorbed
does follow the law of pressures. In natural arterial blood, the
quantity of oxygen which can be obtained from serum is exceed-
ingly small; it does not amount to half a volume in one hundred
volumes of the entire blood to which the serum belonged. It is
evident that the oxygen which is present in blood is in some way
or other peculiarly connected with the red corpuscles. Now the
distinguishing feature of the red corpuscles is the presence of
hæmoglobin. We have already seen (p. 54), that this constitutes
90 per cent. of the dried red corpuscles. There can be *à priori*
little doubt that this must be the substance with which oxygen is
associated; and to the properties of this body we must, therefore,
direct our attention.

Hæmoglobin; its properties and derivatives.

When separated from the other constituents of the serum,
hæmoglobin appears as a substance, either amorphous or crystal-
line, readily soluble in water (especially in warm water and in
serum.

Since hæmoglobin is soluble in serum, and since the identity of the
crystals observed occasionally within the corpuscles with those obtained
in other ways shows that the hæmoglobin as it exists in the corpuscle is
the same thing as that which is artificially prepared from blood, it is
evident that some peculiar relationship between the stroma and the hæmo-
globin must, in natural blood, keep the latter from being dissolved by
the serum. Hence in preparing hæmoglobin it is necessary first of all to
break up the corpuscles. This may be done by the addition of water, of
ether, of chloroform, or of bile salts, or by repeatedly freezing and thaw-
ing. It is also of advantage previously to remove the alkaline serum as
much as possible so as to operate only on the red corpuscles. The cor-
puscles being thus broken up, a solution of hæmoglobin is the result.
The alkalinity of the solution, when present, being reduced by the
cautious addition of dilute acetic acid, and the solvent power of the
aqueous medium being diminished by the addition of one-fourth its bulk
of alcohol, the mixture set aside in a temperature of 0° C. in order still
further to reduce the solubility of the hæmoglobin, readily crystallizes,
when the blood used is that of the dog, cat, horse, rat, guinea-pig, etc.

In the case of the dog, indeed, it is simply sufficient to add ether to the blood and then to let it stand in a cold place; the mixture soon becomes a mass of crystals. The crystals may be separated by filtration, redissolved in water and recrystallized.

Hæmoglobin from the blood of the rat, guinea-pig, squirrel, hedgehog, horse, cat, dog, goose, and some other animals, crystallizes readily, the crystals being generally slender four-sided prisms, belonging to the rhombic system, and often appearing quite acicular. The crystals from the blood of the guinea-pig are octahedral, but also belong to the rhombic system; those of the squirrel are six-sided plates. The blood of the ox, sheep, rabbit, pig, and man, crystallizes with difficulty. (Figs. 124, 125, 126.) Why these differences exist is not known; but the com-

[FIG. 131.

Tetrahedral from Blood of the Pig.]
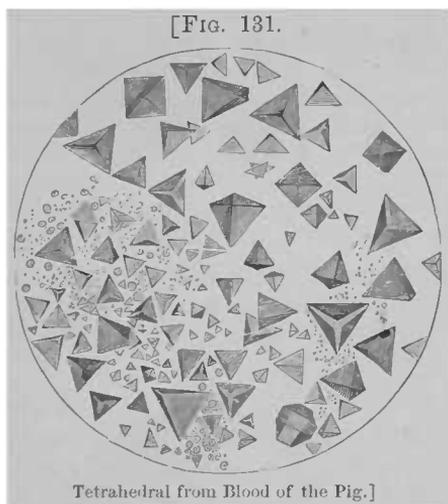
position, and the amount of water of crystallization, vary somewhat in the crystals obtained from different animals. In the dog, the percentage composition of the crystals is, according to Hoppe-Seyler, C. 53.85, H. 7.32, N. 16.17, O. 21.84, S. 0.39, Fe. 0.43, with three to four per cent. of water of crystallization. It will thus be seen that hæmoglobin contains, in addition to the other elements usually present in proteid substances, a certain amount of iron; that is to say, the element iron is a distinct part of the hæmoglobin molecule: a fact which of itself renders hæmoglobin remarkable among the chemical substances present in the animal body.

The crystals, when seen in a sufficiently thick layer under the microscope, have the same bright scarlet color as arterial blood has to the naked eye; when seen in a mass they naturally appear darker. An aqueous solution of hæmoglobin, obtained by dis-

solving purified crystals in distilled water, has also the same
bright arterial color.   A tolerably dilute solution placed before
the spectroscope is found to absorb certain rays of light in a

[FIG. 132.
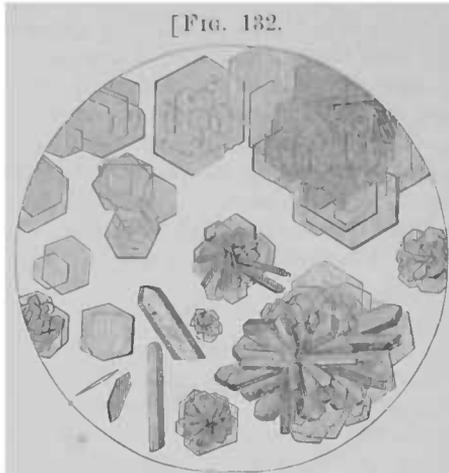
Hexagonal Crystals, from Blood of Squirrel. On these six-sided plates, prismatic crystals,
grouped in a stellate manner, not unfrequently occur.   After FINKE]

peculiar and characteristic manner.   A portion of the red end
of the spectrum is absorbed, as is also a much larger portion of
the blue end ; but what is most striking is the presence of two

[FIG. 133.

Prismatic, from Human Blood]

strongly marked absorption bands, lying between the solar lines D
and E.   See Fig. 134.)   Of these the one towards the red side,
sometimes spoken of as the band a, is the thinnest, but the most

intense, and in extremely dilute solutions (Fig. 134, 1) is the only one visible; its middle lies at some little distance to the blue side of D. Its position may be more exactly defined by expressing it in wave-lengths. As is well known, the rays of light which make up the spectrum differ in the length of their waves, diminishing from the red end where the waves are longest, to the blue end where they are shortest. Thus Frauenhofer's line D corresponds to rays having a wave-length of 589.4 millionths of a millimetre. Using the same unit, the centre of this absorption band a of hæmoglobin corresponds to the wave-length 578; as may be seen in Fig. 134, where however the numbers of the divisions of the scale indicate only 100,000th of a millimetre. The other, sometimes called B, much broader, lies a little to the red side of E, its blue-ward edge, even in moderately dilute solutions (Fig. 134, 2) coming close up to that line; its centre corresponds to about wave-length 539. Each band is thickest in the middle, and gradually thins away at the edges. These two absorption bands are extremely characteristic of a solution of hæmoglobin. Even in very dilute solutions both bands are visible (they may be seen in a thickness of 1 c.m. in a solution containing 1 grm. of hæmoglobin in 10 litres of water), and that when scarcely any of the extreme red end, and very little of the blue end, is cut off. They then appear not only faint but narrow. As the strength of the solution is increased, the bands broaden, and become more intense; at the same time both the red end, and still more the blue end, of the whole spectrum, are encroached upon (Fig 134, 3). This may go on until the two absorption bands become fused together into one broad band (Fig. 134, 4). The only rays of light which then pass through the hæmoglobin solution are those in the green between the blue-ward edge of the united bands and the general absorption which is now rapidly advancing from the blue end, and those in the red between the united bands and the general absorption at the red end. If the solution be still further increased in strength, the interval on the blue side of the united bands becomes absorbed also, so that the only rays which pass through are the red rays lying to the red side of D; these are the last to disappear, and hence the natural red color of the solution as seen by transmitted light. Exactly the same appearances are seen when crystals of hæmoglobin are examined with a micro-spectroscope. They are also seen when arterial blood itself (diluted with saline solutions so that the corpuscles remain in as natural condition as possible) is examined with the spectroscope, as well as when a drop of blood, which from the necessary exposure to air is always arterial, is examined with the micro-spectroscope. In fact, the spectrum of hæmoglobin is the spectrum of normal arterial blood.

FIG. 134.
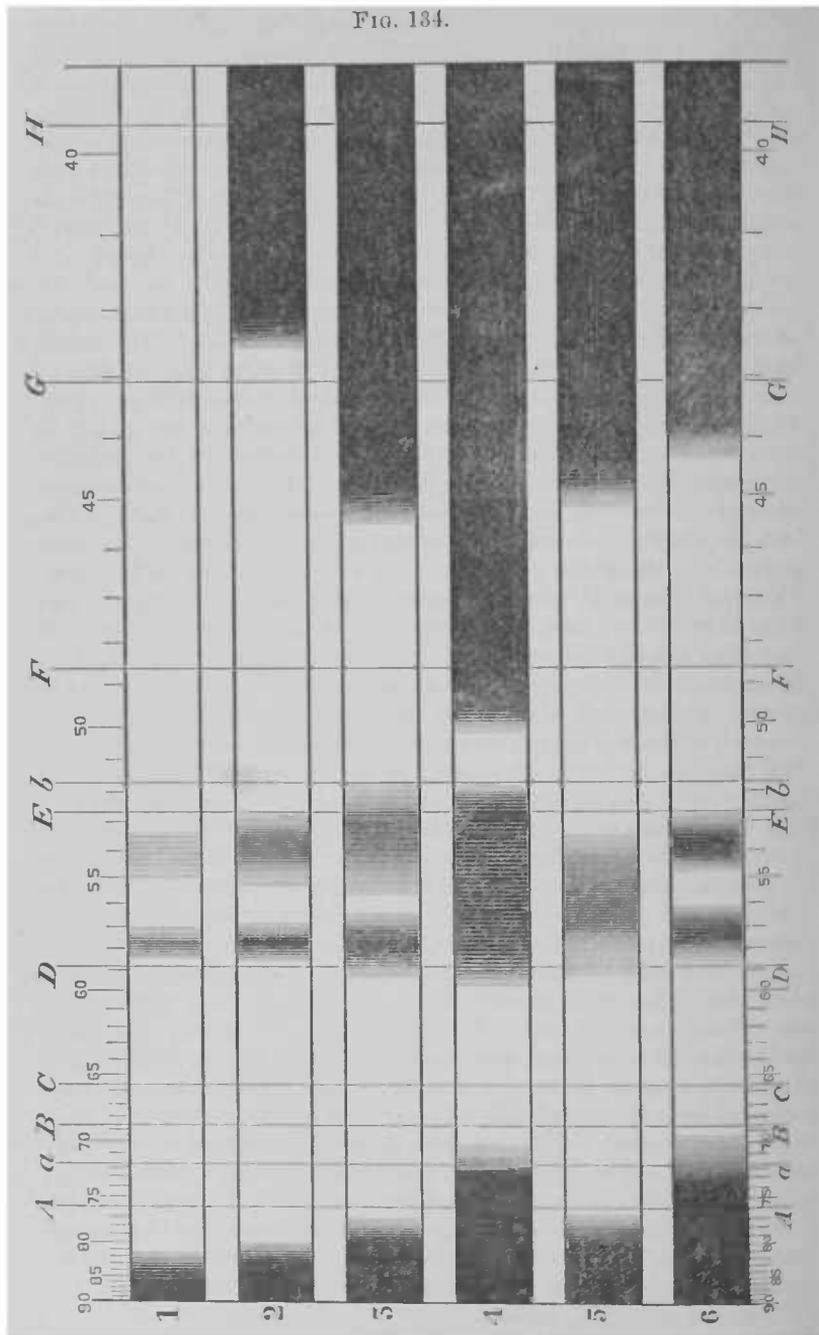
1. Solution of oxyhæmoglobin containing less than 0 01 per cent.
2. Solution of oxyhæmoglobin containing 0.09 per cent.
3. Solution of oxyhæmoglobin containing 0 37 per cent.
4. Solution of oxyhæmoglobin containing 0.8 per cent.
5. Solution of (reduced) hæmoglobin containing about 0.2 per cent.
6. Solution of carbonic-oxide-hæmoglobin.

In each of the six cases the layer brought before the spectroscope was 1 cm in thickness.

The letters (A, a, etc.) indicate Frauenhofer's lines, and the figures wave-lengths expressed in 100,000th of a millimetre.

When crystals of hæmoglobin, prepared in the way already described, are subjected to the vacuum of the mercurial air-pump, they give off a certain quantity of oxygen, and at the same time they change in color. The quantity of oxygen given off is definite, 1 grm. of the crystals giving off 1.59 c.cm. of oxygen. In other words, the crystals of hæmoglobin over and above the oxygen which enters intimately into their composition (and which alone is given in the elementary composition stated on p. 399), contain another quantity of oxygen, which is in loose combination only, and which may be dissociated from them by subjecting them to a sufficiently low pressure. The change of color which ensues when this loosely combined oxygen is removed, is characteristic; the crystals become darker and more of a purple hue, and at the same time dichroic, so that while the thin edges appear green, the thicker ridges are purple.

An ordinary solution of hæmoglobin, like the crystals from which it is formed, contains a definite quantity of oxygen in a similarly peculiar loose combination; this oxygen it also gives up at a sufficiently low pressure, becoming at the same time of a purplish hue. This loosely combined oxygen may also be removed by passing a stream of hydrogen or other indifferent gas through the solution, whereby dissociation is effected. It may also be got rid of by the use of reducing agents. Thus if a few drops of ammonium sulphide or of an alkaline solution of ferrous sulphate, kept from precipitation by the presence of tartaric acid, be added to a solution of hæmoglobin, or even to an unpurified solution of blood corpuscles such as is afforded by the washings from a blood-clot, the oxygen in loose combination with the hæmoglobin is immediately seized upon by the reducing agent. This may be recognized at once, by the characteristic change of color; from a bright scarlet the solution becomes of a purplish-claret color, when seen in any thickness, but green when sufficiently thin: the color of the reduced solution is exactly like that of the crystals from which the loose oxygen has been removed by the air-pump.

Examined by the spectroscope, this reduced solution, or solution

of reduced hæmoglobin as we may now call it, offers a spectrum (Fig. 134, 5) entirely different from that of the unreduced solution. The two absorption bands have disappeared, and in their place there is seen a single, much broader, but at the same time much fainter band whose middle occupies a position about midway between the two absorption bands of the unreduced solution, though the red-ward edge of the band shades away rather further towards the red than does the other edge towards the blue; its centre corresponds to about wave-length 555. At the same time the general absorption of the spectrum is different from that of the unreduced solution; less of the blue end is absorbed. Even when the solutions become tolerably concentrated, many of the bluish-green rays to the blue side of the single band still pass through. Hence, the difference in color between hæmoglobin which retains the loosely combined oxygen,[1] and hæmoglobin which has lost its oxygen and become reduced. In tolerably concentrated solutions, or tolerably thick layers, the former lets through the red and the orange-yellow rays, the latter the red and the bluish-green rays. Accordingly, the one appears scarlet, the other purple. In dilute solutions, or in a thin layer, the reduced hæmoglobin lets through so much of the green rays that they preponderate over the red, and the resulting impression is one of green. In the unreduced hæmoglobin or oxyhæmoglobin, the potent yellow which is blocked out in the reduced hæmoglobin makes itself felt, so that a very thin layer of oxyhæmoglobin, as in a single corpuscle seen under the microscope, appears yellow rather than red.

When the hæmoglobin solution (or crystal) which has lost its oxygen by the action either of the air-pump or of a reducing agent or by the passage of an indifferent gas, is exposed to air containing oxygen, an absorption of oxygen at once takes place. If sufficient oxygen be present, the whole of the hæmoglobin seizes upon its complement, each gramme taking up in combination 1.59 c.cm. of oxygen; if there be an insufficient quantity of oxygen, a part only of the hæmoglobin gets its allowance and the remainder continues reduced. If the amount of oxygen be sufficient, the solution (or crystals), as it takes up the oxygen, regains its bright scarlet color, and its characteristic absorption spectrum, the single band being replaced by the two. Thus if a solution of oxyhæmoglobin in a test-tube after being reduced by the ferrous salt, and showing the purple color and the single band, be shaken up with air, the bright scarlet color at once returns, and when the fluid is placed before the spectroscope, it is seen

[1] For brevity's sake we may call the hæmoglobin containing oxygen in loose combination *oxyhæmoglobin*, and the hæmoglobin from which this loosely combined oxygen has been removed, reduced hæmoglobin or simply hæmoglobin.

that the single faint broad band of the reduced hæmoglobin has wholly disappeared, and that in its place are the two sharp thinner bands of the oxyhæmoglobin. If left to stand in the test-tube, the quantity of reducing agent still present is generally sufficient again to rob the hæmoglobin of the oxygen thus newly acquired, and soon the scarlet hue fades back again into the purple, the two bands giving place to the one. Another shake and exposure to air will, however, again bring back the scarlet hue and the two bands; and once more these may disappear. In fact, a few drops of the reducing fluid will allow this game of taking oxygen from the air and giving it up to the reducer to be played over and over again, and at each turn of the game the color shifts from scarlet to purple, and from purple to scarlet, while the two bands exchange for the one, and the one for the two.

Color of Venous and Arterial Blood.—Evidently we have in these properties of hæmoglobin an explanation of at least one-half of the great respiratory process, and they teach us the meaning of the change of color which takes place when venous blood becomes arterial or arterial venous. In venous blood, as it issues from the right ventricle, the oxygen present is insufficient to satisfy the whole of the hæmoglobin of the red corpuscles; much reduced hæmoglobin is present, hence the purple color of venous blood.

When ordinary venous blood, diluted without access of oxygen, is brought before the spectroscope, the two bands of oxyhæmoglobin are seen. This is explained by the fact that in a mixture of oxyhæmoglobin and (reduced) hæmoglobin, the two sharp bands of the former are always much more readily seen than the much fainter band of the latter. Now in ordinary venous blood there is always some loose oxygen, removable by diminished pressure or otherwise; there is always some—indeed, a considerable quantity—of oxyhæmoglobin as well as (reduced) hæmoglobin. It is only in the very last stages of asphyxia that all the loose oxygen of the blood disappears; and then the two bands of the oxyhæmoglobin vanish too. So distinct are the two bands of even a small quantity of oxyhæmoglobin in the midst of a large quantity of hæmoglobin that a solution of (completely reduced) hæmoglobin may be used as a test for the presence of oxygen.

As the blood passes through the capillaries of the lungs, this reduced hæmoglobin takes from the pulmonary air its complement of oxygen, all or nearly all the hæmoglobin of the red corpuscles becomes oxyhæmoglobin, and the purple color forthwith shifts into scarlet.

The hæmoglobin of arterial blood is saturated or nearly satu-

rated with oxygen. By increasing the pressure of the oxygen, an additional quantity may be driven into the blood, but this, after the hæmoglobin has become completely saturated, is effected by simple absorption. The quantity so added is extremely small compared with the total quantity combined with the hæmoglobin, but its physiological importance is increased by its being present at a high tension.

Passing from the left ventricle to the capillaries, some of the oxyhæmoglobin gives up its oxygen to the tissues, becomes reduced hæmoglobin, and the blood in consequence becomes once more venous, with a purple hue. Thus the red corpuscles, by virtue of their hæmoglobin, are emphatically oxygen-carriers. Undergoing no intrinsic change in itself, the hæmoglobin combines in the lungs with oxygen, which it carries to the tissues; these, more greedy of oxygen than itself, rob it of its charge, and the reduced hæmoglobin hurries back to the lungs in the venous blood for another portion. The change from venous to arterial blood is then in part (for, as we shall see, there are other events as well) a peculiar combination of hæmoglobin with oxygen, while the change from arterial to venous is, in part also, a reduction of oxyhæmoglobin; and the difference of color between venous and arterial blood depends almost entirely on the fact that the reduced hæmoglobin of the former is of purple color, while the oxyhæmoglobin of the latter is of a scarlet color.

There may be other causes of the change of color, but these are wholly subsidiary and unimportant. When a corpuscle swells, its refractive power is diminished, and in consequence the number of rays which pass into and are absorbed by it are increased at the expense of those reflected from its surface; anything, therefore, which swells the corpuscles, such as the addition of water, tends to darken blood; and anything, such as a concentrated saline solution, which causes the corpuscles to shrink, tends to brighten blood. Carbonic acid has apparently some influence in swelling the corpuscles, and therefore may aid in darkening the venous blood.

We have spoken of the combination of hæmoglobin with oxygen as being a peculiar one. The peculiarity consists in the facts that the oxygen may be associated and dissociated, without any general disturbance of the molecule of hæmoglobin, and that dissociation may be brought about very readily. Hæmoglobin combines in a wholly similar manner with other gases. If carbonic oxide be passed through a solution of hæmoglobin, a change of color takes place, a peculiar bluish tinge making its appearance. At the same time, the spectrum is altered; two bands are still visible, but on accurate measurement it is seen that they are placed more towards the blue end than are the otherwise similar

bands of oxyhæmoglobin (see Fig. 134, 6); their centres corresponding respectively to about wave-lengths 572, and 533, while those of oxyhæmoglobin, as we have seen, correspond to 578 and 539. When a known quantity of carbonic oxide gas is sent through a hæmoglobin solution, it will be found on examination that a certain amount of the gas has been retained, an equal volume of oxygen appearing in its place in the gas which issues from the solution. If the solution so treated be crystallized, the crystals will have the same characteristic color, and give the same absorption spectrum as the solution; when subjected to the action of the mercurial pump, they will give off a definite quantity of carbonic oxide, 1 grm. of the crystals yielding 1.59 c.cm. of the gas. In fact, hæmoglobin combines loosely with carbonic oxide just as it does with oxygen; but its affinity with the former is greater than with the latter. While carbonic oxide readily turns out oxygen, oxygen cannot so readily turn out carbonic oxide. Indeed, carbonic oxide has been used as a means of driving out and measuring the quantity of oxygen present in any given blood. This property of carbonic oxide explains its poisonous nature. When the gas is breathed, the reduced and the unreduced hæmoglobin of the venous blood unite with the carbonic oxide, and hence the peculiar bright cherry-red color observable in the blood and tissues in cases of poisoning by this gas. The carbonic-oxide-hæmoglobin, however, is of no use in respiration; it is not an oxygen-carrier, nay more, it will not readily, though it does so slowly and eventually, give up its carbonic oxide for oxygen, when the poisonous gas ceases to enter the chest and is replaced by pure air. The organism is killed by suffocation, by want of oxygen, in spite of the blood not assuming any dark venous color. As Bernard phrased it, the corpuscles are paralyzed.

Hæmoglobin similarly forms a compound, having a characteristic spectrum, with nitric oxide, more stable even than that with carbonic oxide.

It has been supposed by some that the oxygen thus associated with hæmoglobin is in the condition known as ozone; but the arguments urged in support of this view are inconclusive.

Although a crystalline body, hæmoglobin diffuses with great difficulty. This arises from the fact that it is in part a proteid body; it consists of a colorless proteid, associated with a colored compound named *hæmatin*. All the iron belonging to the hæmoglobin is in reality attached to the hæmatin. A solution of hæmoglobin, when heated, coagulates, the exact degree at which the coagulation takes place depending on the amount of dilution; at the same time it turns brown from the setting free of the hæmatin. If a strong solution of hæmoglobin be treated with

acetic (or other) acid, the same brown color, from the appearance
of hæmatin, is observed.   The proteid constituent however is not
coagulated, but by the action of the acid passes into the state of
acid-albumin.   On adding ether to the mixture, and shaking,
the hæmatin is dissolved in the supernatant acid ether, which it
colors a dark red, and which, examined with the spectroscope, is
found to possess a well-marked spectrum, the spectrum of the so-
called acid hæmatin of Stokes.   The proteid in the water below
the ether appears in a coagulated form owing to the action of the
ether.   In a somewhat similar manner alkalies split up hæmo-
globin into a proteid constituent and hæmatin.

The exact nature of the proteid constituent of hæmoglobin
has not as yet been clearly determined.   It was supposed to be
globulin (hence the name hæmatoglobulin contracted into hæmo-
globin), but though belonging to the globulin family, has char-
acters of its own ; it is possibly a mixture of two or more distinct
proteids.   It has been provisionally named *globin* and is said to be
free from ash.   Hæmatin when separated from its proteid fellow,
and purified, appears as a dark brown amorphous powder, or as
a scaly mass with a metallic lustre, having the probable com-
position of $C_{32}H_{34}N_4FeO_5$.   It is fairly soluble in dilute acid or
alkaline solutions, and then gives characteristic spectra.

An interesting feature in hæmatin is that its *alkaline* solution
is capable of being reduced by reducing agents, the spectrum
changing at the same time, and that the reduced solution will,
like the hæmoglobin, take up oxygen again on being brought
into contact with air or oxygen.   This would seem to indicate
that the oxygen-holding power of hæmoglobin is connected ex-
clusively with its hæmatin constituent.   By the action of strong
sulphuric acid hæmatin may be robbed of all its iron.   It still
retains the feature of possessing color, the solution of iron-free
hæmatin being a dark rich brownish-red ; but is no longer
capable of combining loosely with oxygen.   This indicates that
the iron is in some way associated with the peculiar respiratory
functions of hæmoglobin ; though it is obviously an error to
suppose, as was once supposed, that the change from venous to
arterial blood consists essentially in a change from a ferrous to a
ferric salt.

Though not crystallizable itself, hæmatin forms with hydro-
chloric acid a compound, occurring in minute rhombic crystals,
known as hæmin crystals.

In conclusion, the condition of oxygen in the blood is as
follows.   Of the whole quantity of oxygen in the blood, only a
minute fraction is simply absorbed or dissolved, according to the
law of pressures (the Henry-Dalton law).   The great mass is in
a state of combination with the hæmoglobin, the connection being

of such a kind that while the hæmoglobin readily combines with the oxygen of the air to which it is exposed, dissociation readily occurs at low pressures, or in the presence of indifferent gases, or by the action of substances having a greater affinity for oxygen than has hæmoglobin itself. The difference between venous and arterial blood, as far as oxygen is concerned, is that while in the latter there is an insignificant quantity of reduced hæmoglobin, in the former there is a great deal; and the characteristic colors of venous and arterial blood are in the main due to the fact that the color of reduced hæmoglobin is purple, while that of oxyhæmoglobin is scarlet.

The Relations of the Carbonic Acid in the Blood.

The presence of carbonic acid in the blood appears to be determined by conditions more complex in their nature and at present not so well understood as those which determine the presence of oxygen. The carbonic acid is not simply dissolved in the blood; its absorption by blood does not follow the law of pressures. It exists in association with some substance or substances in the blood, and its escape from the blood is a process of dissociation. We cannot however speak of it as being associated, to the same extent as is the oxygen, with the hæmoglobin of the red corpuscles. So far from the red corpuscles containing the great mass of the carbonic acid, the quantity of this gas which is present in a volume of serum is according to some observers actually greater than that which is present in an equal volume of blood—*i. e.*, an equal volume of mixed corpuscles and serum.

When serum is subjected to the mercurial vacuum, by far the greater part of the carbonic acid is given off; but a small additional quantity (2 to 5 vols. per cent.) may be extracted by the subsequent addition of an acid. This latter portion may be spoken of as "fixed" carbonic acid in distinction to the larger "loose" portion which is given off to the vacuum. When however the whole blood is subjected to the vacuum, all the carbonic acid is given off, so that when serum is mixed with corpuscles all the carbonic acid may be spoken of as "loose;" and it is stated that the excess of carbonic acid in serum over that present in entire blood, corresponds to the fixed portion in serum which has to be driven off by an acid. Moreover, even those who maintain that the quantity of carbonic acid in blood is less than that in an equal volume of serum, admit that the *tension* of the carbonic acid in blood is greater than in serum.

If these statements be accepted, it seems probable that the carbonic acid exists associated with some substance or substances

in the serum, but that the conditions of its association (and therefore of its dissociation) are determined by the action of some substance or substances present in the corpuscles. It is further probable that the association of the carbonic acid in the serum is with sodium as sodium bicarbonate, and it is even possible that the hæmoglobin of the corpuscles plays a part in promoting the dissociation of the sodium bicarbonate or even the carbonate, and thus keeping up the carbonic acid tension of the entire blood. Other observers however maintain that the serum does not hold this exclusive possession of the carbonic acid, but that a considerable quantity of this gas is in some way associated with the red corpuscles. Indeed further investigations are necessary before the matter can be said to have been placed on a satisfactory footing.

The Relations of the Nitrogen in the Blood.

The small quantity of this gas which is present in both arterial and venous blood seems to exist in a state of simple solution.

SEC. 4.—THE RESPIRATORY CHANGES IN THE LUNGS.

The Entrance of Oxygen.

We have already seen that the blood in passing through the lungs takes up a certain variable quantity (from 8 to 12 vols. per cent.) of oxygen. We have further seen that the quantity so taken up, putting aside the insignificant fraction simply absorbed, enters into direct but loose combination with the hæmoglobin. In drawing a distinction between the oxygen simply absorbed and that entering into combination with the hæmoglobin, it must not be understood that the latter is wholly independent of pressure. On the contrary all chemical compounds are in various degrees subject to dissociation at certain pressures and temperatures; and the existence of the somewhat loose compound of oxygen and hæmoglobin is dependent on the partial pressure of oxygen in the atmosphere to which the hæmoglobin is exposed. A solution of hæmoglobin or a quantity of blood will either absorb oxygen and thus undergo association or will undergo dissociation and give off oxygen according to the partial pressure of oxygen in the atmosphere to which it is exposed is high or low, and the amount taken up or given off will depend on the degree of the partial pressure. But the law according to which absorption or escape thus takes place is quite

different from that observed in the simple absorption of oxygen by liquids. The association or dissociation is further especially dependent on temperature, a high temperature favoring dissociation so that at a high temperature less oxygen is taken up than would be taken up (or more given off as the case may be than would be given off) at a lower temperature, the partial pressure of the oxygen in the atmosphere remaining the same.

Hence the question arises, Are the conditions in which hæmoglobin and oxygen exist in ordinary venous blood as it flows to the lungs, of such a kind that the venous blood in passing through the pulmonary capillaries will find the partial pressure of the oxygen in the pulmonary alveoli sufficient to bring about the association of the additional quantity of oxygen whereby the venous is converted into arterial blood?

The oxygen of expired air contains (in man) as we have seen about 16 per cent. of oxygen. The air in the pulmonary alveoli must contain rather less than this, since the expired air consists of tidal air mixed by diffusion with the stationary air. How much less it contains we do not exactly know, but probably the difference is not very great. The question therefore stands thus, Will venous blood, exposed at the temperature of the body to a partial pressure of less than 16 per cent. of oxygen take up sufficient oxygen (from 8 to 12 vols. per cent.) to convert it into arterial blood? Numerous experiments have been made (chiefly on the dog) to determine on the one hand the oxygen-tension of both arterial and venous blood (i. e., the partial pressure of oxygen in an atmosphere exposed to which the arterial blood neither gives up nor takes in oxygen, and the same for venous blood), and on the other hand the behavior at the temperature of the body or at ordinary temperature of blood or of solutions of hæmoglobin (for the two behave in this respect very much alike) towards an atmosphere in which the partial pressure of oxygen is made to vary. Without going into detail, we may state that these experiments show that the partial pressure of oxygen in the lungs is amply sufficient to bring about, at the temperature of the body, the association of that additional amount of oxygen by which venous blood becomes arterial. When a solution of hæmoglobin or when blood is successively exposed to increasing oxygen pressures, as the partial pressure of oxygen is gradually increased, the curve of absorption rises at first very rapidly but afterwards more slowly, that is to say, the later additions of oxygen at the higher pressures are proportionately less than the earlier ones, at the lower pressures. And this is consonant with what appears to be the fact that the hæmoglobin of arterial blood though nearly saturated with oxygen—i. e., associated with almost its full complement of oxygen, is not quite saturated. When arterial blood

is thoroughly exposed to air, it takes up rather more than 1 vol. per cent. of oxygen : and that appears to represent the difference between exposing blood to air as it enters the mouth in inspiration and exposing blood to the air as it exists in the pulmonary alveoli.

The greater relative absorption at the lower pressures has a beneficial effect inasmuch as it still permits a considerable quantity of oxygen to be absorbed even when the partial pressure of oxygen in the air in the lungs is largely reduced, as in ascending to great heights.

The statements made so far refer to ordinary breathing, but the question may be asked, what happens when the renewal of the air in the pulmonary alveoli ceases, as when the trachea is obstructed ? In such a case the oxygen in the alveoli is found to diminish rapidly, so that the partial pressure of oxygen in them soon falls below the oxygen tension of ordinary venous blood. But in such a case the blood is no longer ordinary venous blood ; instead of containing a comparatively small amount, it contains a large and gradually increasing amount, of reduced hæmoglobin. And as the reduced hæmoglobin increases in amount, the oxygen tension of the venous blood decreases ; it thus keeps below that of the air in the lungs. Hence even the last traces of oxygen in the lungs are taken up by the blood, and carried away to the tissues ; so that with the last heart's beat, when the oxygen in the lungs has sunk to a mere fraction, the bands of oxyhæmoglobin may still, it is said, be detected for a moment in the blood of the left side of the heart, showing that oxygen has even still been absorbed.

The Exit of Carbonic Acid.

It seems natural to suppose that the carbonic acid would escape by diffusion from the blood of the alveolar capillaries into the air of the alveoli. But in order that diffusion should thus take place, the carbonic acid tension of the air in the pulmonary alveoli must always be less than that of the venous blood of the pulmonary artery, and indeed ought not to exceed that of the blood of the pulmonary vein. There are, however, many practical difficulties in the way of an exact determination of the carbonic acid tension of the pulmonary alveoli (for though it must be greater than that of the expired air, it is difficult to say how much greater), and of the carbonic acid tension of the blood at the same time, so as to be in a position to compare the one with the other. In the case of oxygen, there is always present in the lungs a surplus of the gas, a portion only being absorbed at each breath ; in the case of carbonic acid, the whole

quantity comes direct from the blood, and any modifications in breathing seriously affect the amount given out. Thus when the breath is held for some time the percentage of carbonic acid in the expired air reaches 7 or 8 per cent., but we cannot take this as a measure of the normal percentage of carbonic acid in the pulmonary alveoli, since by the mere holding of the breath the carbonic acid in the blood and in the pulmonary alveoli is increased beyond the normal.

The difficulties of the problem seem, however, to have been overcome by an ingenious experiment in which there is introduced into the bronchus of the lung of a dog a catheter, round which is arranged a small bag; by the inflation of this bag the bronchus, whenever desired, can be completely blocked up. Thus, without any disturbance of the general breathing, and therefore without any change in the normal proportions of the gases of the blood, the experimenter is able to stop the ingress of fresh air into a limited portion of the lung. At the same time, he is enabled by means of the catheter to withdraw a sample of the air of the same limited portion, and, by analysis, to determine its carbonic acid tension. The blood passing through the alveolar capillaries of this limited portion of the lung naturally possesses the same carbonic acid tension as the rest of the venous blood flowing through the pulmonary artery, a tension which, though varying slightly from moment to moment, will maintain a normal average. On the supposition that carbonic acid passes simply by diffusion from the pulmonary blood into the air of the alveoli, because the carbonic acid tension of the latter is normally lower than that of the former, one would expect to find that the air in the occluded portion of the lung would continue to take up carbonic acid until an equilibrium was established between it and the carbonic acid tension of the venous blood. Consequently, if after an occlusion, say of some minutes (by which time the equilibrium might fairly be assumed to have been established), the carbonic acid tension of the air of the occluded portion were determined, it ought to be found to be equal to, and not more than equal to, the carbonic acid tension of the venous blood of the pulmonary artery. And this is the result which has been arrived at; it has been found that the tensions of the carbonic acid of the occluded air and of the venous blood of the right side of the heart are just about equal, that of the occluded air being, if anything, slightly less than that of the venous blood. So that the evidence, so far as it goes, is distinctly in favor of the view that the escape of carbonic acid from the blood into the pulmonary alveoli is simply due to diffusion, and that there is no need to seek for any further explanation. There is, for instance, no necessity to suppose that the epithelium of the pulmonary alveoli

has any specific secretory power of discharging carbonic acid from the blood independently of or in antagonism to the influence of pressures.

Sec. 5.—The Respiratory Changes in the Tissues.

In passing through the several tissues the arterial blood becomes once more venous. A considerable quantity of the oxyhæmoglobin becomes reduced, and a quantity of carbonic acid passes from the tissues into the blood. The amount of change varies in the various tissues, and in the same tissue may vary at different times. Thus, in a gland at rest, as we have seen, the venous blood is dark, showing the presence of a large quantity of reduced hæmoglobin; when the gland is active, the venous blood in its color, and in the amount of hæmoglobin which it contains, resembles closely arterial blood. The blood, therefore, which issues from a gland at rest is more "venous" than that from an active gland; though, owing to the more rapid flow of blood which, as we saw in an earlier section, accompanies the activity of the gland, the total quantity of carbonic acid discharged into the blood from the gland in a given time may be greater in the latter. The blood, on the other hand, which comes from an active—i. e., a contracting—muscle, is, in spite of the more rapid flow, not only richer in carbonic acid, but also, though not to a corresponding amount, poorer in oxygen than the blood which flows from a muscle at rest.

In all these cases the great question which comes up for our consideration is this: Does the oxygen pass from the blood into the tissues, and does the oxidation take place in the tissues, giving rise to carbonic acid, which passes in turn away from the tissues into the blood? or do certain oxidizable reducing substances pass from the tissues into the blood, and there become oxidized into carbonic acid and other products, so that the chief oxidation takes place in the blood itself?

There are, it is true, reducing oxidizable substances in the blood, but these are small in amount, and the quantity of carbonic acid to which they give rise when the blood containing them is agitated with air or oxygen, is so small as scarcely to exceed the errors of observation.

On the other hand, it will be remembered that in speaking of muscle, we drew attention to the fact that a frog's muscle removed from the body (and the same is true of the muscles of other animals) contains no free oxygen whatever; none can be obtained from it by the mercurial air-pump. Yet such a muscle will not

quantity, but also when it contracts evolve a very considerable quantity of carbonic acid. Moreover, this discharge of carbonic acid will go on for a certain time in muscles under circumstances in which it is impossible for them to obtain oxygen from without. Oxygen, it is true, is necessary for the life of the muscle; when venous instead of arterial blood is sent through the bloodvessels of a muscle, the irritability speedily disappears, and unless fresh oxygen be administered the muscle soon dies. The muscle may, however, during the interval in which irritability is still retained after the supply of oxygen has been cut off, continue to contract vigorously. The supply of oxygen, though necessary for the *maintenance* of irritability, is not necessary for the *manifestation* of that irritability, is not necessary for that explosive decomposition which develops a contraction. A frog's muscle will continue to contract and to produce carbonic acid in an atmosphere of hydrogen or nitrogen—that is, in the total absence of free oxygen both from itself and from the medium in which it is placed.

Thus, on the one hand, the muscle seems to have the property of taking up and fixing in some way or other the oxygen to which it is exposed, of converting it into intramolecular oxygen, in which condition it cannot be removed by simple diminished pressure, so that the tension of oxygen in the muscular substance may be considered as always nil; while, on the other hand, the muscular substance is always undergoing a decomposition of such a kind that carbonic acid is set free, sometimes, as when the muscle is at rest, in small, sometimes, as during a contraction, in large, quantities. But, if the oxygen tension of the muscular tissue be thus always nil, the oxygen of the blood-corpuscles, in which it is at a comparatively high tension, will be always passing over, through the plasma, through the capillary walls, the lymph spaces, and the sarcolemma, into the muscular substance, and as soon as it arrives there will be hidden away as intramolecular oxygen, leaving the oxygen tension of the muscular substance once more nil. Conversely, the carbonic acid produced by the decomposition of the muscular substance will tend to raise the carbonic acid tension of the muscle until it exceeds that of the blood; whereupon it will pass from the muscle into the blood, its place in the muscular substance being supplied by freshly generated carbonic acid. There will always, in fact, be a stream of oxygen from the blood to the muscle, and of carbonic acid from the muscle to the blood. The respiration of the muscle, then, does not consist in throwing into the blood oxidizable substances there to be oxidized into carbonic acid and other matters, but it does consist in the assumption of oxygen (as intramolecular oxygen), in the building up by help of that oxygen of explosive

decomposable substances, and in the occurrence of decompositions whereby carbonic acid and other matters are discharged first into the substance of the muscle and subsequently into the blood. We cannot as yet trace out the steps taken by the oxygen from the moment it slips into its intramolecular position to the moment when it issues united with carbon as carbonic acid. The whole mystery of life lies hidden in the story of that progress, and for the present we must be content with simply knowing the beginning and the end.

Our knowledge of the respiratory changes in muscle is more complete than in the case of any other tissue; but we have no reason to suppose the phenomena of muscle are exceptional. On the contrary, all the available evidence goes to show that in all tissues the oxidation takes place in the tissue, and not in the adjoining blood. It is a remarkable fact, that lymph, serous fluids, bile, urine, and milk contain a mere trace of free or loosely combined oxygen, and saliva or pancreatic juice a very small quantity only, while the tension of carbonic acid in peritoneal fluid and probably in the tissues of the intestinal walls is higher than that of venous blood, and in bile and urine is still greater. The tension of carbonic acid in lymph, while higher than that of arterial blood, is lower than that of the general venous blood; but this probably is due to the fact that the lymph in its passage onwards is largely exposed to arterial blood in the connective tissues and in the lymphatic glands, where the production of carbonic acid is slight as compared to that going on in muscles. All these facts point to the conclusion, that it is the tissues, and not the blood, which become primarily loaded with carbonic acid, the latter simply receiving the gas from the former by diffusion, except the (probably) small quantity which results from the metabolism of the blood-corpuscles; and that the oxygen which passes from the blood into the tissues is at once taken up in some combination, so that it is no longer removable by diminished tension.

In further support of this view may be urged the fact that if, in a frog, the whole blood of the body be replaced by normal saline solution, the total metabolism of the body is, for some time, unchanged. The saline medium is able, owing to the low rate of metabolism, and large respiratory surface of the animal, to supply the tissues with all the oxygen they need, and to remove all the carbonic acid they produce. It is difficult to believe that, in such an experiment, the oxidation took place in the saline solution itself while circulating in the bloodvessels and tissue-spaces of the animal.

We may add, that the oxidative power which the blood itself

undoubtedly oxidized in the body is so small that it may be neglected in the present considerations. If grape-sugar be added to blood, or to a solution of hæmoglobin, the mixture may be kept for a long time at the temperature of the body, without undergoing oxidation. Even within the body a slight excess of sugar in the blood, over a certain percentage, wholly escapes oxidation, and is discharged unchanged. Many easily oxidized substances, such as pyrogallic acid, pass largely through the blood of a living body without being oxidized. The organic acids, such as citric, even in combination with alkaline bases, are only partially oxidized; when administered as acids, and not as salts, they are hardly oxidized at all. It is, of course, quite possible that the changes which the blood undergoes when shed might interfere with its oxidative action, and hence the fact that shed blood has little or no oxidizing power, is not a satisfactory proof that the unchanged blood within the living vessels may not have such a power. But did oxidation take place largely in the blood itself, one would expect even highly diffusible substances to be oxidized in their transit; whereas, if we suppose the oxidation to take place in the tissues, it becomes intelligible why such diffusible substances as those which the tissues in general refuse to take up largely, should readily pass unchanged from the blood through the secreting organs.

We have seen that in muscle the production of carbonic acid is not directly dependent on the consumption of oxygen. The muscle produces carbonic acid in an atmosphere of hydrogen. What is true of muscle is true also of other tissues, and of the body at large. Spallanzani and W. Edwards showed long ago that animals might continue to breathe out carbonic acid in an atmosphere of nitrogen or hydrogen; and more recently Pflüger has shown, by a remarkable experiment, that a frog kept at a low temperature will live for several hours, and continue to produce carbonic acid, in an atmosphere absolutely free from oxygen. The carbonic acid produced during this period was made by help of the oxygen inspired in the hours anterior to the commencement of the experiment. The oxygen then absorbed was stowed away from the hæmoglobin into the tissues, it was made use of to build up the explosive compounds, whose explosions later on gave rise to the carbonic acid. Or, to adopt Pflüger's simile, the oxygen helps to wind up the vital clock; but once wound up the clock will go on for a period without further winding. The frog will continue to live, to move, to produce carbonic acid for a while without any fresh oxygen, as we know of old it will without any fresh food; it will continue to do so till the explosive compounds which the oxygen built up are exhausted; it will go on till the vital clock has run down.

To sum up, then, the results of respiration in its chemical aspects.   As the blood passes through the lungs, the low oxygen tension of the venous blood permits the entrance of oxygen from the air of the pulmonary alveolus, through the thin alveolar wall, through the thin capillary sheath, through the thin layer of blood-plasma, to the red corpuscle, and the reduced hæmoglobin of the venous blood becomes wholly, or all but wholly, oxyhæmoglobin.   Hurried to the tissues, the oxygen, at a *comparatively* high tension in the arterial blood, passes largely into them.   In the tissues, the oxygen tension is always kept at an exceedingly low pitch, by the fact that they, in some way at present unknown to us, pack away at every moment into some stable combination each molecule of oxygen which they receive from the blood.   With much but not all of its oxyhæmoglobin reduced, the blood passes on as venous blood.   How much hæmoglobin is reduced will depend on the activity of the tissue itself. The quantity of hæmoglobin in the blood is the measure of limit of the oxidizing power of the body at large; but within that limit the amount of oxidation is determined by the tissue, and by the tissue alone.

We cannot trace the oxygen through its sojourn in the tissue. We only know that sooner or later it comes back combined in carbonic acid (and other matters not now under consideration). Owing to the continual production of carbonic acid, the tension of that gas in the extravascular elements of the tissue is always higher than that of the blood; the gas accordingly passes from the tissue into the blood, and the venous blood passes on not only with its hæmoglobin reduced—*i. e.*, with its oxygen tension decreased, but also with its carbonic acid tension increased.   Arrived at the lungs, the blood finds the pulmonary air at a lower carbonic acid tension than itself.   The gas accordingly streams through the thin vascular and alveolar walls, till the tension without the bloodvessel is equal to the tension within.   At the same time, the blood finds in the air of the pulmonary alveoli a supply of oxygen more than adequate to convert the greater part of the reduced hæmoglobin back again to oxyhæmoglobin.   Thus, the air of the pulmonary alveoli, having given up oxygen to the blood and taken up carbonic acid from the blood, having a higher carbonic acid tension and a lower oxygen tension than the tidal air in the bronchial passages, mixes rapidly with this by diffusion. The mixture is further assisted by ascending and descending currents; and the tidal air issues from the chest at the breathing out poorer in oxygen and richer in carbonic acid than the tidal air which entered at the breathing in.

Sec. 6.—The Nervous Mechanism of Respiration.

Breathing is an involuntary act. Though the diaphragm and all the other muscles employed in respiration are voluntary muscles—*i. e.*, muscles which can be called into action by a direct effort of the will, and though respiration may be modified within very wide limits by the will, yet we habitually breathe without the intervention of the will ; the normal breathing may continue, not only in the absence of consciousness, but even after the removal of all the parts of the brain above the medulla oblongata.

We have already seen how complicated is even a simple respiratory act. A very large number of muscles are called into play. Many of these are very far apart from each other, such as the diaphragm and the nasal muscles; yet they act in harmonious sequence in point of time. If the lower intercostal muscles contracted before the scaleni, or if the diaphragm contracted alternately with the other chest-muscles, the satisfactory entrance and exit of air would be impossible. These muscles, moreover, are coördinated also in respect of the amount of their several contractions; a gentle and ordinary contraction of the diaphragm is accompanied by gentle and ordinary contractions of the intercostals, and these are preceded by gentle and ordinary contractions of the scaleni. A forcible contraction of the scaleni, followed by simply a gentle contraction of the intercostals, would perhaps hinder rather than assist inspiration, and at all events would be waste of power. Further, the whole complex inspiratory effort is often followed by a less marked but still complex expiratory action. It is impossible that all these so carefully coördinated muscular contractions should be brought about in any other way than by coördinate nervous impulses descending along efferent nerves from a coördinating centre. By experiment we find this to be the case.

When in a rabbit the trunk of a phrenic nerve is cut, the diaphragm on that side remains motionless, and respiration goes on without it. When both nerves are cut, the whole diaphragm remains quiescent, though the respiration becomes excessively labored.

When an intercostal nerve is cut, no active respiratory movement is seen in that space, and when the spinal cord is divided below the origin of the seventh cervical spinal nerve, costal respiration ceases, though the diaphragm continues to act and that with increased vigor. When the cord is divided just below the medulla, all thoracic movements cease, but the respiratory actions of the nostrils and glottis still continue. These, however,

disappear when the facial and recurrent laryngeal are divided. We have already stated that after removal of the brain above the medulla, respiration still continues very much as usual, the modifications which ensue from loss of the brain being unessential. Hence, putting all these facts together, it is clear that the respiratory movements are, as we suggested, brought about by coördinated impulses which, originated in the medulla, find their way thence along the several efferent nerves. The proof is completed by the fact that the removal or extensive injury of the medulla alone is, save in exceptional cases, at once followed by the cessation of all respiratory movements, even though every muscle and every nerve concerned be left intact. Nay, more, if only a small portion of the medulla, a tract whose limits are not as yet exactly fixed, but which lies below the vaso-motor centre, between it and the *calamus scriptorius*, be removed or injured, respiration ceases, and death at once ensues. Hence this portion of the nervous system was called by Flourens the vital knot, or ganglion of life, *nœud vital.* We shall speak of it as the respiratory centre.

The nature of this centre must be exceedingly complex; for while even in ordinary respiration it gives rise to a whole group of coördinate nervous impulses of inspiration followed in due sequence by a smaller but still coördinate group of expiratory impulses, in labored respiration fresh and larger impulses are generated, though still in coördination with the normal ones, the expiratory events being especially augmented; and in the cases of more extreme dyspnœa and asphyxia impulses overflow, so to speak, from it in all directions, though only gradually losing their coördination, until almost every muscle in the body is thrown into contractions.

We must not, however, conceive of this centre as one of such a kind that the impulses leave it fully coördinated and equipped so that nothing remains for them but to travel, unchanged, along the several efferent nerve-fibres to their several muscular destinations. On the contrary we have reason to think that the respiratory motor nerves, like other special nerves as they are about to issue from the spinal cord, are connected with a nervous ganglionic machinery,—a point which we shall consider more fully in treating of the spinal cord; and that the respiratory impulses pass into and are modified by such spinal nervous machinery immediately before they issue along the motor nerve-roots. Indeed recent observations show that under particular conditions, and especially in young animals, respiratory movements may be carried out in the entire absence of the medulla oblongata. Thus in a kitten, after removal of the medulla, if the excitability of the spinal cord be heightened by small doses of strychnia, not

only may respiratory movements of the chest be induced in a reflex manner, by pinching or by blowing on the skin, but even transient spontaneous efforts of breathing may with care be observed. These are the exceptional instances mentioned above; and they show that the respiratory nervous mechanism is not confined, as was once thought, to the centre in the medulla, but also embraces other subsidiary centres in the spinal cord below. The respiratory nervous system seems in fact in many ways analogous to the vaso-motor nervous system, with its head centre in the mudulla, and secondary centres elsewhere, and to the cardiac nervous system with its potent ganglia in the sinus, and its secondary ganglia in the auricles, and auriculo-ventricular groove. The matter is not at present thoroughly worked out, but we shall probably not greatly err in continuing to speak of the centre in the medulla as being "the respiratory centre" while admitting that it works through other nervous machinery placed lower down in the spinal cord, and that this subordinate machinery may, in exceptional cases, carry out, though inadequately, the work of the chief centre.

Admitting then the existence of this medullary respiratory centre the question naturally arises, Are we to regard its rhythmic action as due essentially to changes taking place in itself, or as due to afferent nervous impulses or other stimuli which affect it in a rhythmic manner from without? In other words, Is the action of the centre automatic or purely reflex? We know that the centre may be influenced by impulses proceeding from without, and that the breathing may be affected by the action of the will, or by an emotion, or by a dash of cold water on the skin, or in a hundred other ways; but the fact that the action of the centre may be thus modified from without, is no proof that the continuance of its activity is dependent on extrinsic causes.

In attempting to decide this question we naturally turn to the pneumogastric as being the nerve most likely to serve as the channel of afferent impulses setting in action the respiratory centre. If both vagi be divided, respiration still continues though in a modified form. This proves distinctly that afferent impulses ascending those nerves are not the efficient cause of the respiratory movements. We have seen that when the spinal cord is divided below the medulla, the facial and laryngeal movements still continue. This proves that the respiratory centre is still in action, though its activity is unable to manifest itself in any thoracic movement. But when the cord is thus divided, the respiratory centre is cut off from all sensory impulses, save those which may pass into it from the cranial nerves; and the division of these cranial nerves by themselves, when the medulla and spinal cord are left intact, does not destroy respiration. Hence

we may infer that the respiratory impulses proceeding from the respiratory centre are not simply afferent impulses reaching the centre along afferent nerves and transformed by reflex action in that centre. They evidently start *de novo* from the centre itself, however much their characters may be affected by afferent impulses reaching that centre at the time of their being generated. The action of the centre is automatic, not simply reflex.

Among the afferent impulses which affect the automatic action of the centre, the most important are those which ascend along the vagi. If one vagus be divided, the respiration becomes slower; if both be divided, it becomes very slow the pauses between expiration and inspiration being excessively prolonged. The character of the respiratory movement too is markedly changed; each respiration is fuller and deeper, so much so indeed that according to some observers, what is lost in rate is gained in extent, the amount of carbonic acid produced and oxygen consumed in a given period remaining after division of the nerves about the same as when these were intact. Without insisting too much on the exactness of this compensation we may at least conclude from the effects of section of the vagi, in the first place, that during life afferent impulses are continually ascending the vagi and modifying the action of the respiratory centre, and in the second place, that the modification bears chiefly on the distribution in time of the efferent respiratory impulses, and not so much on the amount to which they are generated.

These afferent impulses are probably started in the lungs by the condition of the blood in the pulmonary capillaries acting as a stimulus to the peripheral endings of the nerves, though possibly the altered air in the air-cells may also act as a stimulus to the nerve-endings. It has further been suggested that the mere movements of expansion and contraction may also serve as a stimulus. Thus when air is mechanically driven into the chest, an expiratory movement follows, and when air is drawn out, an inspiratory; and this not only with atmospheric air but with indifferent gases, such as nitrogen; when both vagi are cut, these effects do not appear. So also, when in an animal, after division of the spinal cord below the medulla, artificial respiration is kept up, the respiratory movements of the nostrils follow the rhythm of the artificial respiration so long as the vagi are intact; when these are divided the movements of the nostrils exhibit a rhythm independent of those of the chest. From this it is inferred that the mere mechanical expansion of the lungs transmits along the vagus an impulse tending to inhibit inspiration and to generate an expiration, and the mechanical contraction of the lungs an impulse tending to inhibit expiration and to generate an inspiration. That is to say, the very expansion of the lungs, which is

the natural effect of an inspiration, tends of itself to cut short that inspiration and to inaugurate the sequent expiration, and similarly the contraction of an expiration promotes the following inspiration. The lungs in fact may be spoken of as being so far self-regulating.

The influence of the vagus is further shown by the following experiment. If the medulla oblongata be carefully divided in the middle line, respiration may continue to go on in quite a normal fashion, indicating that the centre is composed of two lateral halves placed one on each side of the median line. If however one vagus be then divided, the respiratory movements both costal and diaphragmatic, on the side of the body on which division of the vagus has taken place, become slower than those on the other side, so that the two sides are no longer synchronous. Obviously the vagus influences primarily the respiratory centre of its own side; though under normal conditions the two halves of the centre work in harmony and synchronism.

When after division of both vagi, the medulla being intact, the central stump of one vagus is stimulated with a gentle interrupted current, the respiration, which from the division of the nerves had become slow, is quickened again; and with care, by a proper application of the stimulus, the normal respiratory rhythm may for a time be restored. Upon the cessation of the stimulus, the slower rhythm returns. If the current be increased in strength, the rhythm may in some cases be so accelerated that at last the diaphragm is brought into a condition of prolonged tetanus, and a standstill of respiration in an extreme inspiratory phase is the result.

If the central end of the superior laryngeal branch of the vagus be stimulated, whether the main trunk of the nerve be severed or not, a slowing of the respiration takes place, and this may by proper stimulation be carried so far that a complete standstill of respiration in the phase of rest is brought about— i. e., the respiratory apparatus remains in the condition which obtains at the close of an ordinary expiration, the diaphragm being completely relaxed. In other words, the superior laryngeal nerve contains fibres, the stimulation of which produces afferent impulses whose effect is to inhibit the action of the respiratory centre; while the main trunk of the vagus contains fibres, the stimulation of which produces afferent impulses whose effect is to accelerate or augment the action of the respiratory centre. In some cases stimulation of the main trunk of the vagus also causes a slowing or even standstill of the respiration, as for instance in deep chloral narcosis or when the nerve has become exhausted by previous stimulation. Stimulation of the superior laryngeal frequently produces not only a complete

cessation of all inspiratory movements, as indicated by the perfectly lax diaphragm, but also contractions of the abdominal muscles indicating an expiratory effort; and it is obvious that the commencement of an expiration must be preceded by a cessation of inspiratory effects, just as similarly inspiration must be preceded by the cessation of expiration. Hence the influences which inhibit inspiration are often spoken of as expiratory though they may not go so far as to produce an actual expiration.

Corresponding to these antagonistic influences we may suppose the existence of separate fibres, augmentative or inspiratory fibres, the stimulation of which leads to inspiratory movements, and inhibitory or expiratory fibres the stimulation of which checks inspiration and subsequently gives rise to expiration. But it must be remembered that the existence of these fibres is hypothetical, and that some other explanation may eventually be given of the facts which we have just described. Indeed we are not able at present to give a wholly consistent and satisfactory explanation of the nature and working of the respiratory centre. Apparently we must conceive of its consisting of two parts, an inspiratory and an expiratory: and direct stimulation of the medulla produces sometimes inspiration, sometimes expiration; but the two parts must be considered as coördinated in such a way as to act alternately. Of the two the inspiratory centre is in ordinary life the more important, the more sensitive and the more active, since in normal breathing active expiratory effects are scanty, and the emptying of the chest is chiefly the result of the cessation of inspiration. Under conditions, however, which we shall speak of presently under the name of dyspnœa, the expiratory centre comes distinctly into play, since actual expiratory efforts come to the front and, as we shall see, the greater the difficulty of breathing the more and more prominent they become. We may picture to ourselves, as Rosenthal has done, that the inspiratory centre is the seat of two conflicting processes, one tending to the discharge of inspiratory impulses and the other offering resistance to that discharge, the former gathering head during a period of rest and so at last overcoming the latter, and effecting an actual discharge. After this the accumulation of inspiratory processes once more begins, and once more terminates in a discharge, thus leading to the rhythm of respiration. We may further suppose that the augmentative impulses ascending the vagi, produce their effects by diminishing the processes of resistance, and thus bring about movements which are at once quicker and less ample. But we have to add to this conception some view as to the relation of the expiratory to the inspiratory centre in order to explain why the impulses inhibitory to the latter should be augmentative to the former.

Indeed the whole matter becomes too complicated to be discussed any further here; and we have introduced the view not because we regard it as an adequate explanation of the phenomena, but because it affords a useful graphic conception of the molecular activity of these and other automatic nervous centres. We may be at present content with the knowledge that, as far as the vagus is concerned, the respiratory centre as a whole may be influenced by augmentative or inspiratory impulses which run chiefly in the trunk of the nerve and by inhibitory or expiratory impulses which run certainly in the superior laryngeal, apparently also in the recurrent laryngeal, and to a certain extent in the trunk also; in the latter case, however, their presence is manifested under certain conditions only. And while, from the results of simple section of the main trunk, it is clear that the accelerating influences are continually at work, it is not so clear that the inhibitory influences are always in action, since section even of both superior laryngeals does not necessarily quicken respiration.

This double or alternate respiratory action of the vagi may be taken as in a general way illustrative of the manner in which other afferent nerves and various parts of the cerebrum are enabled to influence respiration. As we know from daily experience, of all the apsychical nervous centres, the respiratory centre is the one which is most frequently and most deeply affected by nervous impulses from various quarters. Besides the changes brought about by the will (and when we breathe voluntarily we probably make use to some extent of the normal nervous machinery of respiration, working through this, rather than sending independent volitional impulses direct to the diaphragm and other respiratory muscles), we find that emotions, and painful sensations alter profoundly the character of the respiratory movements. Sometimes the breathing thereby becomes quicker and flatter, sometimes it is deepened as well as hurried; at other times it may be slowed or for a while stopped altogether, while occasionally expiratory efforts are made prominent. And though these effects may be partly indirect, the emotion modifying the heart-beat, and so influencing the flow of blood through the respiratory centre, they are chiefly due to the direct actions of nervous impulses reaching that centre from higher parts of the brain. So also impulses from almost every sentient surface, or passing along almost every sensory nerve, may modify respiration in one direction or another, the slighter feebler impulses tending apparently to quicken, and the stronger larger impulses to arrest or inhibit the respiratory discharges. The influences in this way of stimuli applied to the skin is well known to all; but perhaps next to the vagus the nerve most closely connected with the respiratory centre is the fifth nerve, branches of which guard the

nasal respiratory channels; the slightest stimulation of the nostrils at once affecting the breathing and most frequently arresting it. Thus the working of the respiratory centre is made to respond delicately to the varying needs of the economy.

Besides these nervous influences, however, there is another circumstance which perhaps above all others affects the respiratory centre, and that is the condition of the blood in respect to its respiratory changes; the more venous (less arterial) the blood, the greater is the activity of the respiratory centre. When by reason either of any hindrance to the entrance of air into the chest, or of a greater respiratory activity of the tissues, as during muscular exertion, the blood becomes less arterial, more venous —*i. e.*, with a smaller charge of oxyhæmoglobin and more heavily laden with carbonic acid, the respiration from being normal becomes labored. We may speak of normal breathing as *eupnœa*, and say that this, when the blood is insufficiently arterialized, passes into *dyspnœa*, an intermediate stage in which the respiratory movements are simply exaggerated being known as *hyperpnœa*. This effect of deficient arterialization of blood is very different from that of section of the vagi: it is no mere change in the distribution of impulses; the breathing is quicker as well as deeper, there is an increase in the sum of efferent impulses proceeding from the centre, and the expiratory impulses, which in normal respiration are very slight, acquire a pronounced importance. As the blood becomes, in cases of obstruction, less and less arterial, more and more venous, the discharge from the respiratory centre becomes more and more vehement, and instead of confining itself to the usual tracts, and passing down to the ordinary respiratory muscles, overflows into other tracts, puts into action other muscles, until there is perhaps hardly a muscle in the body which is not made to feel its effects. And this discharge may, as we shall see in speaking of asphyxia, continue till the nervous energy of the respiratory centre is completely exhausted. The effect of venous blood then is to augment these natural explosive decompositions of the nerve-cells of the respiratory centre which give rise to respiratory impulses; it increases their amount, and also quickens their rhythm. The later change however is much less marked than the former, the respiration being much more deepened than hurried, and the several respiratory acts are never so much hastened as to catch each other up, and so to produce an inspiratory tetanus like that resulting from stimulation of the vagus. On the contrary, especially as exhaustion begins to set in, the rhythm becomes slower out of proportion to the weakening of the individual movements.

On the other hand, the blood may be made not more but less venous than usual. When we attempt to hold our breath, we

find that we can only do this for a limited time; sooner or later a breath must come; but the time during which we can remain without breathing may be much prolonged, if we first of all take a series of deep breaths. By this increased ventilation we bring our respiratory centre into such a condition that it takes a much longer time for the succeeding respiratory impulses to become irresistible. A similar but even more pronounced condition may be brought about in an animal by making it inspire oxygen, or breathe ordinary air more rapidly and more forcibly than the needs of the economy require. If in a rabbit artificial respiration is carried on very vigorously for a while, and then suddenly stopped, the animal does not immediately begin to breathe. For a variable period no respiration takes place at all, and when it does begin, occurs gently and normally, only passing into dyspnœa if the animal is unable to breathe of itself; and even then the transition is quite gradual. Evidently during this period the respiratory centre is in a state of complete rest, no explosions are taking place, no respiratory impulses are being generated, and the quiet transition from this condition to that of normal respiration shows that the subsequent generation of impulses is attended by no great disturbance. The cause of this state of things, which is known as that of *apnœa*, is to be sought for in the condition of the blood. By the increased vigor of the artificial respiratory movements, the hæmoglobin of the arterial blood, which in normal breathing is not quite saturated, becomes almost completely so, and the quantity of oxygen simply dissolved is increased, its tension being largely augmented. Respiration is arrested because the blood is more highly arterialized than usual. Thus, we have in apnœa the converse to dyspnœa; and both states point to the same conclusion, that the activity of the respiratory centre is dependent on the condition of the blood, being augmented when the blood is less arterial and more venous, being depressed when it is more arterial and less venous than usual.

The question now arises, Does this condition of the blood affect the respiratory centre directly, or does it produce its effect by stimulating the peripheral ends of afferent nerves in various parts of the body, and, by the creation there of afferent impulses, indirectly modify the action of the centre? Without denying the possibility that the latter mode of action may help in the matter, as regards not only the vagi, but all afferent nerves, it is clear from the following reasons that the main effect is produced by the direct action of the blood on the respiratory centre itself. If the spinal cord be divided below the medulla oblongata, and both vagi be cut, want of proper aëration of the blood still produces an increased activity of the respiratory centre, as shown

by the increased vigor of the facial respiratory movements. If the supply of blood be cut off from the medulla by ligature of the bloodvessels of the neck, dyspnœa is produced, though the operation produces no change in the blood generally, but simply affects the respiratory condition of the medulla itself, by cutting off its blood-supply, the immediate result of which is an accumulation of carbonic acid and a paucity of available oxygen in the protoplasm of the nerve-cells in that region. If the blood in the carotid artery in an animal be warmed above the normal, dyspnœa is at once produced. The overwarm blood hurries on the activity of the nerve-cells of the respiratory centre, so that the supply of blood, even though greater than normal owing to the bloodvessels of the medulla becoming dilated by the increased temperature, is yet insufficient for their needs. The condition of the blood, then, affects respiration by acting directly on the respiratory centre itself.

Deficient aeration produces two effects in blood : it diminishes the oxygen, and increases the carbonic acid. Do both of these changes affect the respiratory centre, or only one, and if so, which? When an animal is made to breathe an atmosphere containing nitrogen only, the exit of carbonic acid by diffusion is not affected, and the blood, as is proved by actual analysis, contains no excess of carbonic acid. Yet all the phenomena of dyspnœa are present. In this case, these can only be attributed to the deficiency of oxygen. On the other hand, if an animal be made to breathe an atmosphere rich in carbonic acid, but at the same time containing abundance of oxygen, though the breathing becomes markedly deeper and also somewhat more frequent, there is no culmination in a convulsive asphyxia, even when the quantity of carbonic acid in the blood, as shown by direct analysis, is very largely increased. On the contrary, the increase in the respiratory movements after a while passes off, the animal becoming unconscious, and appearing to be suffering rather from a narcotic poison than from simple dyspnœa. It does not seem certain that the increased respiratory movements seen at first are the direct result of the action of the carbonic acid on the respiratory centre; it is possible that the carbonic acid may affect the respiratory centre in an indirect way, by stimulating the respiratory passages, or by its action on higher parts of the brain ; and in all cases there is a marked contrast between the slow development and evanescent character of the hyperpnœa of carbonic acid poisoning, and the rapid onset and speedy culmination in convulsions and death of the dyspnœa due to the absence of oxygen. There can, in fact, be no doubt that the action of deficiently arterialized blood on the respiratory centre, as manifested in an augmentation of

the respiratory explosions, is due primarily to a want of oxygen, and in a secondary manner only to an excess of carbonic acid.

[The action of drugs upon the respiratory centres and peripheral pulmonic vagi nerves, is both physiologically and therapeutically of considerable interest. Thus, it has been found that ammonia stimulates the respiratory centres ; belladonna first stimulates, afterwards paralyzes (?) them ; and salicylic acid in small doses stimulates and in large doses paralyzes the centres. Apomorphia stimulates the peripheral nerves, and in rabbits the centres also. Aconite, hydrocyanic acid, opium, caffein, ether, chloral, nitrite of amyl, veratria, and many other drugs paralyze the centres.]

Cheyne-Stokes Respiration.—A remarkable abnormal rhythm of respiration, first observed by Cheyne, but afterwards more fully studied by Stokes, and hence called by their combined names, occurs in certain pathological cases. The respiratory movements gradually decrease both in extent and rapidity until they cease altogether, and a condition of apnœa, lasting it may be for several seconds, ensues. This is followed by a feeble respiration, succeeded in turn by a somewhat stronger one, and thus the respiration returns gradually to the normal, or may even rise to hyperpnœa or slight dyspnœa, after which it again declines in a similar manner. A secondary rhythm of respiration is thus developed, periods of normal or slightly dyspnœic respiration alternating by gradual transitions with periods of apnœa. The cause of the phenomena is not thoroughly understood. Stokes connected it with a fatty condition of the heart, but it has been met with in various maladies. Closely similar phenomena have been observed during sleep, under perfectly normal conditions. It presents a striking analogy with the " groups " of heart-beats so frequently seen in the frog's ventricle placed under abnormal circumstances.

Sec. 7.—The Effects of Respiration on the Circulation.

We have seen, while treating of the circulation, that the blood-pressure curves are marked by undulations, which, since their rhythm is synchronous with that of the respiratory movements, are evidently in some way connected with respiration.

When these undulations of the blood-pressure curve are compared carefully with the respiratory movements or with the variations of intrathoracic pressure, it is seen that while in general the blood-pressure rises during inspiration and falls during expiration neither the rise nor the fall of the former is

exactly synchronous with either inspiration or expiration. Fig. 135 shows two tracings from a dog taken at the same time, one, *a*, being the ordinary blood-pressure curve from the carotid, and the other, *b*, representing the condition of the intrathoracic pressure as obtained by carefully bringing a manometer into connection with the pleural cavity. On comparing the two

FIG. 135.

COMPARISON OF BLOOD-PRESSURE CURVE WITH CURVE OF INTRATHORACIC PRESSURE.
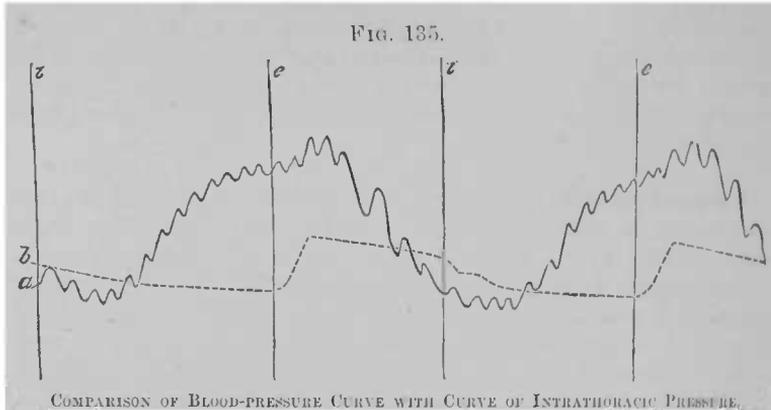
is the blood-pressure curve, with its respiratory undulations, the slower beats on the descent being very marked. *b* is the curve of intrathoracic pressure obtained by connecting one limb of a manometer with the pleural cavity. Inspiration begins at *i*, expiration at *e*. The intrathoracic pressure rises very rapidly after cessation of the inspiratory effort, and then slowly falls as the air issues from the chest; at the beginning of the inspiratory effort the fall becomes more rapid.

curves, it is evident that neither the maximum nor the minimum of arterial pressure coincides exactly either with inspiration or with expiration. At the beginning of inspiration (*i*) the arterial pressure is seen to be falling; it soon however begins to rise, but does not reach the maximum until some time after expiration (*e*) has begun; the fall continues during the remainder of expiration, and passes on into the succeeding inspiration.

This suggests the idea that, while inspiration tends to increase and expiration to diminish the blood-pressure, there are causes at work which in each case delay the effect. Extended observations however show that such a relation as that shown in the figure though frequent is not constant. In fact the effects of the respiratory movements on blood-pressure are found to vary very widely according as the respiration is quick or slow, easy and shallow or labored and deep, and especially as the air enters into the chest readily or with difficulty. A similar variety of effect is seen in sphygmographic tracings, and these further show that the respiratory movements bring about changes not only in the mean blood-pressure but in the form and characters of each

pulse-wave. In Fig. 136, which represents a state of things frequently occurring, but which must not be considered as illustrating what always takes place, it will be seen that during the greater part of expiration the pulse-wave is high and the dicrotic wave is not very prominent, while during inspiration the height of the wave is diminished, and dicrotism becomes much more

FIG. 136.

EXPIRATION   INSPIRATION
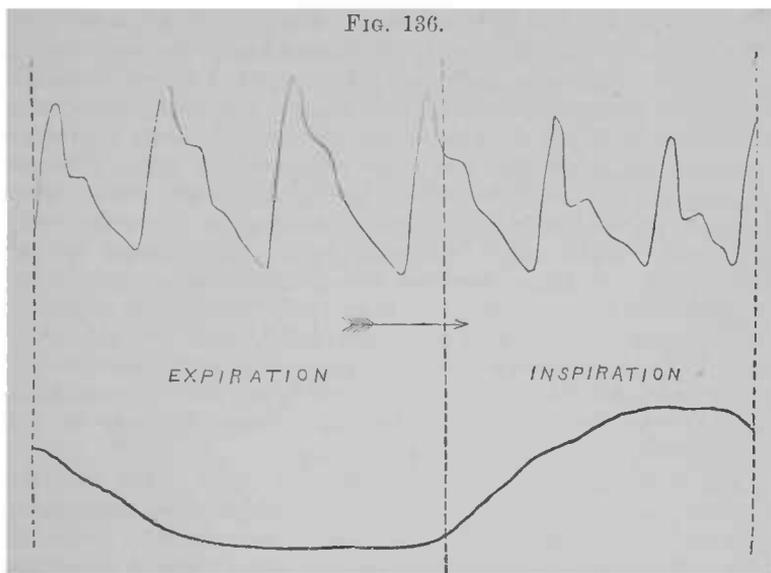
Influence of respiration on the form of the pulse-wave and the medium blood-pressure The upper curve gives the radial pulse from a healthy man 27 years of age, and with an extra-arterial pressure of 70 mm. mercury. The lower curve gives the movements of the chest-wall, the points of the recording levers of both instruments being in the same vertical line. It can be seen that during inspiration the pulse-waves diminish in height and become more dicrotic, while during expiration the height of the pulse-waves is increased and their form tends more towards that of the pulse-wave with a raised arterial pressure.

marked; the former indicates a higher and the latter a lower blood-pressure.

These variations in the exact relations of the respiratory undulations to the respiratory movements themselves will prepare the reader for the statement that the causation of the undulations is complex. Apparently the respiratory act affects the vascular system in several different ways, and the general effect varies according as one or other influence is predominant. These several actions are sufficiently interesting and important to deserve discussion.

When the brain of a living mammal is exposed by the removal of the skull, a rhythmic rise and fall of the cerebral mass, a

pulsation of the brain, quite distinct from the movements caused by the pulse in the arteries of the brain, is observed; and upon examination it will be found that these movements are synchronous with the respiratory movements, the brain rising up during expiration and sinking during inspiration.   They disappear when the arteries going to the brain are ligatured, or when the venous sinuses of the dura mater are laid open so as to admit of a free escape of the venous blood.   They evidently arise from the expiratory movements in some way hindering and the inspiratory movements assisting the return of blood from the brain.   We have already (p. 167) stated that during inspiration the pressure of blood in the great veins may become negative— *i. e.*, sink below the pressure of the atmosphere; and a puncture of one of these veins may cause immediate death by air being actually drawn into the vein and thus into the heart during an inspiratory movement.   When the veins of an animal are laid bare in the neck and watched, the so-called *pulsus venosus* may be observed in them—that is, they swell up during expiration and diminish again during inspiration.   And indeed a little consideration will show that the expansion and contraction of the chest must have a decided effect on the flow of blood through the thoracic portion of, and thus indirectly on that through the whole of the vascular system.

The heart and great bloodvessels are, like the lungs, placed in the air-tight thoracic cavity, and are subject like the lungs to the pumping action of the respiratory movements.   Were the lungs entrely absent from the chest, the whole force of the expansion of the thorax in inspiration would be directed to drawing blood from the extrathoracic vessels towards the heart, and conversely the effect of the contraction of the thorax in expiration would be to drive the blood back again from the heart towards the extrathoracic vessels.   In the presence of the lungs, however, the free entrance of air into the interior of the chest tends to maintain the pressure around the heart and great vessels within the thorax equal to the ordinary atmospheric pressure on the vessels of the rest of the body outside the thorax, but it is unable completely to equalize the two pressures.   Did the air enter as freely into the lungs as it does into the pleural cavities when wide openings are made in the thoracic walls, the respiratory movements would have very little effect indeed on the flow of blood to and from the heart, just as when such free openings exist they are ineffectual in promoting the entrance and exit of air to and from the lungs.   But the air does *not* pass into the pulmonary alveoli as freely as it would do into a pleural cavity through an opening in the thoracic wall.   Before the inspired air can fill a pulmonary alveolus, the walls of the alveolus have to

be distended *at the expense of the pressure which causes the inspired air to enter.* Part of the atmospheric pressure, in fact, which causes the entrance of the air into the lung is spent in overcoming the elasticity of the pulmonary passages and cells. Consequently, any structure lying within the thorax but outside the lungs, is never, even at the conclusion of an inspiration when the lungs are filled with air, subject to a pressure as great as that of the atmosphere. The pressure on such a structure always falls short of the pressure of the atmosphere by the amount of pressure necessary to counterbalance the elasticity of the pulmonary passages and cells. And, since the fraction of the atmospheric pressure which is thus spent in distending the lungs increases as the lungs become more and more stretched, it follows that the fuller the inspiration the greater is the difference between the pressure on structures within the thorax but outside the lungs and the ordinary pressure of the atmosphere. Now we have seen that the pressure necessary to counterbalance the elasticity of the lungs when they are completely at rest (in the pause between expiration and inspiration), is in man about 5 to 7 mm. of mercury, and that when the lungs are fully distended, as at the end of a forcible inspiration, the pressure rises to as much as 30 mm. of mercury. Hence, at the height of a forcible inspiration the pressure exerted on the heart and great vessels within the thorax is 30 mm. less than the ordinary atmospheric pressure of 760 mm., and even when the chest is completely at rest, at the end of an expiration, the pressure on the heart and great vessels is slightly (by about 5 mm. mercury) below that of the atmosphere.

During an inspiration, then, the pressure around the heart and great bloodvessels becomes considerably less than that of the atmosphere on the vessels outside the thorax. During expiration this pressure returns towards that of the atmosphere, but in ordinary breathing never quite reaches it. It is only in forcible expiration that the pressure on the thoracic vascular organs exceeds that of the atmosphere. But if during inspiration the pressure bearing on the right auricle and the venæ cavæ becomes less than the pressure which is bearing on the jugular, subclavian, and other veins outside the thorax, this must result in an increased flow from the latter into the former. Hence, during each inspiration a larger quantity of blood enters the right side of the heart. This probably leads to a stronger stroke of the heart, and at all events causes a large quantity to be ejected by the right ventricle ; this causes a larger quantity to escape from the left ventricle, and thus more blood is thrown into the aorta, and the arterial tension proportionately increased. During expiration the converse takes place. The pressure on the intrathoracic bloodvessels returns to the normal, the flow of

blood from the veins outside the thorax into the venæ cavæ and right auricle is no longer assisted, and in consequence less blood passes through the heart into the aorta, and arterial tension falls again. During forced expiration, the intrathoracic pressure may be so great as to afford a distinct obstacle to the flow from the veins into the heart.

The effect of the respiratory movements on the arteries is naturally different from that on the veins. During inspiration the diminution of pressure in the thorax around the aortic arch tends to draw the blood from the arteries outside the thorax back to the arch of the aorta, or, in other words, tends to check the onward flow of blood. At the same time, and this is the point to which we wish to call attention, the aortic arch itself tends to expand; in consequence the pressure of blood within it—*i. e.*, the arterial tension, tends to diminish. During expiration, the increase of pressure outside the aortic arch of course tends to increase also the blood-pressure within it, acting in fact just in the same way as if the coats of the aorta themselves contracted. Thus, as far as arterial blood-pressure is concerned, the effects of the respiratory movements on the great veins and great arteries respectively are antagonistic to each other; the effect on the veins being to increase arterial tension during inspiration and to diminish it during expiration, while the effect on the arteries is to diminish arterial tension during inspiration and to increase it during expiration. But we should naturally expect the effect on the thin-walled veins to be greater than that on the stout thick-walled arteries, so that the total effect of inspiration would be to increase, and the total effect of expiration to diminish, arterial tension. This is to say, we should expect the blood-pressure to rise during inspiration and to fall during expiration. This as we have seen is frequently the case, and indeed when the breathing is deep and labored the influence in this direction on the blood-pressure curve of the pumping action of the chest is unmistakable.

In addition to the influence thus exerted by the thoracic movements on the great veins leading to, and the great arteries leading from the heart, we have to consider the behavior of the pulmonary vessels themselves under the varying thoracic pressure. These, like the venæ cavæ and aorta, tend to expand under the influence of the inspiratory expansion of the chest, and thus to become fuller of blood, very much as they would if the whole lung were placed under a large cupping-glass. The first effect of this increased filling of the pulmonary vessels would be to retain for a while a certain quantity of blood in the lungs and thus to lessen the amount falling into the left auricle. But this would be temporary only; and the widening of the pulmonary vessels would speedily produce an exactly contrary effect, namely,

an increased flow through the lungs due to the diminished resistance offered by the widened passages. Conversely the first effect of expiration would be an increased flow into the left auricle due to the additional quantity of blood driven onwards by the partial collapse of the pulmonary vessels, followed by a more significant diminished flow caused by the greater resistance now offered by the narrower vascular channels. Thus the effect of inspiration in this way would be first to diminish the flow into the left auricle and so into the left ventricle and thus to diminish for a brief initial period the blood-pressure in the aorta, but afterwards, for the rest of the inspiration until the beginning of expiration, to increase the flow into the ventricle and thus to raise the arterial pressure; while conversely the effect of expiration would be first, for a brief period, to increase and afterwards, during the rest of the movement, to diminish the flow of blood into the left ventricle, and through that the amount of arterial pressure. Further, while this may be considered as the effect on the pulmonary vessels, large and small taken together, the influence both of the thoracic negative pressure during inspiration, and the return in a positive direction during expiration, will bear more on the thin-walled pulmonary veins than on the stouter pulmonary artery; that is to say, as inspiration becomes established, there will be a diminution of pressure in the pulmonary veins greater than that in the pulmonary artery, and this will be an additional influence favoring the flow into the left ventricle; during expiration a similar difference of effect will be felt in the contrary direction. The general effect then of the movements of the chest on the pulmonary vessels will be during the beginning inspiration to continue the lowering of arterial pressure which was taking place during expiration, but subsequently to raise the arterial pressure; and conversely at the beginning of expiration to continue the rise of arterial pressure which was taking place during inspiration, but subsequently to lower arterial pressure. In ordinary breathing, as we have seen, what may be considered as the normal relations of blood-pressure to the respiratory movements are precisely of this kind; and it seems exceedingly probable that they are, to a large extent at least, produced in this way.

In attempting, however, to estimate the action of the thorax, we must bear in mind what is taking place in the abdomen. In easy inspiration the descent of the diaphragm compresses the abdominal viscera, and so, while at the very first it drives a quantity of blood onward along the inferior vena cava, subsequently hinders the upward flow from the abdomen and lower limbs; at the same time by compressing the abdominal aorta, it tends to raise the pressure in the thoracic aorta and its branches. The effect of

easy expiration would be the converse of this; but in forced
expiration the pressure of the contracting abdominal muscles
would, as in inspiration, first tend to drive the blood onward
along the vena cava, but subsequently hinder the flow both along
the vena cava and the aorta.   The effect of the abdominal
movements therefore is mixed and variable, and the influence on
the blood-pressure in the femoral artery must be different from
that on the radial artery or other branch of the thoracic aorta.
It is difficult to predict what in all cases the effect would be, but
it is stated that section of the phrenic nerves, leading to quies-
cence of the diaphragm largely diminishes, and sometimes causes
the total disappearance of, even the normal respiratory un-
dulations.

Effects of the respiratory movements are seen not only in
natural but also in artificial respiration.   When, for instance, in
an animal under urari, artificial is substituted for natural respir-
ation, undulations of the blood-pressure curve, synchronous with
the respiratory movements, are still observed (Fig. 137), though
generally less in extent than those seen under natural conditions.
Now in artificial respiration, the mechanical conditions under
which the thoracic viscera are placed as regards pressure are
the exact opposite of those existing during natural respiration;
for when air is blown into the trachea to distend the lungs, the
pressure within the chest is increased instead of diminished.

Under these circumstances we should expect to find that
while the first effect of an artificial inspiration would be to drive
an additional quantity of blood out of the lungs into the left
ventricle, and thus to raise arterial pressure, this would be in
turn followed by a fall of arterial pressure due to the increased
resistance offered both to the passage of blood through the lungs
and to the entrance of blood through the venæ cavæ into the
right auricle.   Conversely the effect of the succeeding expiration
would be an initial continuance of the fall of arterial pressure
succeeded by a rise.   In other words, we should expect to find in
artificial respiration effects exactly the reverse of those which we
find in normal respiration ; and, indeed, in many curves of blood-
pressure taken during artificial respiration, this is the case ; but
here, as in natural respiration, the features of the blood-pressure
curve vary according as the breathing is hurried or slow, shallow
or deep.

We may add that another explanation than those given above
has been offered of these effects of the respiratory movements.
It has been suggested that when the lung is expanded, the
increase in the area of the wall of each pulmonary alveolus tends
to stretch and elongate the capillaries lying in the alveolar walls,
and in elongating them necessarily narrows them, just as an

India-rubber tube is narrowed when it is stretched lengthways. This narrowing of the capillaries would present an obstacle to the passage of blood through them; and hence the expansion of the alveoli in inspiration, other things being equal, would be unfavorable to the flow of blood through the lungs. It has been further suggested that the first effect of the expansion of the alveolus and narrowing of the capillaries would be to drive out suddenly the blood at the moment contained in them, and thus for the instant to produce a passing increase of flow; and conversely that the first effect of the collapse of the alveolus and consequent widening of the capillaries would be to find room for an extra quantity of blood, and thus for a moment to check the flow. Whether in each case the first or the second phase becomes predominant would depend on the rate and depth of the breathing. There are difficulties, however, in accepting this view, and the one previously given seems to be the more valid one.

From what has been said, it is clear that the influences of the respiratory movements are not only many but conflicting, and that the exact effect at any one moment will vary according as circumstances render one or other factor predominant. It will hardly be profitable to make any further attempt to unravel the complexity of the several cases.

The relations between respiration and circulation which we have just discussed are of a mechanical nature, but there are also ties of a nervous kind between the two systems. One striking feature of the respiratory undulation in the blood-pressure curve of the dog[1] is the fact that the pulse-rate is quickened during the rise of the undulation and becomes slower during the fall. The quickening of the beat might be considered as itself partly accounting for the rise, or, on the other hand, it might be urged that the increased flow of blood which causes the rise, at the same time leads to the quickening, were it not for one fact, viz., that the difference is at once done away with, without any other essential change in the undulations, by section of both vagi. Evidently the slower pulse during the fall is caused by a coincident stimulation of the cardio-inhibitory centre in the medulla oblongata, the quicker pulse during the rise being due to the fact that, during that interval, the centre is comparatively at rest. We have here most important indications that, while the respiratory centre in the medulla oblongata is at work, sending out rhythmic impulses of inspiration and expiration, the neighboring cardio-inhibitory centre is, as it were by sympathy, thrown

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[1] In the rabbit, the respiratory undulations, though well marked, present a very small difference of pulse-rate in the rise and fall.

into an activity of such a kind that its influence over the heart waxes and wanes with each respiratory movement.

But if the cardio-inhibitory centre is thus synchronously affected, ought we not to expect that the vaso motor centre should also be influenced? We have, indeed, evidence that the action of the vaso-motor centre is largely dependent on the respiratory changes of blood.

FIG. 137.

TRAUBE-HERING CURVES.   To be read from left to right.
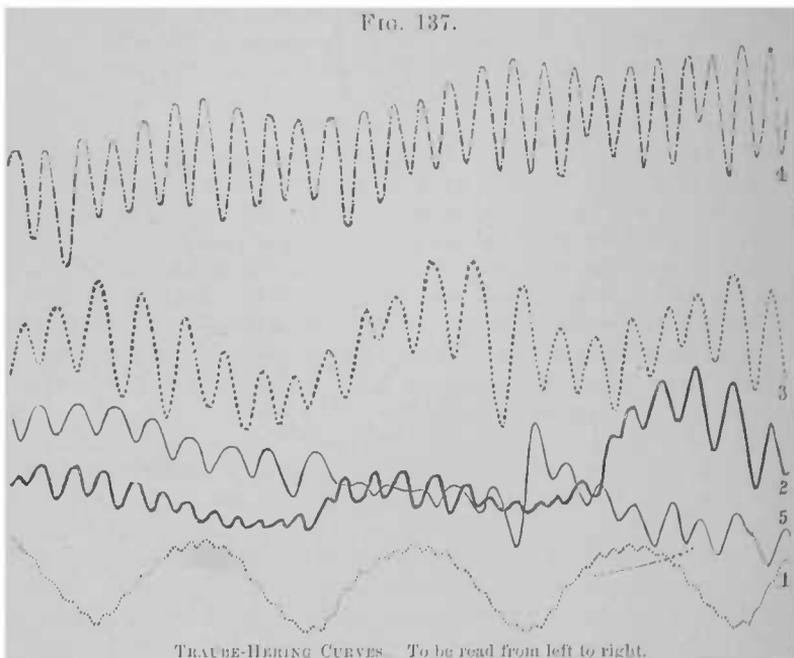
The curves 1, 2, 3, 4, 5 are portions selected from one long continuous tracing forming the record of a prolonged observation, so that the several curves represent successive stages of the same experiment. Each curve is placed in its proper position relative to the base line, which, to save space, is omitted, and it is obvious, that starting from the stage represented by 1, the blood-pressure rises in stages 2, 3, and 4, but falls again in stage 5. Curve 1 is taken from a period when artificial respiration was being kept up, and the undulations visible are those the nature of which have been discussed; the vagi having been cut, the pulsations on the ascent and descent of the undulations do not differ. When the artificial respiration was suspended, these undulations for a while disappeared, and the blood-pressure rose steadily while the heart beats became slower. Soon, as shown in curve 2, new undulations appeared. A little later, the blood-pressure was still rising, the heart-beats still slower, but the undulations still more obvious (curve 3). Still later (curve 4), the pressure was still higher, but the heart-beats were quicker and the undulations flatter. The pressure then began to fall rapidly (curve 5), and continued to fall until some time after artificial respiration was resumed.

When artificial respiration is stopped, a very large but steady rise of pressure is observed. This may be in part due to the

increased force of the cardiac beat, caused by the increasingly venous character of the blood ; but only in part, and that a small part. The rise so witnessed is very similar to that brought about by powerfully stimulating a number of vaso-constrictor nerves ; and there can be no doubt that it is due to the venous blood stimulating the vaso-motor centre in the medulla, and thus causing constriction of the small arteries of the body, particularly, perhaps, those of the splanchnic area. We say, "stimulating the medullary vaso-motor centre," because, though we must admit that, since a rise of pressure follows upon dyspnœa when the spinal cord has been previously divided below the medulla, the venous blood may stimulate other vaso-motor centres in the spinal cord, and possibly even act directly on local peripheral mechanisms, or on the muscular coats of the small arteries themselves, yet the fact that the rise of pressure is much less under these circumstances shows that the medullary centre plays the chief part. Upon the cessation of the artificial respiration, the respiratory undulations cease also, so that the blood-pressure curve rises at first steadily in almost a straight line ; yet after a while new undulations, the so-called Traube or Traube-Hering curves, make their appearance (Fig. 137, 2, 3), very similar to the previous ones, except that their curves are larger and of a more

FIG. 138.

BLOOD-PRESSURE CURVE OF A RABBIT, RECORDED ON A SLOWLY MOVING SURFACE TO SHOW TRAUBE-HERING CURVES.
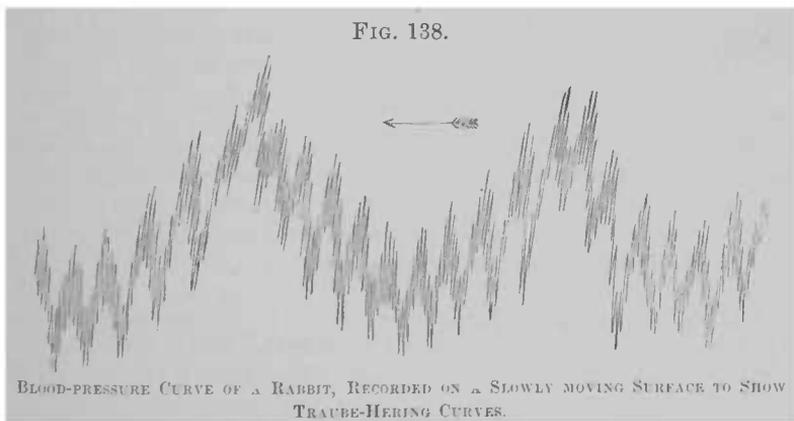
In each heart-beat the upward and downward strokes are very close together, but may be easily distinguished by the help of a lens. The undulations of the next order are those of respiration. The wider sweeps are the Traube-Hering curves, of which two complete curves and portions of two others are shown. Each Traube-Hering curve comprises about nine respiratory curves, and each respiratory curve about the same number of heart-beats.

sweeping character. These new undulations, since they appear in the absence of all thoracic or pulmonary movements, passive or active, and are witnessed even when both vagi are cut, must be of vaso-motorial origin ; the rhythmic rise must be due to a

rhythmic constriction of the small arteries, and this probably is caused by a rhythmic discharge from vaso-motor centres, and especially from the medullary vaso-motor centre. The undulations are maintained as long as the blood-pressure continues to rise. With the increasing venosity of the blood, however, both the vaso-motor centres and the heart become exhausted; the undulations disappear, and the blood-pressure rapidly sinks.

The appearance of these Traube-Hering curves is not, however, dependent on the cessation of the respiratory movements, and on an abnormally venous condition of the blood. They sometimes (Fig. 138) are seen in an animal whose breathing is fairly normal. We need not discuss them any further now, and have introduced them chiefly to illustrate the fact that the vaso-motor nervous system is apt to fall into a condition of rhythmic activity. It has been suggested that the normal respiratory undulations may be as to a rhythmic rise and fall of the activity of the vaso-motor centre, synchronous, like that of the cardio-inhibitory centre, with the respiratory movements. A review of all the evidence, however, goes to show that the respiratory variations in blood-pressure are due to the mechanical conditions discussed above, and that vaso-motor influences intervene but little if at all.

Sec. 8.—The Effects of Changes in the Air Breathed.

The Effects of Deficient Air. Asphyxia.

When, on account of occlusion of the trachea, or by breathing in a confined space, a due supply of air is not obtained, normal respiration gives place, through an intermediate phase of dyspnœa, to the condition known as asphyxia; this, unless remedial measures be taken, rapidly proves fatal.

Phenomena of Asphyxia.—As soon as the oxygen in the arterial blood sinks below the normal, the respiratory movements become deeper and at the same time more frequent; both the inspiratory and expiratory phases are exaggerated, the supplementary muscles spoken of at p. 388 are brought into play, and the rate of the rhythm is hurried. In this respect, dyspnœa, or hyperpnœa as this first stage has been called, contrasts very strongly with the peculiar respiratory condition caused by section of the vagi, in which the respiratory movements, while much more profound than the normal, are diminished in frequency.

As the blood continues to become more and more venous the respiratory movements continue to increase both in force and

frequency, a larger number of muscles being called into action and that to an increasing extent. Very soon, however, it may be observed that the expiratory movements are becoming more marked than the inspiratory. Every muscle which can in any way assist in expiration is in turn brought into play; and at last almost all the muscles of the body are involved in the struggle. The orderly expiratory movements culminate in expiratory convulsions, the order and sequence of which are obscured by their violence and extent. That these convulsions, through which dyspnœa merges into asphyxia, are due to a stimulation of the medulla oblongata by the venous blood, is proved by the fact that they fail to make their appearance when the spinal cord has been previously divided below the medulla, though they still occur after those portions of the brain which lie above the medulla have been removed. It is usual to speak of a "convulsive centre" in the medulla, the stimulation of which gives rise to these convulsions; but if we accept the existence of such a centre we must at the same time admit that it is connected by the closest ties with the normal expiratory division of the respiratory centre, since every intervening step may be observed between a simple slight expiratory movement of normal respiration and the most violent convulsion of asphyxia. An additional proof that these convulsions are carried out by the agency of the medulla is afforded by the fact that convulsions of a wholly similar character are witnessed when the supply of blood to the medulla is suddenly cut off by ligaturing the bloodvessels of the head. In this case the nervous centres, being no longer furnished with fresh blood, become rapidly asphyxiated through lack of oxygen, and expiratory convulsions quite similar to those of ordinary asphyxia, and preceded like them by a passing phase of dyspnœa, make their appearance. Similar "anæmic" convulsions are seen after a sudden and large loss of blood from the body at large, the medulla being similarly stimulated by the lack of arterial blood.

Such violent efforts speedily exhaust the nervous system; and the convulsions after being maintained for a brief period suddenly cease and are followed by a period of calm. The calm is one of exhaustion; the pupils, dilated to the utmost, are unaffected by light; touching the cornea calls forth no movement of the eyelids, and indeed no reflex actions can anywhere be produced by the stimulation of sentient surfaces. All expiratory active movements have ceased; the muscles of the body are flaccid and quiet; and though from time to time the respiratory centre gathers sufficient energy to develop respiratory movements, these resemble those of quiet normal breathing, in being, as far as muscular actions are concerned, almost entirely inspi-

ratory. They occur at long intervals, like those after section of the vagi; and like them are deep and slow. The exhausted respiratory centre takes some time to develop an inspiratory explosion; but the impulse when it is generated is proportionately strong. It seems as if the resistance which had in each case to be overcome was considerable, and the effort in consequence, when successful, productive of a large effect.

As time goes on, these inspiratory efforts become less frequent; their rhythm becomes irregular; long pauses, each one of which seems a final one, are succeeded by several somewhat rapidly repeated inspirations. The pauses become longer, and the inspiratory movements shallower. Each inspiration is accompanied by the contraction of accessory muscles, especially of the face, so that each breath becomes more and more a prolonged gasp. The inspiratory gasps spread into a convulsive stretching of the whole body, and with extended limbs and a straightened trunk, with the head thrown back, the mouth widely open, the face drawn, and the nostrils dilated, the last breath is taken in.

Thus we are able to distinguish three stages in the phenomena which result from a continued deficiency of air: (1) A stage of dyspnœa, characterized by an increase of the respiratory movements both of inspiration and expiration. (2) A convulsive stage, characterized by the dominance of the expiratory efforts, and culminating in general convulsions. (3) A stage of exhaustion, in which lingering and long-drawn inspirations gradually die out. When brought about by sudden occlusion of the trachea these events run through their course in about 4 or 5 minutes in the dog, and in about 3 or 4 minutes in the rabbit. The first stage passes gradually into the second, convulsions appearing at the end of the first minute. The transition from the second stage to the third is somewhat abrupt, the convulsions suddenly ceasing early in the second minute. The remaining time is occupied in the third stage.

The duration of asphyxia varies not only in different animals, but in the same animal under different circumstances. Newly born and young animals need much longer immersion in water before death by asphyxia occurs than do adults. Thus while in a full-grown dog recovery from drowning is unusual after $1\frac{1}{2}$ minutes, a new-born puppy has been known to bear an immersion of as much as 50 minutes. The cause of the difference lies in the fact that in the quite young, or rather just born animal, the respiratory changes of the tissues are much less active. These consume less oxygen, and the general store of oxygen in the blood has a less rapid demand made upon it. The respiratory activity of the tissues may also be lessened by a deficiency in the circulation; hence bodies in a state of syncope at the

time when the deprivation of oxygen begins can endure the loss for a much longer period than can bodies in which the circulation is in full swing. There being the same store of oxygen in the blood in each case, the quicker circulation must of necessity bring about the speedier exhaustion of the store. In many cases of drowning, death is hastened by the entrance of water into the lungs.

By training, the respiratory centre may be accustomed to bear a scanty supply of oxygen for a much longer time than usual before dypsnœa sets in, as seen in the case of divers.

The phenomena of slow asphyxia, where the supply of air is gradually diminished, are fundamentally the same as those resulting from a sudden and total deprivation. The same stages are seen, but their development takes place more slowly.

The Circulation in Asphyxia.—If the carotid or other artery of an animal be connected with a manometer during the development of the asphyxia just described, the following facts may be observed. During the first and second stages the blood-pressure rises rapidly, attaining a height far above the normal. During the third stage it falls even more rapidly, repassing the normal and becoming *nil* as death ensues. The respiratory undulations of the pressure-curve are abrupt and somewhat irregular, the inspiratory movements being accompanied by a fall of pressure. When the animal has been previously placed under urari, so that the respiratory impulses cannot manifest themselves by any muscular movements, the rise of the pressure-curve, as we have already said, is at first steady and unbroken, but after a variable period Traube's curves make their appearance. As during the third stage the pressure sinks, these undulations pass away.

The heart-beats are at first somewhat quickened, but speedily become slow, while at the same time they acquire great force; so that the pulse-curves on the tracing are exceedingly bold and striking, Fig. 137. Even while the blood-presure is sinking, the pulse-curves still maintain somewhat these characters, and the heart continues to beat for some seconds after the respiratory movements have ceased, the strokes at last rapidly failing in frequency and strength.

If the chest of an animal be opened under artificial respiration, and asphyxia brought on by cessation of the respiration, it will be seen that the heart during the second and third stages becomes completely gorged with venous blood, all the cavities as well as the large veins being distended to the utmost. If the heart be watched to the close of the events, it will be seen that the feebler strokes which come on towards the end of the third

stage are quite unable to empty its cavities; and when the last beat has passed away its parts are still choked with blood. The veins spirt out when pricked, and it may frequently be observed that the beats recommence when the over-distention of the heart's cavities is relieved by puncture of the great vessels. When rigor mortis sets in after death by asphyxia, the left side of the heart is more or less emptied of its contents; but not so the right side. Hence in an ordinary post-mortem examination in cases of death by asphyxia, while the left side is found comparatively empty, the right appears gorged.

These various phenomena of asphyxia are probably brought about in the following way:

The increasingly venous character of the blood augments the action of the general vaso-motor centre, and thus leads to a general constriction of the small arteries. This is the cause of the markedly increased blood-pressure; though, as we have already said, the venous blood may also act directly on the other spinal vaso-motor centres and possibly on peripheral vaso-motor mechanisms or on the muscular arterial coats, or may even affect the peripheral resistance by modifying the changes in the capillary regions.

This increased peripheral resistance, while indirectly helping to augment the force of the heart's beat, is a direct obstacle to the heart emptying itself of its contents. On the other hand, the increased respiratory movements favor the flow of venous blood towards the heart, which in consequence becomes more and more full. This repletion is moreover assisted by the marked infrequency of the heats. This in turn depends in part on the cardio-inhibitory centre in the medulla being stimulated by the venous blood; since when the vagi are divided the infrequency is much less pronounced. It does not however disappear altogether; and we are therefore driven to suppose it is in part due to the venous blood acting in an inhibitory manner directly on the heart itself. The increased resistance in front, the augmented supply from behind, and the long pauses between the strokes, all concur in distending the heart more and more.

When the large veins have become full of blood the inspiratory movements can no longer have their usual effect in increasing the blood-pressure. The whole force of the chest movement, as far as the circulation is concerned, is spent in diminishing the pressure around the large arteries; and hence the sinking of the blood-pressure during each inspiratory movement.

The distention of the cardiac cavities, at first favorable to the heart-beat, as it increases becomes injurious. At the same time the cardiac tissues, which at first probably are stimulated, after

awhile become exhausted by the action of the venous blood ; and the strokes of the heart become feebler as well as slower.

On account of this increasing slowness and feebleness of the heart's beat, the blood-pressure, in spite of the continued arterial constriction, begins to fall, since less and less blood is pumped into the arterial system ; the boldness of the pulse-curves at this stage being chiefly due to the infrequency of the strokes. As the quantity which passes from the heart into the arteries becomes less second by second, the pressure gets lower and lower, the descent being assisted by the exhaustion of the vaso-motor centre, until almost before the last beats it has sunk to zero. Thus at the close of asphyxia, while the heart and venous system are distended with blood, the arterial system is less than normally full.

The Effects of an Increased Supply of Air. Apnœa.

We have already (p. 427) seen that when artificial respiration is carried on too vigorously, a condition of peculiar breathlessness known as "apnœa"[1] is brought about. We have further seen that the essential feature of apnœa consists in the blood containing for the time being more oxygen than usual. In consequence of this a longer time is needed before the deficiency of oxygen in the blood of the capillaries of the medulla oblongata, or rather in the nerve-cells constituting the respiratory centre, reaches the limit which determines the discharge of a respiratory impulse. As we have seen, the molecular processes of these cells are so arranged, that whenever the oxygen which is available for their use sinks below a certain level, respiratory explosions occur whereby a fresh supply of oxygen is gained. We must suppose that the changes going on in these cells, like those taking place in other cells and tissues, are oxidative in character ; but they possess this peculiar feature, that the absence or diminution of oxygen acts as it were as a stimulus, leading to an explosive decomposition. The facts previously (p. 427) discussed lead us to adopt this view, though we cannot explain why oxygen has this remarkable effect on these particular cells. By increasing their available oxygen, the explosive action of the cells is deferred and diminished ; that is, apnœa is established. Similarly when the supply of oxygen is diminished, the explosions are hastened and increased ; that is, dyspnœa is brought about. The different conditions of the respiratory centre during apnœa,

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[1] It is to be regretted that this name is used by some medical authorities in a sense almost identical with asphyxia. In its physiological sense, as here used, it is the very opposite of asphyxia.

normal breathing or eupnœa, and dyspnœa, are well shown by
the different effects produced by stimulating the afferent fibres
of the trunk of the vagus with the same stimulus during the
three stages. If the current chosen be of such a strength as
will gently increase the rhythm of normal breathing, it will be
found to have no effect at all in apnœa, while in dyspnœa it may
produce almost convulsive movements. Indeed, in well-marked
apnœa even strong stimulation of the vagus may produce no
effect whatever.

The Effects of Changes in the Composition of the Air Breathed.

We have already discussed the effects of such changes as are
produced by the act of respiration itself, viz., a deficiency of oxy-
gen and an excess of carbonic acid. We have only to add, that
the result of an excess of oxygen, except in the cases of extreme
pressure to be mentioned immediately, is simply apnœa, and that
variations in amount of nitrogen have of themselves no effect, this
gas being eminently an indifferent gas as far as physiological
processes are concerned.

Poisonous Gases.—Carbonic oxide produces the same effects as
deficiency of oxygen, inasmuch as it preoccupies the hæmoglobin
and so prevents the blood from becoming properly oxygenated
(see p. 406). Sulphuretted hydrogen produces similar effects,
but in a different manner; it acts as a reducing agent (see p.
403). Some gases are irrespirable, on account of their causing
spasm of the glottis, and this is said to be, to a certain extent,
the case with carbonic acid.

The Effects of Changes in the Pressure of the Air Breathed.

Gradual Diminution of Pressure.—The symptoms are those of
deficiency of oxygen; the animals die of asphyxia. The blood
contains less and less oxygen as the pressure is reduced, the
quantity present in the arterial blood soon becoming less than
that in normal venous blood. The quantity of carbonic acid in
the blood is also diminished. The increasing dyspnœa is accom-
panied by great general feebleness; and convulsions, though
frequent, are not invariable. The occurrence of these seems to
depend on the suddenness with which the oxygen of the blood is
diminished.

Sudden Diminution.—Death in these cases ensues from the
liberation of gases within the bloodvessels and the consequent
mechanical interference with the circulation. The gas which is

found in the bloodvessels on examination after death consists
chiefly of nitrogen.

Increase of Pressure.—Up to a pressure of several atmospheres
of air, the only symptoms which present themselves are those
somewhat resembling narcotic poisoning. At a pressure, how-
ever, of four atmospheres of oxygen, corresponding to twenty
atmospheres of air, and upwards, a very remarkable phenomenon
presents itself. The animals die of asphyxia and convulsions,
exactly in the same way as when oxygen is deficient. Cor-
responding with this it is found that the production of carbonic
acid is diminished. That is to say, when the pressure of the
oxygen is increased beyond a certain limit, the oxidations of the
body are diminished, and with a still further increase of the
oxygen are arrested altogether. The oxidation of phosphorus is
quite analogous; at a high pressure of oxygen, phosphorus will
not burn. Not only animals, but plants, bacteria, and organized
ferments, are similarly killed by a too great pressure of oxygen.

Sec. 9.—Modified Respiratory Movements.

The respiratory mechanism with its adjuncts, in addition to its
respiratory function, becomes of service, especially in the case of
man, as a means of expressing emotions. The respiratory column
of air, moreover, in its exit from the chest, is frequently made
use of in a mechanical way to expel bodies from the upper air-
passages. Hence arise a number of peculiarly modified and
more or less complicated respiratory movements, sighing, cough-
ing, laughter, etc., adapted to secure special ends which are not
distinctly respiratory. They are all essentially reflex in char-
acter, the stimulus determining each movement, sometimes
affecting a peripheral afferent nerve, as in the case of coughing,
sometimes working through the higher parts of the brain as in
laughter and crying, sometimes possibly, as in yawning and
sighing, acting on the respiratory centre itself. Like the simple
respiratory act, they may with more or less success be carried
out by a direct effort of the will.

Sighing is a deep and long-drawn inspiration chiefly through
the nose followed by a somewhat shorter, but correspondingly
large expiration.

Yawning is similarly a deep inspiration, deeper and longer
continued than a sigh, drawn through the widely open mouth,
and accompanied by a peculiar depression of the lower jaw and
frequently by an elevation of the shoulders.

Hiccough consists in a sudden inspiratory contraction of the diaphragm, in the course of which the glottis suddenly closes, so that the further entrance of air into the chest is prevented, while the impulse of the column of air just entering, as it strikes upon the closed glottis, gives rise to a well-known accompanying sound. The afferent impulses of the reflex act are conveyed by the gastric branches of the vagus. The closure of the glottis is carried out by means of the inferior laryngeal nerve. See *Voice*.

In *sobbing* a series of similar convulsive inspirations follow each other slowly, the glottis being closed earlier than in the case of hiccough, so that little or no air enters into the chest.

Coughing consists in the first place of a deep and long-drawn inspiration by which the lungs are well filled with air. This is followed by a complete closure of the glottis, and then comes a sudden and forcible expiration, in the midst of which the glottis suddenly opens, and thus a blast of air is driven through the upper respiratory passages. The afferent impulses of this reflex act are in most cases, as when a foreign body is lodged in the larynx or by the side of the epiglottis, conveyed by the superior laryngeal nerve; but the movement may arise from stimuli applied to other afferent branches of the vagus, such as those supplying the bronchial passages and stomach and the auricular branch distributed to the *meatus externus*. Stimulation of other nerves also, such as those of the skin by a draught of cold air, may develop a cough.

In *sneezing* the general movement is essentially the same, except that the opening from the pharynx into the mouth is closed by the contraction of the anterior pillars of the fauces and the descent of the soft palate, so that the force of the blast is driven entirely through the nose. The afferent impulses here usually come from the nasal branches of the fifth. When sneezing however is produced by a bright light, the optic nerve would seem to be the afferent nerve.

Laughing consists essentially in an inspiration succeeded, not by one, but by a whole series, often long continued, of short spasmodic expirations, the glottis being freely open during the whole time, and the vocal cords being thrown into characteristic vibrations.

In *crying*, the respiratory movements are modified in the same way as in laughing; the rhythm and the accompanying facial expressions are however different, though laughing and crying frequently become indistinguishable.

CHAPTER III.

THE skin is divided into two principal portions : the *epidermis*, cuticle or scarf-skin, and the *derma*, or true skin. These layers can readily be demonstrated by maceration.

The *epidermis*, or most superficial layer, is a cellular structure, composed entirely of superimposed stratifications of epithelium cells, which differ in character in the superficial and deep layers.

FIG. 139.
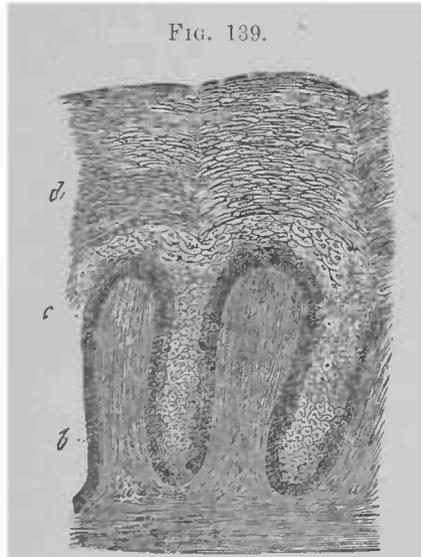
Skin of the Negro, in a Vertical Section ; magnified 250 diameters. *a, a,* cutaneous papillæ ; *b,* undermost and dark colored layer of prismoidal epidermis cells of the mucous or Malpighian layers ; *d,* horny layer. After SHARPEY.

The superficial layers are composed of flat, nucleated horny epithelium cells, which are detached from the cutaneous surface in the form of scales. In the deeper layers, the cells are rounded or prismoidal in form, soft and pigmented. The pigment is most abundant in the layers of cells which immediately surround the papillary layer of the derma, and gradually becomes less abundant as the superficial layers of the epidermis are approached. The difference in the color of the skin of different races is due to the pigmentary deposit in those cells. The superficial layers of the

epidermis are termed the horny layers; the deeper layers are termed the *rete mucosum*, Malpighian or mucous layers. (Fig. 139.) The cells, which are being constantly desquamated from the horny layers, are replaced by cells from the deeper layers, which undergo the modifications in form from a prismoidal to a rounded and ultimately to a flattened condition as they are pushed up by the new cells, which are continually being reproduced in the *rete mucosum*. The epidermis forms a protective covering for the body, by preserving the soft and more delicate superficial structures from the effects of friction, by diminishing the evolution of heat, and by limiting the amount of watery evaporation.

The *derma* or true skin is composed of two layers, the *papillary layer* and the *corium*.

The *corium* or deep layer is dense, tough, and elastic, and composed of fasciculi of white fibrous tissue, which are inter-
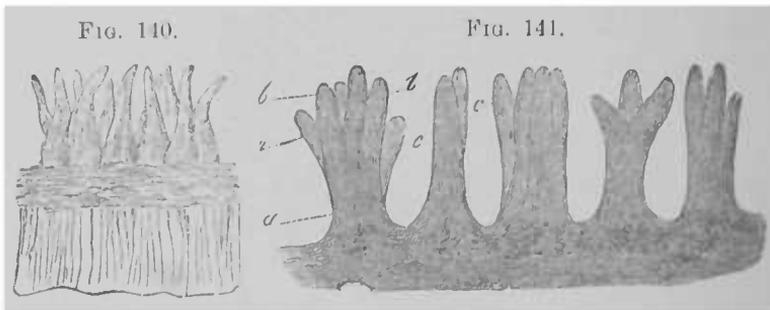
Fig. 140.   Fig. 141.

Fig. 140. Papillæ, as seen with a Microscope, on a portion of the true skin, from which the Cuticle has been removed. After Bourgery.

Fig. 141.—Compound Papillæ from the Palm of the Hand; magnified 60 diameters. *a*, bases of a papilla; *b, b*, divisions or branches of the same; *c, c*, branches belonging to papillæ of which the bases are hidden from view. After Kölliker.

laced in various directions, and forming spaces between their interlacements which are termed *areolæ*. Intermixed with the white fibrous tissue is a variable amount of yellow elastic fibres. In the deeper portions of the corium the fasciculi are not so closely interwoven, and they become blended with the subcutaneous tissue : the areolæ are larger and contain fat, hair-follicles, and cutaneous glands. Approaching the superficial surface the fasciculi become more closely interwoven, and in some parts so closely as to obliterate the areolæ entirely. The most superficial portion of the corium is of a homogeneous nucleated, transparent structure. The *papillary* layer consists of numerous extremely sensitive, vascular, conical projections, which are homogeneous in structure, and appear to be but prolongations

of the corium, from which it has no distinct line of separation. The papillæ are of two kinds: the *simple* and *compound*. The simple papillæ (Fig. 140) are single conical eminences, which are scattered irregularly over the general cutaneous surface. The compound papillæ (Fig. 141) are conical elevations, which have a variable number of simple papillæ projecting from their free
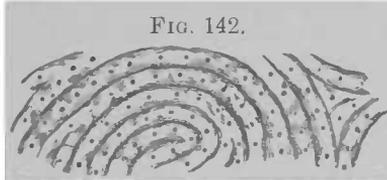
FIG. 142.

Portion of Skin from the Palmar Surface of the end of the Thumb, slightly magnified, showing the curved ridges and intermediate furrows. Upon the ridges are seen the orifices of the ducts of the sweat-glands. After MARSHALL.

extremities. The compound papillæ are most abundant upon the palmar surface of the hands and fingers. As seen in this situation they are arranged in the form of parallel curved ridges,
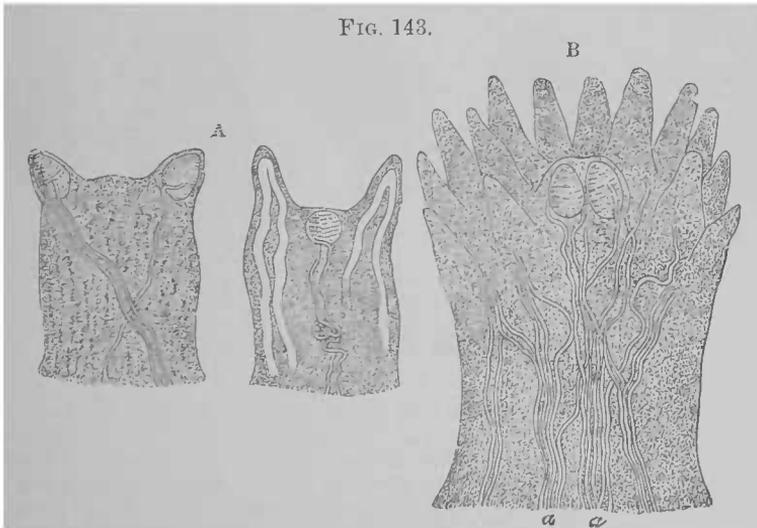
FIG. 143.

End-bulbs in Papillæ (magnified) treated with Acetic Acid. A, from the lips; the white loops in one of them are capillaries. B, from the tongue. Two end-bulbs seen in the midst of the simple papillæ; *a, a*, nerves. After KOLLIKER.

each of which is formed of a double row of papillæ, which are placed in pairs. Transverse grooves are seen upon the surfaces of the ridges, which correspond to the interspaces between the pairs of papillæ forming the rows. In the centre of each trans-

verse groove is a small opening, which is an orifice of a sudori-
parous duct.   (Fig. 142.)

The mode by which the nervous filaments terminate in the
skin is of great physiological interest, but unfortunately our
knowledge on the subject is still unsatisfactory.   Thus far we
know that the nerves after passing through the subcutaneous
cellular tissues form plexuses of minute filaments in the more
superficial layers of the corium.   Some of these are soon lost in
the tissues; others are traced to small corpuscular elements situ-
ated in the papillæ, which are thought to be the essential terminal
organs connected with tactile sensibility.   These corpuscles are
of two kinds: the corpuscles or *terminal bulbs of Krause*, and the
tactile or *axile corpuscles*.   The *bulbs of Krause* (Fig. 143) are
found principally in the conjunctiva, the lips and tongue, and
the glans penis and clitoris.   They are in the form of oval, ob-
long, or rounded bodies, composed of homogeneous structure,
having a delicate connective tissue investment.   The nerve-

Fig. 144.
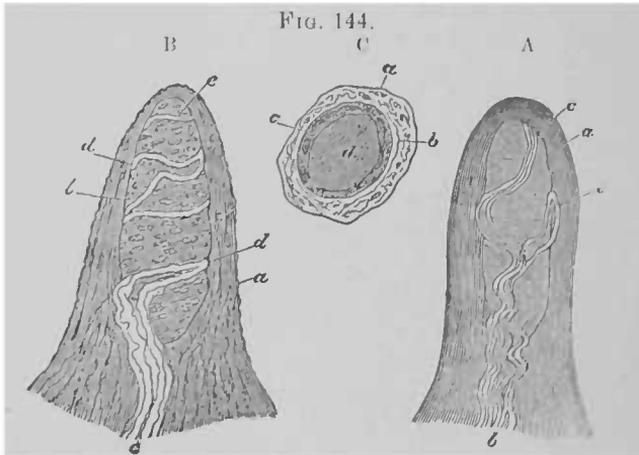
Papillæ from the skin of the Hand, freed from the cuticle and exhibiting the tactile cor-
puscles; magnified 350 diameters.   B, Simple papilla with four nerve-fibres; *a*, tactile cor-
puscle; *b*, nerves.   C, Papilla treated with acetic acid : *a*, cortical layer with cells and fine
elastic filaments; *b*, tactile corpuscle with transverse nuclei; *c*, entering nerve with neuri-
lemma; *d*, nerve-fibres winding round the corpuscle.   A, Papilla viewed from above so as to
appear as a cross-section : *a*, cortical layer; *b*, nerve-fibre; *c*, sheath of the tactile corpuscle
containing nuclei; *d*, core.   After KÖLLIKER.

filament, which consists alone of the axis-cylinder, after entering
the corpuscle becomes very much convoluted, or else appears in
the centre as a straight axial filament.

The *tactile* or *axile* corpuscles (Fig. 144) are found most
thickly distributed where the sense of touch is most acute.   They
appear as oblong or oval bodies, composed of a granular connec-

tive tissue which is almost homogeneous. According to Kölliker, the corpuscles consist of a core of homogeneous or granular connective tissues, which is surrounded by an outer layer or sheath of fibro-elastic tissue, having elongated nuclei, situated transversely. Covering this is a cortex of plasmatic cells and elastic filaments. The nerve filaments, which may be three or four in

FIG. 145.
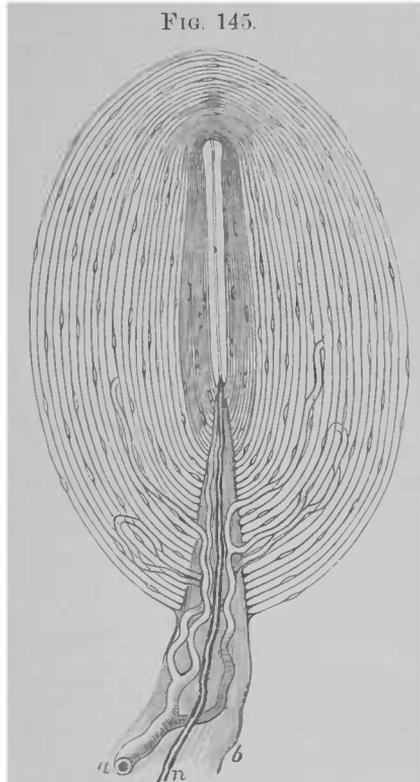
Pacinian Corpuscles from the Mesentery of a Cat; intended to show the general construction of these bodies. The stalk and body, the outer and inner system of capsules with the central cavity are seen. *a*, Arterial twig, ending in capillaries, which form loops in some of the intercapsular spaces, and one penetrates to the central capsule. *b*, The fibrous tissue of the stalk, prolonged from the neurilemma. *n*, Nerve-tube advancing to the central capsule, there losing its white substance, and stretching along the axis to the opposite end, where it is fixed by a tubular enlargement.

number, after reaching the base of the corpuscle, form several irregular spiral coils around it as they approach the apex, at which point they each probably terminate in a filamentous extremity.

Another variety of corpuscle has been described by Pacini. These are known as the *Pacinian corpuscles.* (Fig. 145.) They

are found principally in the subcutaneous cellular tissue of the palmar surface of the hands and feet, and most numerous in the fingers and toes, and are found connected with the nerves of the joints, mesentery, and other parts. They consist of a corpuscular body, which is joined by a pedicle to the nerve with which it is connected. The body is of an oval form, and consists of superimposed concentric layers of connective tissue, which form a series of capsules around a common centre or *bulb*. Between the capsules, especially the most external, spaces exist, which are filled with a clear fluid. The bulb consists of granular nucleated matter, which surrounds the nerve-tube. The nerve loses its medullary substance and sheath as it penetrates the axis of the bulb, and is continued through the bulb to the opposite end, where the filament ends as a tubercular enlargement. The situation of these bulbs in the subcutaneous tissue, as well as in positions of the body not concerned in the tactile sense, indicates that they are not connected with special sensation, but are only one of the modes of termination of the sensory nerves.

Appendages of the Skin.—The nails are formed of modified epithelium cells of the epidermis. They are convex, flattened, smooth, horny structures, which are placed upon the dorsal surface of the last phalanges of the fingers and toes. The nails consist of a *root, body*, and *free edge*. (Fig. 146.) The root is thin, soft, with an irregular margin. It is
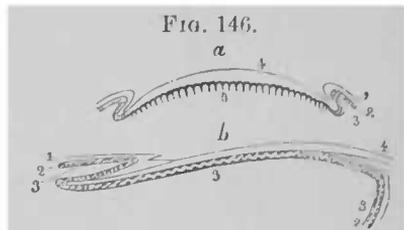
FIG. 146.

Transverse Section of the Nail and its Matrix. *b*, Longitudinal section of the same. Both figures are diagrammatic. 1, the outer cuticular layer; 2, the *rete mucosum*; 3, the cutis; 4, the nail substance; 5, the ridges of the cutis, of which the matrix or end of the nail consists.

covered by a fold of the skin which is extended around the sides of the body. The *body* is that portion which extends from the root to the free edge. It is firmly attached by its under surface to the corium or true skin, which at this point is very vascular and marked by longitudinal rows of papillæ. The portion beneath the body of the nail is termed the *matrix* or bed. At the root of the nail is frequently seen a white semilunar spot, called the *lunula*. The whitish color is due to the lessened vascularity and fewer papillæ, as compared with the rest of the

matrix. The *free* portion of the nails is that part which is detached from the matrix and projects from the cutaneous surface. The nails consist of a superficial hard *horny* layer, and a
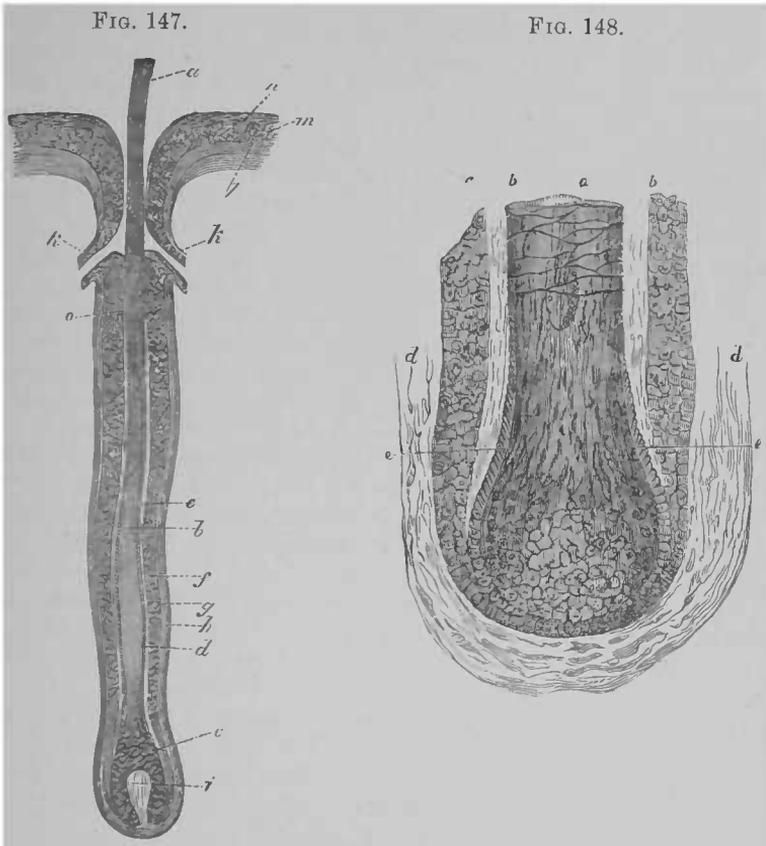
FIG. 147.—Medium-sized Hair in its Follicle ; magnified 50 diameters. *a*, stem cut short ; *b*, root ; *c*, knob ; *d*, hair-cuticle ; *e*, internal, and, *f*, external root-sheath ; *g*, *h*, dermic coat of follicle ; *i*, papilla ; *k*, *k*, ducts of sebaceous glands ; *l*, corium ; *m*, mucous layer of epidermis ; *c*, upper limit of internal root-sheath. After KOLLIKER.

FIG. 148.—Magnified View of the Root of a Hair. *a*, stem or shaft of hair cut across ; *b*, inner, and *c*, outer layer of the epidermal lining of the hair-follicle, called also the inner and outer root-sheath ; *d*, dermal or external coat of the hair-follicle, shown in part ; *e*, imbricated scales about to form a cortical layer on the surface of the hair. The adjacent cuticle of the root-sheath is not represented, and the papilla is hidden in the lower part of the knob where that is represented lighter. After KOHLRAUSCH.

deeper and softer *Malpighian* or *mucous* layer, which rests upon the matrix and completely fills the interpapillary spaces. The nails grow by a continual addition of new cells on their under

surface and root. The Malpighian layer remains stationary, and the horny layer alone is gradually increased in thickness by a deposition of cells underneath and on the root, and is pushed forward by the growth of the root, and worn away at its free edge by attrition, or else cut off.

The *hairs*, like the nails, are formed of modified epidermis cells. They consist of a *root* or bulb, a *shaft* or stem, and a *point*. (Figs. 147, 148.) The shaft is of a flattened cylindrical shape, and is composed of an external portion or *cortex* and an internal *fibrous* substance. The cortex is formed of a layer of fine imbricated cells, having their free extremities looking towards the *point* of a hair. The cortex encloses the *fibrous* structure which constitutes the bulk of the hair substance, and is composed of elongated longitudinal cells, which contain pigment, and occasionally air-cavities. In the axis of the fibrous portion, extending from the root to near the point of the hair, a deposition of granular matter is found, which is composed of irregularly shaped cells, pigment and fat. This is called the *medulla* or *pith*. In the medulla air-cells and air-spaces are found. Kölliker supposes that the dark pigment-granules of the medulla are nothing more than the globules of air in the air-cells.

The *root* or bulb of the hair is enclosed in a follicle which is formed by an involution of the epidermis. In the smaller hairs the follicle merely extends into the corium; in the larger hairs it extends through into the deep layers of the subcutaneous tissue. At its deepest part it is expanded into a bulbous enlargement, which receives the expanded portion of the root, called the *knob*. The follicle is lined by a continuation of the epidermis cells, which forms the *root-sheath* of the hair. This sheath consists of two layers, the *inner* of which is closely attached to the imbricated cells of the cortex and extends to a point below the orifice of the sebaceous ducts. (Fig. 147.) The outer layer is closely attached to the wall of the follicle. The wall of the follicle is formed by a fibro-cellular tissue which is continuous with the corium. A highly nervous and vascular papilla projects from the corium into the bottom of the follicle. On the surface of the papilla the cells are produced which are destined to form the hair. The bulbous portion of the root or *knob* completely envelops the free portion of the papilla, and consists of nucleated cells which are continuous with the cuticular lining of the follicle.

The *sebaceous glands* are found distributed in most portions of the skin, but most abundantly in the scalp and face, and about the nose, mouth, and external ear. They are absent in the palmar surface of the hands and feet.

They are sacculated glands, which are situated either in the

corium or subcutaneous tissue. The walls of the gland consist
of a fibrous tissue, which is lined with a basement membrane
covered with a layer of granular nucleated epithelium cells.

Fig. 149.
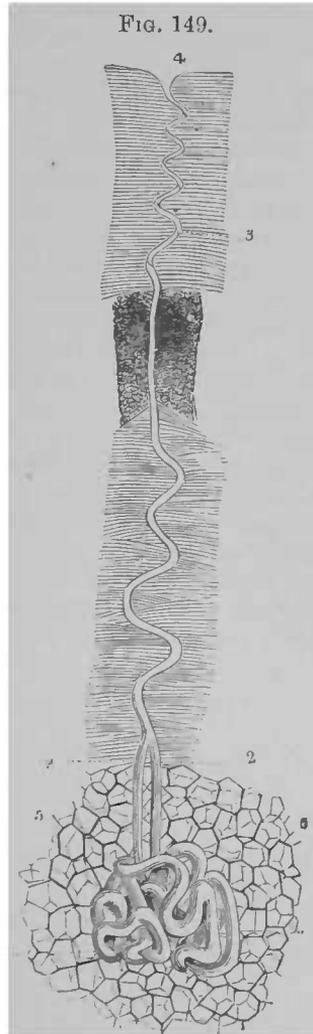
Sudoriparous Gland from the Palm of the Hand ; magnified 40 diameters. 1, 1, contorted
tubes, composing the gland, and uniting in two excretory ducts ; 2, 2, which unite into one
spiral canal that perforates the epidermis at c, and opens its surface at 4 : the gland is em-
bedded in fat-vesicles, which are seen at 5, 5.

These cells contain an opaque, oily matter, which is formed by a
metabolism of the cells, and constitutes the secretion of the gland.

Each gland has a single duct, which is lined with epithelium, and opens by a pivot-like orifice, either on the cutaneous surface or into the upper portion of the hair-follicle. (Fig. 147.)

The *sudoriparous* or sweat glands (Fig. 149) are found profusely distributed over nearly every portion of the skin. Their total number has been estimated to be about 2,400,000. The orifices of the ducts are irregularly dispersed over the general cutaneous surface, between the papillæ. On the palmar surface of the hand and fingers, the orifices are arranged in curved lines in the middle of the double rows of papillæ forming the ridges. (Fig. 142.) These glands are of the tubular variety, and each consists of a tubule, having one extremity terminating in an orifice on the cutaneous surface, and the other extremity forming a convoluted coil, which is located in the subcutaneous tissue. That part of the tubule between the orifice and convoluted portion is called the *duct*. The convoluted portion consists of one or more tubuli, which are formed by the subdivision of the primary tubule. The tubuli end in cæcal extremities. These glands are composed of a fibro-cellular wall, which is lined with granular nucleated epithelium. The duct in its passage from the convoluted portion to the orifice assumes a spiral or undulating course through the corium, becomes straightened in the papillary layer, and again assumes a spiral course, but much more marked, in its passage through the epidermis. They are abundantly supplied with bloodvessels and nerves. The bloodvessels form a capillary plexus around the convoluted portion.]

SECRETION BY THE SKIN.

We have traced the food from the alimentary canal into the blood, and, did the state of our knowledge permit, the natural course of our study would be to trace the food from the blood into the tissues, and then to follow the products of the activity of the tissues back into the blood, and so out of the body. This, however, we cannot as yet satisfactorily do; and it will be more convenient to study first the final products of the metabolism of the body, and the manner in which they are eliminated, and afterwards to return to the discussion of the intervening steps.

Our food consists of certain food-stuffs, viz., proteids, fats, and carbohydrates, of various salts, and of water. In their passage through the blood and tissues of the body, the proteids, fats, and carbohydrates are converted into urea (or some closely allied body), carbonic acid and water, the nitrogen of the urea being furnished by the proteids alone. Many of the proteids contain sulphur, and also have phosphorus attached to them in some combination or other, and some of the fats taken as food contain

phosphorus; these elements ultimately suffer oxidation into phosphates and sulphates, and leave the body in that form in company with the other salts.

Broadly speaking, then, the waste products of the animal economy are urea, carbonic acid, salts, and water. Of these, a large portion of the carbonic acid, and a considerable quantity of water, leave the body by the lungs in respiration; while all (or nearly all) the urea, the greater portion of the salts, and a large amount of water, with an insignificant quantity of carbonic acid, pass away by the kidneys. The work therefore of the remaining excretory tissue, the skin, is confined to the elimination of a comparatively small quantity of salts, a little carbonic acid, and a variable but on the whole large quantity of water in the form of perspiration. The actual excretion by the bowel, that is to say, that portion of the feces which is not simply undigested matter, we have seen to be very small.

The Nature and Amount of Perspiration.

The quantity of matter which leaves the human body by way of the skin is very considerable. Thus it has been estimated that, while 7 grains pass away through the lungs per minute, as much as 11 grains escape through the skin. The amount however varies extremely; it has been calculated, from data gained by enclosing the arm in a caoutchouc bag, that the total amount of perspiration from the whole body in 24 hours might range from 2 to 20 kilos; but such a mode of calculation is obviously open to many sources of error.

Of the whole amount thus discharged, part passes away at once as watery vapor mixed with volatile matters, while part may remain for a time as a fluid on the skin; the former is frequently spoken of as *insensible*, the latter as *sensible* perspiration. The proportion of the insensible to the sensible perspiration will depend on the rapidity of the secretion in reference to the dryness, temperature, and amount of movement, of the surrounding atmosphere. Thus, supposing the rate of secretion to remain constant, the drier and hotter the air, and the more rapidly the strata of air in contact with the body are renewed, the greater is the amount of sensible perspiration which is by evaporation converted into the insensible condition; and conversely when the air is cool, moist, and stagnant, a large amount of the total perspiration may remain on the skin as sensible sweat. Since, as the name implies, we are ourselves aware of the sensible perspiration only, it may and frequently does happen that we seem to ourselves to be perspiring largely, when in reality it is not so much the total perspiration which is being increased as the relative proportion of the sensible perspiration. The rate of secretion may

however be so much increased, that no amount of dryness, or heat, or movement of the atmosphere, is sufficient to carry out the necessary evaporation, and thus the sensible perspiration may become abundant in a hot dry air. And practically this is the usual occurrence, since certainly a high temperature conduces, as we shall point out presently, to an increase of the secretion, and it is possible that mere dryness of the air has a similar effect.

The total amount of perspiration is affected not only by the condition of the atmosphere, but also by the nature and quantity of food eaten, by the amount of fluid drunk, and by the amount of exercise taken. It is also influenced by mental conditions, by medicines and poisons, by diseases, and by the relative activity of the other excreting organs, more particularly of the kidney.

The fluid perspiration, or sweat, when collected, is found to be a clear colorless fluid, with a strong and distinctive odor varying according to the part of the body from which it is taken. Besides accidental epidermic scales, it contains no structural elements. The reaction of the secretion of the sweat glands, apart from that of the sebaceous glands, appears to be alkaline. This is well seen when the sweat becomes abundant. An admixture of sebaceous secretion may, when the sweat itself is scanty, give rise to an acid reaction, probably from the sebaceous fats becoming converted into fatty acids. The average amount of solids is about 1.81 per cent., of which about two-thirds consist of organic substances. The chief normal constituents are: (1) Sodium chloride with small quantities of other inorganic salts. (2) Various acids of the fatty series, such as formic, acetic, butyric, with probably propionic, caproic, and caprylic. The presence of these latter is inferred from the odor; it is probable that many various volatile acids are present in small quantities. Lactic acid, which Berzelius reckoned as a normal constituent, is stated not to be present in health. (3) Neutral fats, and cholesterin; these have been detected even in places, such as the palms of the hand, where sebaceous glands are absent. (4) Though some observers seem to have found a considerable quantity of urea (calculated at 10 grammes in the 24 hours for the whole body) in sweat, the evidence goes to show that neither urea nor any ammonia compound exists in the normal secretion to any extent; apparently some small amount of nitrogen leaves the body by the skin, but this is probably supplied by the epidermis.

In various forms of disease the sweat has been found to contain, sometimes in considerable quantities, blood, albumen, urea (particularly in cholera), uric, acid, calcium oxalate, sugar, lactic acid, indigo, bile and other pigments. Iodine and potassium iodide, succinic, tartaric, and benzoic (partly as hippuric) acids have been found in the sweat when taken internally as medicines.

Cutaneous Respiration.

A frog, the lungs of which have been removed, will continue to live for some time; and during that period will continue not only to produce carbonic acid, but also to consume oxygen. In other words, the frog is able to breathe without lungs, respiration being carried on efficiently by means of the skin. In mammals and in man this cutaneous respiration is, by reason of the thickness of the epidermis, restricted to within very narrow limits; nevertheless, when the body remains for some time in a closed chamber to which the air passing in and out of the lungs has no access (as when the body is enclosed in a large air-tight bag fitting tightly round the neck, or where a tube in the trachea carries air to and from the lungs of an animal placed in an air-tight box), it is found that the air in the chamber loses oxygen and gains carbonic acid. The amount of carbonic acid which is thus thrown off by the skin of an average man in twenty-four hours amounts to about 10 grms., or, according to some observers, to (no more than) about 4 grms., increasing with a rise of temperature, and being very markedly augmented by bodily exercise. It is stated that the amount of oxygen consumed is about equal in volume to that of the carbonic acid given off, but some observers make it rather less. It is evident that the loss which the body suffers through the skin consists chiefly of water.

When an animal, such as a rabbit, is covered over with an impermeable varnish such as gelatine, so that all exit or entrance of gases or liquids by the skin is prevented, death shortly ensues. This result cannot be due, as was once thought, to arrest of cutaneous respiration, seeing how insignificant is the gaseous interchange by the skin as compared with that by the lungs. Nor are the symptoms those of asphyxia, but rather of some kind of poisoning, marked by a very great fall of temperature, which, however, does not seem to be the result of diminished production of heat, since it is said to be coincident with an actual increase of the discharge of heat from the surface. The animal may be restored, or at all events its life may be prolonged with abatement of the symptoms, if the great loss of heat which is evidently taking place be prevented by covering the body thickly with cotton-wool, or keeping it in a warm atmosphere. The symptoms have not as yet been clearly analyzed, but they seem to be due in part to a pyrexia or fever possibly caused by the retention within or reabsorption into the blood of some of the constituents of the sweat, or by the products of some abnormal metabolism, and in part to a dilation of the cutaneous vessels which causes an abnormally large loss of heat, even through the varnish.

The Secretion of Perspiration.

The skin contains, besides the ordinary sudoriparous glands, the sebaceous glands, and the special odoriferous glands of the axilla, anus, and other regions. With regard to the various volatile and odoriferous substances peculiar to sweat, and especially with regard to those peculiar to the sweat of particular regions of the skin, there can be no doubt that these are secreted by the epithelium of the appropriate glands. There can be equally no doubt that the fats which come to the surface of the skin from the sebaceous glands arise from a metabolism of the cells of those glands. And we shall probably not go far wrong in regarding the sweat as a whole as supplied by the sweat-glands alone. For though it seems evident that some amount of fluid must pass by simple transudation through the ordinary epidermis of the portions of skin intervening between the mouths of the glands, yet on the whole it is probable that the portion which so passes is a small fraction only of the total quantity secreted by the skin ; and direct experiment shows that even the simple evaporation of water is much greater from those parts of the skin in which the glands are abundant than from those in which they are scanty.

The Nervous Mechanism of Perspiration. — The secreting activity of the skin, like that of other glands, is usually accompanied and aided by vascular dilation. In one of Bernard's early experiments on division of the cervical sympathetic, it was observed that, in the case of the horse, the vascular dilation of the face on the side operated on was accompanied by increased perspiration. Indeed, the connection between the state of the cutaneous bloodvessels and the amount of perspiration is a matter of daily observation. When the vessels of the skin are contracted, the secretion of the skin is diminished; when they are dilated, it becomes abundant. And in this way, as we shall later on point out, the temperature of the body is largely regulated. When the surrounding atmosphere is warm, the cutaneous vessels are dilated, the amount of sweat secreted is increased, and the consequently augmented evaporation tends to cool down the body. On the other hand, when the atmosphere is cold, the cutaneous vessels are constricted, perspiration is scanty, and less heat is lost to the body by evaporation.

The analogy with the other secreting organs which we have already studied leads us, however, to infer that there are special nerves directly governing the activity of the sudoriparous glands, independent of variations in the vascular supply. And not only

is this view supported by many pathological facts, such as the profuse perspiration of the death agony, of various crises of disease, and of certain mental emotions, and the cold sweats occurring in phthisis and other maladies, in all of which the skin is anæmic rather than hyperæmic; but we have direct experimental evidence of a nervous mechanism of perspiration as complete as the vaso-motor mechanism.

If in the cat[1] the peripheral stump of the divided sciatic nerve be stimulated with the interrupted current, a profuse sweat may readily be observed to break out in the hairless sole of the foot on that side. Not only may the secretion be observed when the cutaneous vessels are thrown into a state of constriction by the stimulus, but it also appears when the aorta or crural artery is clamped previous to the stimulation, or indeed when the leg is amputated. Moreover, when atropin has been injected, the stimulation produces no sweat, though vaso-motor effects follow as usual. The analogy between the sweat-glands of the foot and such a gland as the submaxillary is in fact very close, and we are justified in speaking of the sciatic nerve as containing secretory fibres distributed to the sudoriparous glands of the foot. Similar results may be obtained with the nerves of the forelimb. And in ourselves copious secretion of sweat may be induced by tetanizing through the skin the nerves of the limbs or the face.

If a cat in which the sciatic nerve has been divided on one side be exposed to a high temperature in a heated chamber, the limb, the nerve of which has been divided, remains dry, while the feet of the other limbs sweat freely. This result shows that the sweating which is caused by exposure of the body to high temperatures is brought about not by a local action on the sweat-glands but by the agency of the central nervous system. A high temperature up to a certain limit increases the irritability of the epithelium of the sweat-glands as it does that of other forms of protoplasm; thus stimulation of the sciatic in the cat produces a much more abundant secretion in a limb exposed to a temperature of $35°$ or somewhat above, than in one which has been exposed to a distinctly lower temperature, and in a limb which has been placed in ice-cold water hardly any secretion at all can be gained, but apparently mere rise of temperature without nerve-stimulation will not give rise to a secretory activity of the glands. The sweating caused by a dyspnœic condition of blood, and such appears to be the sweat of the death

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[1] The cat sweats freely in the hairless soles of the feet, but not on any part of the body covered with hairs. The dog also sweats in the same regions, but not so freely as the cat. Rabbits and other rodents appear not to sweat at all. The snout of the pig sweats freely, and the often profuse sweating of the horse is known to all.

agony, is similarly brought about by the agency of the central
nervous system. When an animal with the sciatic nerve divided
on one side is made dyspnoeic, no sweat appears in the hind-limb
of that side, though abundance is seen in the other feet.

Sweating may be brought about as a reflex act. Thus when
the central stump of the divided sciatic is stimulated sweating is
induced in the other limbs, and in ourselves the introduction of
pungent substances into the mouth will frequently give rise to a
copious perspiration over the side of the face. We are thus led
to speak of sweat-centres, analogous to the vaso-motor centres,
as existing in the central nervous system, and, as in the case of
vaso-motor centres, a dispute has arisen as to whether there is a
dominant sweat-centre in the medulla oblongata or whether such
centres are more generally distributed over the whole of the
spinal cord.

It does not at present appear certain whether the sweating
caused by heat is carried out by direct action on the sweat-
centres, or by the higher temperature affecting the skin and so
producing its effect in a reflex manner, but in the case of dyspnoea
at least we may fairly suppose that the action of the venous
blood is chiefly if not exclusively on the nerve centres. Some
drugs, such as pilocarpin, which cause sweating, appear to pro-
duce their effect chiefly by a local action on the glands since the
action continues after the division of the nerves (though pilo-
carpin at least has as well some action on the nerve centres),
and the antagonistic action of atropin is similarly local. Nicotin
appears to produce its sweating action chiefly by acting on the
central nervous system.

The sweat-fibres for the hind-foot (in the cat) appear to leave
the spinal cord by the roots of the last dorsal and first two
lumbar or last two dorsal and first four lumbar nerves, pass
along the *rami communicantes* to the abdominal sympathetic, and
thus reach the sciatic nerve. Similarly the sweat-nerves for the
fore-foot leave the spinal cord by the roots of the fourth (or
fourth, fifth, and sixth) dorsal nerves, pass into the thoracic
sympathetic, thence into the ganglion stellatum, and thus join
the brachial plexus ; the course to the foot is finally along the
median and ulnar nerves respectively. In the horse and pig the
sweat-fibres for the side of face and snout appear to run in
branches of the fifth and not in the facial.

Absorption by the Skin.

Although under normal circumstances the skin serves only as
a channel of loss to the body, it has been maintained that it may,
under particular circumstances, be a means of gain. Cases are

on record where bodies are said to have gained in weight by immersion in a bath, or by exposure to a moist atmosphere during a given period, in which no food or drink was taken, or to have gained more than the weight of the food or drink taken; the gain in such cases must have been due to the absorption of water by the skin. Direct experiments, however, throw doubt on these statements, for they show that under ordinary circumstances such a gain by the skin is slight, being apparently due to mere imbibition of water by the epidermis. It is uncertain whether substances in aqueous solution can be absorbed by the skin when the epidermis is intact, the evidence on this point being contradictory. In the case of the sound human skin the balance of conflicting evidence is in favor of the view that soluble nonvolatile substances are not absorbed, and that volatile substances, such as iodine, which may be detected in the system after a bath containing them, are absorbed not by the skin, but by the mucous membrane of the respiratory organs, the substance making its way to the latter by volatilization from the surface of the bath. In the case of the skin of the frog an absorption of water and of various soluble substances would certainly appear to take place. The lymphatics in the skin of a new-born infant have been found crowded with the particles of the peculiar fatty secretion which covers the skin at birth; and solid particles rubbed into even the sound skin may, especially when applied in a fatty vehicle, as, *ex. gr.*, in the well-known mercury ointment, find their way into the underlying lymphatics. So that possibly absorption to a certain extent may ordinarily take place in this way. By abraded surfaces, where the dermis is laid bare and covered only by the lowest layers of epidermis, absorption takes place very readily.

CHAPTER IV

[Physiological Anatomy of the Kidneys.

THE kidneys are tubular glands. They are invested by a fibrous capsule, which is loosely connected to the surface of the organ by delicate processes and bloodvessels. At the hilum or notch, the capsule is prolonged inwards and forms the lining of the sinus, and a sheath around the bloodvessels. The *pelvis* of the kidney is formed by a trumpet-like expansion of the ureter.

FIG. 150.
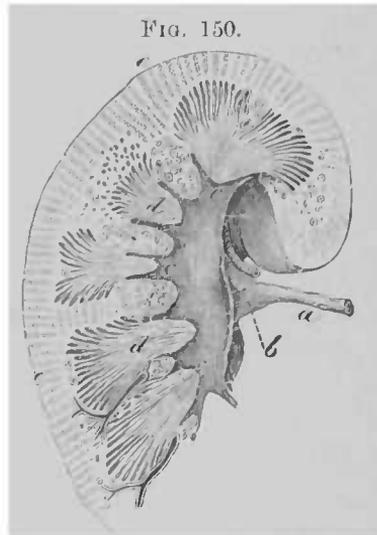
SECTION THROUGH THE KIDNEY, SHOWING THE MEDULLARY AND CORTICAL PORTIONS, AND THE BEGINNING OF THE URETER. HENLE.

a, ureter; *b*, pelvis of the ureter; *c*, papillæ surrounded by calices of the excretory tube; *d*, pyramidal portions; *e*, cortical portion of the kidney.

At its widest part it divides into three infundibula, and these in turn are subdivided into ten or twelve smaller divisions or *calices*, each of which embraces one or more small papillary projections.

If a vertical section be made of the kidney, as is shown in Fig 150, the substance of the gland will appear to consist of two distinct portions, which from their positions are termed the *medullary* and *cortical* portions. The medullary substance consists

of a number of conical-shaped bodies, which are termed the *pyramids of Malpighi*. The bases and sides of these bodies are enveloped by the cortical substance; the apices project into the *calices* as *papillæ*. The pyramids have a striated appearance, and when more minutely examined are seen to consist of a number of diverging tubules, which are bound together by a fibrous stroma containing bloodvessels. The cortical substance constitutes about

FIG. 151.
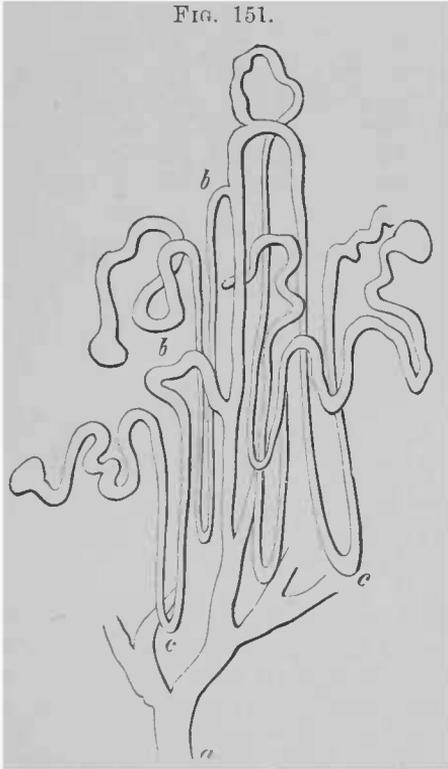
DIAGRAM OF THE COURSE OF THE URINIFEROUS TUBULES.

a, orifice of tubule at apex of Malpighian pyramid; *b*, intermediary portion, continuous with recurrent branches, which form loops, *c*, in the medullary portion of the kidney, and, reascending, terminate in Malpighian capsules in the cortical portion.

three-fourths of the gland substance, and is composed of a mass of convoluted tubules which are continuous with those of the pyramids, and of small reddish bodies called the *Malpighian corpuscles* or *glomeruli*; all of which are embedded in a fibrous matrix which contains bloodvessels, nerves, and lymphatics.

The tubules are called the *tubuli uriniferi*, and are composed of a homogeneous transparent membrane, lined with granular

nucleated epithelium. In their passage from the papillary ori-
fices to the cortex they divide dichotomously at acute angles and
form bundles of straight or slightly wavy tubules, which consti-
tute the pyramids of Ferrein. From these straight tubules
(tubules of Bellini) the intermediary branches arise. (Fig.
151, b.) These branches are somewhat enlarged and more or
less twisted and tortuous; they then become much diminished in

FIG. 152.
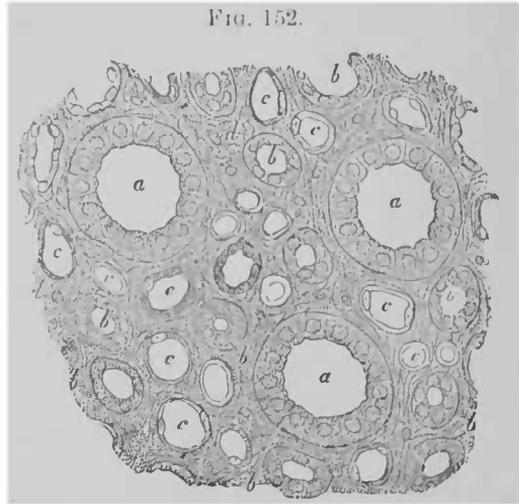
TRANSVERSE SECTION OF A RENAL PAPILLA.

a, larger tubes or papillary ducts; b, smaller tubes of Henle; c, bloodvessels distinguished
by their flatter epithelium; d, nuclei of the stroma. $\frac{200}{1}$. From KOLLIKER.

size, and return towards the papillæ in a direction nearly parallel
with the tubules of Bellini, and after pursuing a variable distance
retrace their way, being still more reduced in size, and then run-
ning into the substance of the cortex, where they become enlarged
and convoluted, finally terminate in saccular dilatations, termed
Malpighian capsules. The recurrent branches or loops above
described are known as the *narrow tubes* or *loops of Henle.*
   The portion of the tubules between the straight tubules of
Bellini and the Malpighian capsules presents three distinct ana-
tomical varieties. The *convoluted* portion ("secreting tubules")
near the capsule, is enlarged and lined throughout with glandular
epithelium; the capsular, or *smaller* portion of the *loop of Henle,*
is about one-fourth the size of the convoluted portion, and is lined
with small clear nucleated cells; the *larger* portion of the loop is
about double the size of the capsular portion, and is lined with
epithelium of a columnar variety, having somewhat of an imbri-
cated arrangement; the *intermediate* or "intercalated" portion,

which connects the loop of Henle with the tubules of Bellini, is lined with an epithelium similar to that which lines the convoluted portion near the capsule. The tubules of Bellini as well as the main tubules are lined by epithelium of a columnar variety, with broad bases.

Each of the *Malpighian corpuscles* is composed of a Malpighian capsule, and an inclosed vascular tuft. (Figs. 153 and 154.)
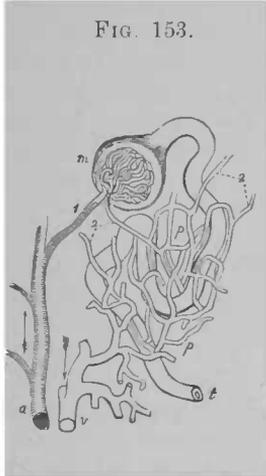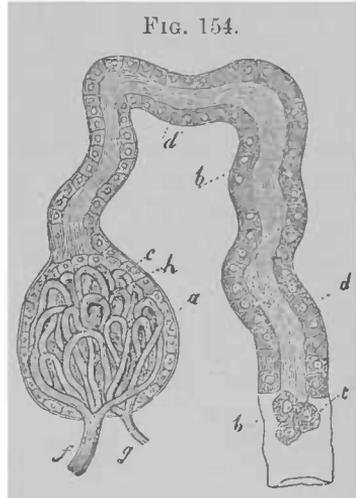
FIG. 153.—Plan of the Renal Circulation in Man and Mammalia. *a*, terminal branch of the artery, giving the terminal twig 1, to the Malpighian tuft *m*, from which emerges the efferent or portal vessel, 2. Other efferent vessels, 2, are seen entering the plexus of capillaries, surrounding the uriniferous tube *t*. From the plexus, the emulgent vein, *v*, springs.

FIG. 154.—Semi-diagrammatic Representation of a Malpighian Body in its relations to the Uriniferous Tube (from KOLLIKER) $\frac{300}{1}$. *a*, capsule of the Malpighian body; *d*, epithelium of the uriniferous tube; *e*, detached epithelium; *f*, afferent vessel; *g*, efferent vessel; *h*, convoluted vessels of the glomerulus.

The tuft is composed of an afferent and efferent vessel and their intermediate plexus of capillaries. The afferent vessel is formed by one of the ramifications of the renal artery, which after piercing the capsule rapidly subdivides into minute capillaries forming an intricate convoluted plexus which finally anastomoses to form one or more efferent vessels or veins. The efferent vessels make their exit adjacent to the point of entrance of the afferent vessel, and then form anastomoses with the efferent vessels of other glomeruli to form dense plexuses of capillaries around the *tubuli uriniferi*. These capillaries finally form larger branches, which ultimately unite to form the renal vein. The system of venous capillaries around the tubules is termed the *renal vena-portal system*. The interior of the capsules is lined by ovoid

granular nucleated cells.   According to some observers, the tuft is covered by a layer of cells similar to those lining the convoluted portion of the tubules.]

SECRETION BY THE KIDNEYS.

The epithelium of the kidney, like that of the alimentary canal, is a secreting tissue.   The protoplasmic cells which line at least a large portion of the *tubuli uriniferi*, elaborate from the blood, in a manner which we shall presently discuss, certain substances, and discharge them into the channels of the tubules.   Besides these distinctly active secreting structures, however, the kidney exhibits in its Malpighian bodies an arrangement very analogous to that which obtains in the lungs.   Just as in the latter the functions of the alveolar epithelium are reduced to a minimum, and the entrance and egress of the gases of respiration are mainly carried on by diffusion, so in the former the epithelium covering the glomerulus has probably but little secreting activity, and the passage of material from the interior of the convoluted bloodvessels into the cavity of the tubule is chiefly carried on by processes which more closely resemble ordinary filtration.   What substances pass in this way, and what substances are secreted by the direct action of the epithelium of the secreting tubules, we shall shortly consider.   The various substances passing, in company with a large amount of water, in either the one or the other way, into the ducts of the gland, constitute the secretion called urine.   And since the substances so thrown out are of no further use in the economy, but are at once carried away, urine is generally spoken of as an excretion.

SEC. 1.— COMPOSITION OF URINE.

The healthy urine of man is a clear, yellowish, slightly fluorescent fluid, of a peculiar odor, saline taste, and acid reaction, having a mean specific gravity of 1.020, and generally holding in suspension a little mucus.   The normal constituents may be arranged in several classes.

1. **Water.**

2. **Inorganic Salts.**—These for the most part exist in urine in natural solution, the composition of the ash almost exactly corresponding with the results of the direct analysis of the fluid; in this respect urine contrasts forcibly with blood, the ash of which

is largely composed of inorganic substances, which previous to the combustion existed in peculiar combination with proteid and other complex bodies. In the ash of urine there is rather more sulphur than corresponds to the sulphuric acid directly determined; this indicates the existence in urine of some sulphur-holding complex body. And there are traces of iron, pointing to some similar iron-holding substance. But, otherwise, all the substances found in the ash exist as salts in the natural fluid. The most abundant and important is sodium chloride. There are found in smaller quantities, calcium chloride, potassium and sodium sulphates, sodium, calcium and magnesium phosphates, with traces of silicates. Alkaline carbonates are frequently found, and nitrates in small quantity are also said to be sometimes present.

The phosphates are derived partly from the phosphates taken as such in food, partly from the phosphorus or phosphates peculiarly associated with the proteids, and partly from the phosphorus of certain complex fats, such as lecithin. When urine becomes alkaline, the calcic and magnesic phosphates are precipitated (Fig. 155), the sodium phosphates remaining in solution. The

[FIG. 155.
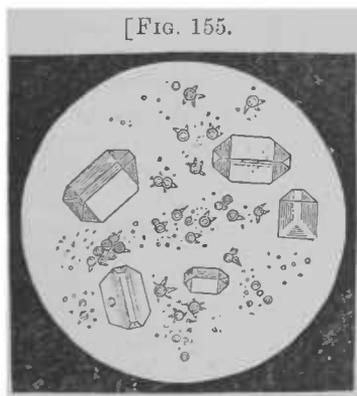
Urinary sediment of triple phosphates (large prismatic crystals) and urate of ammonia, from urine which had undergone alkaline fermentation.]

sulphates are derived partly from the sulphates taken as such in food and partly from the sulphur of the proteids. The carbonates, when occurring in large quantity, generally have their origin in the oxidation of such salts as citrates, tartrates, etc. The bases present depend largely on the nature of the food taken. Thus, with a vegetable diet, the excess of the alkalies in the food reappears in the urine; with an animal diet, the earthy bases in a similar way come to the front.

3. **Nitrogenous Crystalline Bodies**, derivatives of the metabolism of the proteids of the body and food. First and foremost come urea and its immediate ally, uric acid. These will be considered in detail hereafter; they are the typical products of the metabolism of proteids. Existing in much smaller quantities are a number of bodies more or less closely related to urea, which may for the most part be regarded as less completely oxidized products of metabolism. Such are: kreatinin, xanthin, hypoxanthin, and occasionally allantoin. To these may be added: hippuric acid, ammonium oxalurate, and, at times, taurin, cystin, leucin, and tyrosin. These, too, we shall have to consider in dealing with the metabolism of the body.

4. **Non-nitrogenous Bodies.**—These exist in very small quantities, and many of them are probably of uncertain occurrence. They are organic acids, such as lactic, succinic, formic, oxalic, phenylic, etc. It has been maintained that minute quantities of sugar are invariably present in even healthy urine; this, however, has not as yet been placed beyond all doubt.

5. **Pigments.**—These are at present very imperfectly understood. Whether the natural yellow color of urine be due to a single pigment, or to more than one, and what is the exact nature of these pigments, must be left undecided. As has been stated, the urine frequently contains *urobilin;* and the peculiar red color of some rheumatic urines is due to the presence of a body called *purpurin* or *uroerythrin.* The urine of many animals, especially of the dog, and occasionally of man, contains *indican*, which, under certain circumstances, may give rise to the production of indigo-blue.

6. **Other Bodies.**—When urine is treated with many times its volume of alcohol, a granular or flocculent precipitate is thrown down, consisting of phosphates, some substance or substances giving proteid reactions, and probably other bodies in small quantities. An aqueous solution of the precipitate is both amylolytic and proteolytic, from which it appears probable that some of the ferments of the salivary glands, pancreas, stomach, etc., having done their work, escape from the body by the urine.

7. **Gases.**—Those gases which can be extracted from urine by the mercurial pump are chiefly nitrogen and carbonic acid, oxygen occurring in very small quantities or being wholly absent.

The quantities in which these multifarious constituents are present vary within very wide limits, being dependent on the

nature of the food taken, and on the conditions of the body. These points will be considered in the succeeding chapter. What may be called the average composition of human urine is shown in the following table:

Amounts of the Several Urinary Constituents Passed in Twenty-four Hours. After PARKES.

	By an average man of 66 kilos. Grammes.	Per 1 kilo of body weight. Grammes.
Water	1500.000	23.0000
Total solids	72.000	1.1000
Urea	33.180	0.5000
Uric acid	0.555	0.0084
Hippuric acid	0.400	0.0060
Kreatinin	0.910	0.0140
Pigment and other substances	10.000	0.1510
Sulphuric acid	2.012	0.0305
Phosphoric acid	3.164	0.0480
Chlorine	7.000 (8.21)	0.1260
Ammonia	0.770	
Potassium	2.500	
Sodium	11.090	
Calcium	0.260	
Magnesium	0.207	

Acidity of Urine.—The healthy urine of man is acid, owing to the presence of acid sodium phosphate, the absence of free acid being shown by the fact that sodium hyposulphite gives no precipitate. The amount of acidity is about equivalent to 2 grms. of oxalic acid in twenty-four hours, but the degree of acidity at any one time varies much during the day, being in an inverse ratio to the amount of acid secreted by the stomach; thus it decreases after food is taken, and increases as gastric digestion becomes complete. It varies with the nature of the food; with a vegetable diet the excess of alkalies secreted leads to alkalinity, or at least to diminished acidity, whereas this effect is wanting with an animal diet, in which the earthy bases preponderate. Hence the urine of carnivora is generally very acid, while that of herbivora is alkaline. The latter, when fasting, are for the time being carnivorous, living entirely on their own bodies, and hence their urine becomes under these circumstances acid.

The natural acidity increases for some time after urine has been discharged, owing to the formation of fresh acid, apparently by some kind of fermentation. This increase of acid frequently causes a precipitation of urates, which the previous acidity has been insufficient to throw down. After a while, however, the acid reaction gives way to alkalinity. This is caused by a con-

version of the urea into ammonium carbonate through the
agency of a specific ferment. This ferment as a general rule
does not make its appearance except in urine exposed to the
air; it is only in unhealthy conditions that the fermentation
takes place within the bladder.

Abnormal Constituents of Urine.—The structural elements
found in the urine under various circumstances are blood, pus,
and mucous corpuscles, epithelium from the bladder and kidney,
and spermatozoa. Serum-albumin, fibrin (frequently as "casts"),
alkali-albumin, globulin, a peculiar form of albumin (the so-
called hemi-albumose), fats, cholesterin, sugar, leucin, tyrosin,
oxalic acid, bile acids, and bile pigment, may be enumerated as
the most important metabolic products abnormally present in
urine. Besides these the urine serves as the chief channel of
elimination for various bodies not proper constituents of food,
which may happen to have been taken into the system. Thus
various minerals, alkaloids, salts, pigmentary and odoriferous
matters may be passed unchanged. Many substances thus occa-
sionally taken suffer changes in passing through the body; the
most important of these will be considered in a succeeding
chapter.

Sec. 2.—The Secretion of Urine.

We have already called attention to the fact that the kidney,
unlike the other secreting organs which we have hitherto studied,
consists of two parts so distinct in structure that it seems impos-
sible to resist the conclusion that their functions are different,
and that the mechanism by which the urine is secreted is of a
double kind. On the one hand, the tubuli uriniferi with their
characteristic epithelium seem obviously to be actively secreting
structures comparable to the secreting alveoli of the salivary and
other glands. On the other hand, the Malpighian capsules with
their glomeruli are organs of a peculiar nature with an almost
insignificant epithelium, and their structure irresistibly suggests
that they act rather as a filtering than as a truly secreting
mechanism. Hence, the view put forward by Bowman long ago,
that certain constituents only of the urine are secreted after the
fashion of other secreting glands by the tubuli uriniferi, and that
the rest of the constituents, including a great deal of the water
with such highly soluble and diffusible salts as preëxist in con-
siderable quantity in the blood, are, as it were, filtered by the
glomeruli of the Malpighian capsules. This view is, moreover,
as we shall presently see, supported by direct experimental evi-
dence. Assuming for the present the truth of it, we may remark

that the passage of fluids and dissolved substances through membranes being in large part directly dependent on pressure, the extent and rapidity of that part of the whole process of the secretion of urine which is a kind of filtration will be directly affected by the amount of arterial pressure in the renal arteries, while the effect of variations of arterial pressure on that part of the process which is a real active secretion will be an indirect one only. Hence, the discharge of urine by the kidneys must be to a much greater extent than is the case with the secretion of saliva or of gastric juice a mere matter of pressure; and it will consequently be of advantage to study the relations of urinary secretion to blood-pressure before we enter upon the discussion of the active secretion itself.

The Relation of the Secretion of Urine to Arterial Pressure.

Recent observations have shown experimentally that the kidney is supplied with a vaso-motor mechanism as well developed, perhaps, as that of any other part of the body.

By means of a modification of the plethysmograph, we can readily observe the variations which take place in the volume of the kidney, and the same method can be applied also to other internal organs.

The instrument consists of two parts, one of which (Fig. 156) called by Dr. C. S. Roy, who introduced it, an oncometer,[1] is applied to the organ about to be studied, while the other (Fig. 157), called the oncograph, is the recording part of the apparatus. Any diminution in the volume of the organ (Fig. 156, K), kidney, spleen, etc., as the case may be, diminishes the pressure on the fluid in the chamber a; some of the fluid in the chamber M (Fig. 157) accordingly passes through the tube K and the tube T to the chamber a; the piston D accordingly falls and with it the lever H. Similarly an increase in the volume of the organ causes the lever to rise.

The volume of the kidney may be increased by a swelling of its constituent cells and other structural elements, by an accumulation of lymph in its lymph-spaces and by a distention of its bloodvessels. Compared with the third, the two former causes are in health so insignificant and problematical that they may be disregarded. Further the distention of the bloodvessels will in general depend on the constriction or dilation of the renal arteries and their ramifications, for distention due to venous obstruction will only occur in special cases. Hence variations in the volume of the kidney may be taken as a measure of variations in its vascular supply, increase of volume indicating dilated renal vessels, and decrease of volume indicating constriction of the renal vessels.

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[1] From oncos, bulk.

When, by means of the instrument just described a tracing is taken of the volume of a kidney in what may be considered a normal condition, some such result as that shown in Fig. 158 is obtained.

The volume of the kidney is seen to be so delicately responsive to changes in the mean arterial pressure that the curve

FIG. 156.
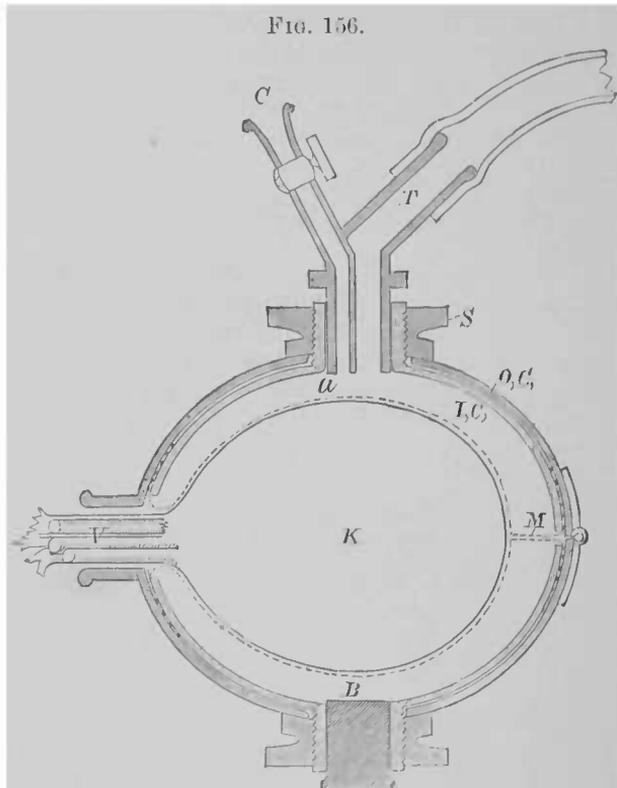
RENAL ONCOMETER.

Seen in section (semi-diagrammatic). *K* kidney, *V* vessels and nerves embedded in fat, etc., entering hilus of organ, *O C* and *I C* outer and inner metal capsules screwed together by the screw *S*, and holding between them the edge of the membrane *M*, which applies itself to the surface of the kidney and forms with the metal capsule two chambers *a* and *B*, one of which (*B*) is closed by a plug filling the opening *B*, while the other (*a*) communicates by a tube *T*, with the recording instrument. The other opening *C* (which is closed by a small tap) is for the purpose of filling the chamber *a* with warm oil, after the kidney has been placed in the box, the other chamber *B* having been previously partly filled, the quantity introduced into it depending upon the size of the kidney.

reproduces almost exactly a blood-pressure curve, showing not only the respiratory undulations, but even the rise and fall due to the individual heart-beats. With each rise of mean arterial

pressure more blood is driven into the renal vessels and the kidney swells; with each fall of pressure less blood enters and

FIG. 157.
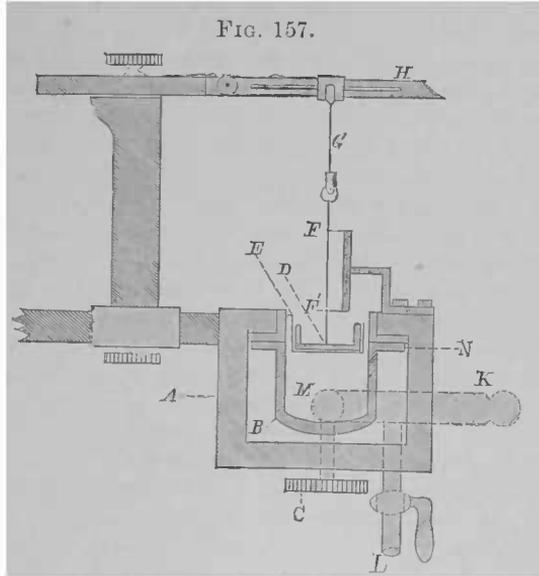
SEMI-DIAGRAMMATIC SECTIONAL VIEW OF ONCOGRAPH. Half natural size.

K tube connecting instrument with oncometer. *D* piston floating on oil contained in the cavity *M*; the oil is prevented from escaping by the side of the piston, by the delicate flexible membrane *E*, which does not interfere with the movements of the piston. *H*, recording lever connected with the piston by a needle *G*, passing through the guides *F*, *F'*. The screw *C* is for the purpose of clamping the edge of the membrane between the two ring-shaped surfaces at *N*, while the side tube *L* is for the purpose of filling the instrument.

FIG. 158.

BLOOD PRESSURE

KIDNEY CURVE

BLOOD-PRESSURE TRACING, AND CURVE FROM RENAL ONCOMETER. Natural size.
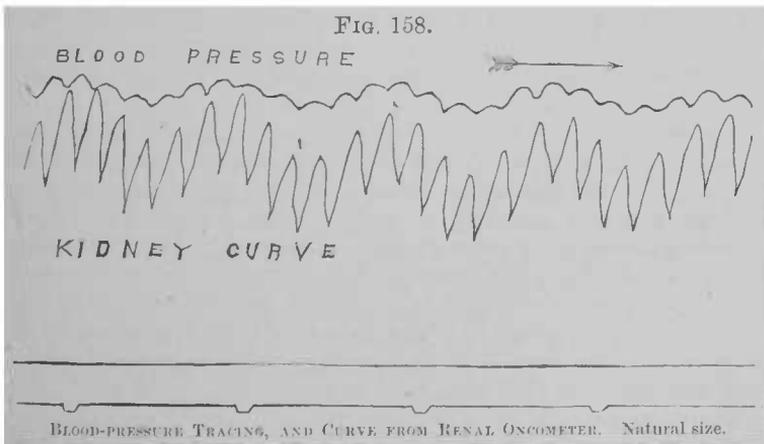
The blood-pressure abscissa line has been raised 2.75 cm. (the actual medium blood-pressure having been 115 mm. Hg.). The time-curve gives interruptions recurring every three seconds,

the kidney shrinks. On other tracings taken in the same way may often be seen the wider variations corresponding to the Traube-Hering curves, but it will be observed that in these the kidney shrinks with the rise of pressure and swells with the fall. For as we have seen (p. 440) the rise in the Traube-Hering undulation is due to an augmentation of peripheral resistance caused by the constriction of minute arteries, and this constriction occurs in the kidney as elsewhere; the renal arterioles take their share in producing the result, and in consequence of their constriction the kidney shrinks. Similarly the relaxation of the renal vessels contributes to bring about the sequent fall.

Other variations in the volume of the kidney are seen to arise from various influences. When respiration is stopped the increasingly venous blood, acting on the medullary or spinal vaso-motor centres, leads to constriction of the renal as well as of other arteries, as shown by the shrinking of the kidney. Stimulation of the medulla oblongata causes a very marked shrinking of the kidney, indicating powerful constriction of its arteries, as does also stimulation of the splanchnic nerve; the effect when the splanchnic on one side is stimulated, frequently affects the kidney on the opposite side as much as that on the same side. Stimulation of a sensory nerve causes shrinking of the kidney, in spite of a rise of mean pressure, which in itself would tend to swell the kidney, taking place at the same time; this is an instance of reflex constriction as that of stimulation of the splanchnic nerve is of direct constriction. A direct constriction may also be brought about by stimulation of the renal nerves. When all the renal nerves are divided (an operation by no means easy), stimulation of nerves in other parts of the body does not cause a constriction but an expansion of the kidney, since it gives rise to an increase of blood-pressure, through which the renal vessels are passively filled to a greater extent.

The same method further shows that the vaso-motor mechanism of the kidney is remarkably sensitive to changes in the chemical constitution of the blood. The injection into the blood of even a small quantity of water causes a shrinking of the kidney followed by a more lasting expansion. The injection of urea and some other diuretics produces the same effect to a more marked degree, while the injection of normal saline solution and especially of such diuretics as sodium acetate causes an expansion from the very first, the primary shrinking being absent. It is, moreover, worthy of note that these effects of diuretics and of chemical changes in blood appear even after all the renal nerves have apparently been completely severed, indicating that these bodies induce vascular changes by acting either upon some

peripheral vaso-motor mechanism, or even more directly, on the bloodvessels themselves. It may be added that they will produce considerable effects in the kidney itself without appreciably modifying the general blood-pressure.

As yet this method has not disclosed any distinct vaso-dilator fibres passing to the kidney from other parts, positive dilation having been observed only as the result of chemical agents. But, even if these prove eventually to be really absent, enough has been said to show that the kidney has an ample and well-developed vaso-motor supply. In many of the observations referred to above, the flow of urine was determined at the same time as the volume of the kidney, by measuring the escape from the ureter of the kidney experimented upon through a canula tied into it. And it was found that unless special causes intervened, expansion of the kidney was accompanied by an increase, and contraction by a decrease in the flow of urine. But before we attempt to illustrate the working of the vaso-motor mechanism just described, it will be as well to call attention to the fact that, as far as filtration is concerned, the chief circumstance of the vascular condition of the kidney which we have to consider is the extent of pressure present in the small vessels of the renal glomeruli. The more the pressure of the blood in these exceeds the pressure of the fluid in the channels of the uriniferous tubules, the more rapid and extensive will be the filtration from the one into the other.

This local blood-pressure in the small vessels of the glomeruli may be *increased :*

1. By an increase of the general blood-pressure, brought about (*a*) by an increased force, frequency, etc., of the heart's beat, (*b*) by the constriction of the small arteries supplying areas other than the kidney itself.

2. By a relaxation of the renal artery, which, as we have previously pointed out (p. 263), while diminishing the pressure in the artery itself, increases the pressure in the capillaries and small veins which the artery supplies. It need hardly be added that this local relaxation must either be accompanied by constriction in other vascular areas, or, at all events, must not be accompanied by a sufficiently compensating dilation elsewhere.

The same local pressure may be similarly *diminished—*

1. By a constriction of the renal artery and its branches, which, while increasing the pressure on the cardiac side of the artery, diminishes the pressure in the capillaries and veins which are supplied by the artery. This again must either be accompanied by dilation in other vascular areas, or at least not accompanied by a compensating constriction.

2. By a lowering of the *general* blood-pressure brought about (*a*) by diminished force, etc., of the heart's beat, (*b*) by a general dilation of the small arteries of the body at large, or by a dilation of vascular areas other than the kidneys.

Bearing these facts in mind, it becomes apparently easy to explain many of the instances in which an increase or diminution of urine is produced by natural or artificial means. Thus, section of the spinal cord below the medulla causes a great diminution, and indeed in many cases a complete or almost complete arrest of the secretion of urine. This operation, as we have seen in discussing the vaso-motor system, leads to a very general vascular dilation, in consequence of which there ensues a great fall of the general blood-pressure. At present it seems uncertain whether the renal arteries really possess a normal tone like that of most other arteries, and we do not know whether they, in consequence of the operation, share in the general dilation. Even if they do, their expansion apparently is insufficient to compensate the great diminution of general blood pressure. It has been stated that the effect of section of the medulla is so marked and constant that when, in the dog, the blood-pressure sinks at least below 30 mm. mercury the secretion of urine is invariably arrested. It would appear, however, that this is not always the case, and that secretion is sometimes observed to continue when the blood-pressure sinks even below this point. Section of the spinal cord in the dorsal region similarly depresses the general blood-pressure and similarly arrests or diminishes the secretion of urine. This is an operation, however, from which an animal may, if duly tended, recover, and live for a long time with the lumbar spinal cord quite separated from the brain and upper parts of the spinal cord. In such a case the secretion of urine is soon reëstablished; but the general blood-pressure is also reëstablished, so that this condition of things also illustrates the connection between blood-pressure and the secretion of urine.

Stimulation of the spinal cord below the medulla, though acting in the converse direction, brings about the same result, arrest of the secretion. By the stimulation the action of the vaso-motor nerves is augmented, and constriction of the renal arteries, as well as of other arteries in the body, is brought about. The increase of general blood-pressure thus produced is insufficient to compensate for the increased resistance in the renal arteries; and, as a consequence, the flow of blood into the glomeruli is largely reduced. We have seen that under these circumstances the kidney shrinks; and, indeed, on inspection it is seen to become during the stimulation pale and bloodless.

Section of the renal nerves is followed by a most copious secre-

tion, by what has been called hydruria or polyuria. The section of the nerves, by interrupting the vaso-motor tracts, even if it does not act in the way of destroying a normal tone (the existence of which seems doubtful), prevents the advent of ordinary constricting impulses, and thus indirectly leads to dilation of the renal arteries, and so to increased pressure in the small vessels of the glomeruli. If, after section of the renal nerves, the cord be divided below the medulla, the polyuria disappears; for the diminution of general blood-pressure thus produced more than compensates for the special dilation of the renal arteries. Conversely, if after section of the renal nerves the cord be stimulated, the flow of urine is still further increased, since the rise of general blood-pressure due to the general arterial constriction caused by the stimulation tends to throw still more blood into the renal arteries, on which, owing to the division of their nerves, the spinal stimulation is powerless. The section of the renal nerves sometimes leads to the appearance of albumin in the urine, but this is probably due to some other effects than those of variations in blood-pressure simply.

Section of the splanchnic nerves produces also an increased flow of urine. But the augmentation in this case is smaller and less certain than in the case of section of the renal nerves themselves, partly because the vaso-motor tracts from the spinal cord to the kidneys do not run exclusively in the splanchnic nerves, but reach the kidney along some other path or paths, and partly because the splanchnic nerves govern the whole splanchnic area, and hence a large portion of the increased supply of blood is diverted from the kidney to other abdominal organs. On the other hand, stimulation of the splanchnic nerves is able to arrest the flow of urine by producing constriction of the renal arteries.

The experimental phenomena recorded above are thus seen to receive a fairly satisfactory explanation when they are referred exclusively to variations in blood-pressure. And many of the natural variations in the flow of urine may be interpreted in the same way. No fact in the animal economy is oftener or more strikingly brought home to us than the correlation of the skin and the kidney as far as their secretions are concerned; and this seems to be, in part at least, maintained by means of the vaso-motor nervous mechanism. Thus, when the skin is cold, its bloodvessels are, as we know, constricted. This, by causing an increase of general blood-pressure, will augment the flow through the kidneys, and conversely, the dilated condition of the arteries of a warm skin, with the consequent diminution of general blood-pressure, will give rise to a diminished renal discharge. It is probable, however, that a more direct connection exists between the skin and the kidneys, so that a warm skin leads to constric-

tion and a cold skin to dilation of the renal vessels; and it is further possible that the one may react on the other in another way, viz., by changes induced in the blood. The effects of emotions may possibly, also, be explained as essentially vaso-motor phenomena.

Secretion by the Renal Epithelium.

While thus recognizing the importance of the relations of the flow of urine to blood-pressure, we must not be led into the error of supposing that the work of the kidney is wholly a matter of filtration. The glomerular mechanism, so specially fitted for filtration, is, after all, a small portion only of the whole kidney, and the epithelium over a large part of the course of the *tubuli uriniferi* bears most distinctly the characters of an active secreting epithelium. These facts would lead us *à priori* to suppose that the flow of urine is in part the result of an active secretion comparable to that of the salivary or other glands which we have already studied. And we have experimental and other evidence that such is the case.

In the first place, a flow of urine may be artificially excited even when the natural flow has been arrested by diminution of blood-pressure. Thus if, when the urine has ceased to flow in consequence of a section of the medulla oblongata, certain substances, such as urea, sodium acetate, etc., be injected into the blood, a more or less copious secretion is at once set up. This secretion is, or at least may be, unaccompanied by any rise of blood-pressure sufficient to account for the flow on the filtration hypothesis. A very similar result is illustrated by the common experience that the flow of urine is largely increased after taking fluids, especially in large quantities. We cannot explain this by a reference to blood-pressure, since we have seen (p. 271) that the quantity of blood may be increased largely without raising the blood-pressure. On the other hand, observations with the oncometer have shown us that the kidney is remarkably sensitive to changes in the chemical constitution of the blood, an expansion, preceded or not by a passing constriction, being caused by the injection into the blood of even small quantities of water, sodium chloride, and other substances. We have further seen that the expansion of the kidney, or rather the dilation of the renal vessels which is the cause of that expansion, brought about in this way, is dependent on a local peripheral action of some kind or other, since it will take place after complete severance of all the renal nerves. It is, of course, open for us to suppose that this very dilation of the renal vessels is the cause of the increased flow at the same time, since, the general blood-pressure remain-

ing the same, it will lead to increased pressure in the glomeruli. So that the activity of the kidney which follows upon food and drink, or upon the injection of urea and other substances into the blood, may be taken as really illustrating the dependence of the flow of urine on blood-pressure, though the vascular mechanism concerned is limited to the kidney itself and variations of the general blood-pressure play no part in the matter. But it is also open for us to suppose that the presence of these substances in the blood excites the renal epithelium cells to an unwonted activity, causing them to pour into the interior of the tubules a copious secretion, just as the presence of pilocarpin in the blood will cause the salivary cells to pour forth their secretion into the lumen of their ducts; and that this activity of the epithelium cells is accompanied, also, as in the case of the submaxillary and other glands, by a vascular dilation which, though adjuvant and beneficial, is not the distinct cause of the activity. That this latter view is probably the true one, is shown by the following remarkable experiment, from which we learn that of the various substances finding their way into the blood, some pass into the urine through the glomeruli, while others are distinctly secreted by the tubuli uriniferi, their discharge being accompanied by an activity of the secreting cells indicated by the flow of water taking place at the same time.

In the amphibia, the kidney has a double vascular supply: it receives arterial blood from the renal artery, but there is also poured into it venous blood from another source. The femoral vein divides at the top of the thigh into two branches, one of which runs along the front of the abdomen to meet its fellow in the middle line and form the anterior abdominal vein, while the other passes to the outer border of the kidney and branches in the substance of that organ, forming the so-called renal portal system. Now the glomeruli are supplied exclusively by the branches of the renal artery, the renal vena portæ only serving to form the capillary plexus around the tubuli uriniferi, which is also supplied by the efferent vessels of the glomeruli. From this it is obvious that if the renal artery be tied, the blood is shut off entirely from the glomeruli, actual observation of the kidney of the newt having shown that under these circumstances there is no reflux from the capillary network surrounding the tubules back to the glomeruli; thus the kidney by this simple operation is transformed into an ordinary secreting gland devoid of any special filtering mechanism. We owe to Nussbaum the ingenious use of such a kidney to ascertain what substances are excreted by the glomeruli, and what by the tubules in some other part of their course. It is found that sugar and peptones, which injected into the blood readily pass through the untouched kidney and

appear in the urine, do not pass through a kidney the renal arteries of which have been tied. These substances, therefore, are excreted by the glomeruli. Urea, on the other hand, injected into the blood, gives rise to a secretion of urine, when the renal arteries are tied; this substance, therefore, is secreted by the epithelium of the tubules, and in being so secreted gives rise at the same time to a flow of water through the cells into the interior of the tubules.

Additional evidence in favor of the activity of the epithelium cells is afforded by an observation for which we are indebted to Heidenhain. Into the veins of animals in which the urinary flow had been arrested by section of the spinal cord below the medulla, this observer injected a quantity of coloring material known as sodium sulphindigotate.[1] By killing the animals at appropriate times after the injection of the material and examining the kidneys microscopically and otherwise, he was enabled to ascertain that the pigment so injected passed from the blood into the renal epithelium, and thence into the channels of the tubules, where it was precipitated in a solid form. There being no stream of fluid through the tubules, owing to the arrest of urinary flow by means of the preliminary operation, the pigment travelled very little way down the interior of the tubules, and remained very much where it was cast out by the epithelium cells. There were no traces whatever of the pigment having passed by the glomeruli; and the cells which could be seen distinctly to take up and eject it, were those lining such portions of the tubules (viz., the so-called secreting tubules, intercalated tubules and portions of the loops of Henle) as from their microscopic features have been supposed to be the actively secreting portions of the entire tubules. By varying the quantity injected and the time which was allowed to elapse between the injection and subsequent inspection, Heidenhain was able to trace the material step by step into the cells, out of the cells into the interior of the tubules, and for some little distance along the tubules. The advantage of the absence of a large flow of urine is obvious; had this been present, the pigment immediately that it issued from the cells would have been rapidly washed away down the channels of the tubules. One observation he made of a peculiarly interesting character. After injecting a certain quantity of pigment, and allowing such a time to elapse as he knew from previous experiments would suffice for the passage of the material through the epithelium to be pretty well completed, he injected a second quantity. He found that the excretion of

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[1] Sometimes called indigo-carmine, though this name is more properly applied to a crude impure preparation of potassium sulphindigotate.

this second quantity was most incomplete and imperfect. It seemed as if the cells were exhausted by their previous efforts, just as a muscle which has been severely tetanized will not respond to a renewed stimulation.

This observation may be objected to on the ground that this coloring matter does not occur as a constituent of the blood either in health or disease, and especially that the absence of any concomitant discharge of fluid from the cells excites suspicion that the process observed was not really one of secretion, for the injection of such substances as urea or urates into the blood does cause a copious flow of fluid, and indeed thus prevents the microscopic tracking out of their passage, which in the case of urates might be done much in the same way as with the sodium sulphindigotate. Moreover, other observers have maintained that the sodium sulphindigotate does, like ordinary carmine, pass through the glomeruli, but in the case of the amphibian kidney when sodium sulphindigotate is injected after ligature of renal arteries, no urine is found in the bladder, but the pigment can be traced through the epithelium of the secreting portions of the tubuli. Without insisting too much on the value of the sodium sulphindigotate experiments, they may be taken as fairly supporting the view we are considering.

Experimental evidence then justifies the conception which the structure of the kidney led us to adopt. The secretion of urine by the kidney is a double process. It is partly a process of filtration, whose object is to remove as rapidly as possible a quantity of water from the body, and this part of the work of the kidney is directly dependent on blood-pressure. It is also, however, a process of active secretion by the epithelium of the tubuli, and this part of the work of the kidney is, in an indirect manner only, dependent on blood-pressure. Both processes may give rise to a discharge of water from the blood, and both may give rise to the presence of the solid constituents of the urine, in solution in that water. In the first process the discharge of water is the primary object, and the solid matters which escape at the same time are of secondary importance; in the second process the excretion of the solid substance is the primary object, and the accompanying water of secondary importance. The first process is governed (mainly at least) by the vaso-motor nervous system; the second process is excited, as far as we know at present, by substances in the blood acting directly as chemical stimuli to the epithelium, but future researches may disclose the existence of a secretory nervous mechanism analogous to that of other secretory glands. It must also be left for further inquiries to determine exactly which of the two processes, or to what relative extent each of them, is concerned in

bringing about the presence in the urine of its several constituents.

In one respect the kidney as a secreting organ differs markedly from such a gland as the salivary. In the case of the latter, we have seen that the saliva as it flows may cause a pressure in the duct greater than the mean arterial pressure; in the case of the former when a manometer is connected with a canula tied into the ureter of a dog, the mercury may rise to 60 mm., but not much beyond, and often becomes stationary at a lower level, showing that the urine cannot be secreted at a pressure greater than that probably obtaining in the renal vessels; or, at least, if secretion does take place it is counterbalanced by an absorption taking place at the same time. But in this respect the kidney has its fellow in another secreting organ, the liver, for in this, as we have seen, the secretion of bile is arrested when the pressure is raised too high.

One or two words of caution are necessary. In speaking of the glomerulus as a filtering apparatus, it must not be understood that it is thereby really compared to an ordinary filter made of dead material, and that when filtration through it is spoken of, a process exactly like that which takes place in the laboratory is meant. In the glomerulus the elements of the blood have to pass through the living wall of the capillary, and the covering layer of epithelium cells, and the transit must be affected by the condition of these living structures. By virtue of their constitution they allow certain things to pass and not others, and when they become changed the passage of material is changed also. The possible influence of a mere layer of squamous epithelium is shown by experiments on the cornea, which acts absolutely differently as a filter according as the epithelium of Descemet is retained or removed, and in speaking of the circulation we dwelt on the importance of the physiological condition of the capillary walls. The nature of the filtration taking place through the glomerulus will depend therefore on the condition of the capillary walls and their epithelial investment. This is illustrated by the phenomena of albuminuria (or the passage of albumin into the urine), especially as seen in the following interesting experiment by Nussbaum on the artificial production of albuminuria in the frog. The renal arteries being tied, an injection of urea (1 cm. of a 10 per cent. solution) into the blood gave rise to a flow of urine which was free from albumin. Upon loosing the ligatures so as to reëstablish the flow of blood through the glomeruli, the urine at once became albuminous. The arrest of the circulation through the glomeruli had damaged the capillary walls, and so allowed the passage through them into the interior of the Malpighian capsules of

the natural proteids of the blood, which in a normal condition of the capillaries cannot effect such a passage. The injury, however, was temporary only; in a short time the capillary walls were restored to health, and the urine ceased to be albuminous.

We may further quote as showing the peculiar nature of the filtration that ligature of the renal veins arrests the secretion of urine. Apparently the effect which it should produce by increasing the pressure in the glomeruli is more than counterbalanced by other influences. Upon removal of the ligatures, the urine is usually albuminous, showing that in the interval the glomeruli have become changed.

One consideration, of quite secondary importance in the glands which have been previously studied, acquires great prominence when the kidney is being studied. In studying the pancreas and gastric glands, we concluded without much discussion that the zymogen and pepsinogen were formed in the epithelium cells; for no great manufacture of these substances is going on in other parts of the body. The kidney, however, is emphatically an excreting organ: its great function is to get rid of substances produced by the activity of other tissues; its work is not to form but to eject. There can be no doubt, to put forward a strong instance, that with regard to urea it would be absurd to suppose that the whole series of changes from the proteid condition to the urea stage is carried on by the kidney. But there still remains the question, Are any of the stages carried on in the kidney, and if so, what? Is the secreting activity of the renal epithelium confined to picking out the already formed urea from the blood? Or does the secreting cell of the tubule receive from the blood some antecedent of urea, and in the laboratory of its protoplasm convert that antecedent of urea into urea itself? and, if so, what is that antecedent which comes to the kidney in the blood of the renal artery? And so with many other of the urinary constituents.

In order to complete our study of renal activity, this question ought to be considered now; but for many reasons it will be more convenient to defer the matter to the succeeding chapter, in which we deal with the metabolic events of the body in general.

SEC. 3.—MICTURITION.

The urine, like the bile, is secreted continuously; the flow may rise and fall, but, in health, never absolutely ceases for any length of time. The cessation of renal activity, the so-called suppression of urine, entails speedy death. The minute streams passing con-

tinuously, now more rapidly now more slowly, along the collecting and discharging tubules, are gathered into the renal pelvis, whence the fluid is carried along the ureters partly by pressure and gravity and partly by the peristaltic contractions of the muscular walls of those channels (see p. 133) into the urinary bladder. When a ureter is divided in an animal, and a canula inserted, the urine may be observed to flow from the canula drop by drop, slowly or rapidly, according to the rate of secretion. Frequently, after a series of single drops at long intervals, several drops follow in rapid succession, apparently urged by a peristaltic wave. In the urinary bladder, the urine is collected, its return into the ureters being prevented by the oblique entrance into the bladder and valvular nature of the orifices of those tubes ; and its discharge thence in considerable quantity is effected from time to time by a somewhat complex muscular mechanism, of the nature and working of which the following is a brief account.

The involuntary muscular fibres forming the greater part of the vesical walls are arranged partly in a more or less longitudinal direction forming the so-called detrusor urinæ, and partly in a circular manner, the circular fibres being most developed round the neck of the bladder and forming there the so-called sphincter vesicæ. After it has been emptied, the bladder is contracted and thrown into folds ; as the urine gradually collects, the bladder becomes more and more distended. The escape of the fluid is, however, prevented by the resistance offered by the elastic fibres of the urethra, which keep the urethra channel closed. Some maintain that a tonic contraction of the sphincter vesicæ aids in, or indeed is the chief cause of, this retention. The continuity of the sphincter vesicæ with the rest of the circular fibres of the bladder suggests that it probably is not a sphincter, but that its use lies in its contracting after the rest of the vesical fibres, and thus finishing the evacuation of the bladder. On the other hand, the fact that the neck of the bladder can withstand a pressure of twenty inches of water so long as the bladder is governed by an intact spinal cord, but a pressure of six inches only when the lumbar spinal cord is destroyed or the vesical nerves are severed, affords very strong evidence in favor of the view that the obstruction at the neck of the bladder to the exit of urine depends on some tonic muscular contraction maintained by a reflex or automatic action of the lumbar spinal cord.

When the bladder has become full, we feel the need of making water, the sensation being heightened if not caused by the trickling of a few drops of urine from the full bladder into the urethra. We are, then, conscious of an effort ; during this effort the bladder is thrown into a long-continued contraction of an obscurely peri-

staltic nature, the force of which is more than sufficient to over-
come the elastic resistance of the urethra, and the urine issues in
a stream, the sphincter vesicæ, if it act as a sphincter, being at
the same time either relaxed after the fashion of the sphincter
ani, or at least overcome.   In its passage along the urethra, the
exit of the urine is forwarded by irregularly rhythmic contrac-
tions of the bulbo-cavernosus or ejaculator urinæ muscle, and the
whole act is further assisted by pressure on the bladder exerted
by means of the abdominal muscles, very much the same as in
defecation.

We said, just now, " when the bladder has become full," but
this must not be understood to mean, " when the bladder has
received a certain quantity of fluid."   On the contrary, it is a
matter of common experience that we feel the desire to make
water sometimes when a large quantity and sometimes when a
small quantity of urine has accumulated in the bladder.   We
have evidence that the bladder possesses to a very high degree
that obscure continuous contraction which we speak of as "tone;"
and, further, that the amount of its tone is exceedingly variable,
the organ, quite independently of distinct efforts at micturition,
being at one time contracted and at another flaccid and distended.
When it is in a contracted state, a small quantity of fluid may
exert the same pressure on the vesical walls as a larger quantity
when the bladder is flaccid.   Hence, the determining cause of
the desire to make water is the pressure of the urine upon the
vesical walls, the quantity needed to produce fulness being de-
pendent on the amount of tonic contraction of the muscular
fibres existing at the time.

Micturition as sketched above seems at first sight, and espe-
cially when we appeal to our own consciousness, a purely volun-
tary act.   A voluntary effort throws the bladder into contrac-
tions, an accompanying voluntary effort throws the ejaculator
and abdominal muscles also into contractions, and, the resistance
of the urethra being thereby overcome, the exit of the urine
naturally follows.   If we adopt the view of a sphincter vesicæ
being relaxed at the same time, we have to add to the above
simple statement the supposition that the will, while causing the
detrusor urinæ to contract, also lessens the tone of the sphincter,
probably by inhibiting its centre in the lumbar cord.

There are facts, however, which prevent the acceptance of so
simple a view.   In the first place, in cases of urethral obstruc-
tion, where the bladder cannot be emptied when it reaches its
accustomed fulness, the increasing distention sets up fruitless but
powerful contractions of the vesical walls, contractions which are
clearly involuntary in nature, which wane or disappear, and
return again and again in a rhythmic manner, and which may

be so strong and powerful as to cause great suffering. It seems that the fibres of the bladder, like all other muscular fibres, have their contractions augmented in proportion as they are subjected to tension. Just as a previously quiescent ventricle of a frog's heart may be excited to a rhythmic beat by distending its cavity with blood, so the quiescent bladder may, quite independent of the will, be excited, by the distention of its cavity, to a peristaltic action which in normal cases is never carried beyond a first effort, since with that the bladder is emptied and the stimulus is removed, but which in cases of obstruction is enabled clearly to manifest its rhythmic nature.

In the second place, it has been shown that quite normal micturition may take place in a dog in which the lumbar region of the spinal cord has been completely and permanently separated by section from the dorsal region. In such a case there can be no exercise of volition, and the whole process appears as a reflex action. When under these circumstances the bladder becomes full (and otherwise apparently the act fails) and slight stimulus, such as sponging the anus or slight pressure on the abdominal walls, causes a complete act of micturition; the bladder is entirely emptied, and the stream of urine towards the end of the act undergoes rhythmical augmentations due to contractions of the ejaculator urinæ. These facts can only be interpreted on the view that there exists in the lumbar cord (of the dog) what we may speak of as a micturition centre capable of being thrown into action by appropriate afferent impulses, the action of the centre being such as to cause a contraction of the walls of the bladder and of the ejaculator urinæ, and possibly at the same time to suspend the tone of the sphincter vesicæ.

Moreover, we have, in the case both of man and of other animals, experimental and other evidence that contraction of the bladder is frequently brought about by reflex action. Thus the pressure within the bladder when observed for any length of time is found to be subject to considerable and manifold variations. Over and above passive changes in pressure due to the respiratory movements, when the bladder is pressed upon at each descent of the diaphragm, active contractions, of a strength inadequate to bring about micturition, are from time to time observed. These in some instances appear to be spontaneous, or be the result of emotions, but they may be readily induced in a reflex manner, by stimulating various sentient surfaces or sensory nerves. And common experience affords many instances where vesical contractions thus brought about in a reflex manner acquire strength adequate to empty the bladder.

Observations of vesical pressure may be most conveniently carried out by introducing into the bladder a catheter connected either with an

oncograph, or some other similar registering apparatus, so arranged as to allow fluid to be driven into or received from the bladder at pleasure.

Involuntary micturition obviously of reflex nature has frequently been observed in cases of paralysis from disease or injury of the spinal cord ; and the involuntary micturition which is common in children, as the result of irritation of the pelvis and genital organs, and which sometimes occurs in the adult as the result of emotions, or at least sensory impressions, appears to be the result of reflex action. In these several cases we may fairly suppose that the centre in the lumbar cord is affected by afferent impulses reaching it along various sensory nerves or descending from the brain. Hence, we are led to the conception that when we make water by a conscious effort of the will, what occurs is not a direct action of the will on the muscular walls of the bladder, but that impulses started by the will descend from the brain after the fashion of afferent impulses and thus in a reflex manner throw into action the micturition centre in the lumbar spinal cord. Nor is this view negatived by the fact that paralysis of the bladder, or rather inability to make water either voluntarily or in a reflex manner, is a common symptom of cerebral or spinal disease or injury. Putting aside the cases in which the reflex act is not called forth because the appropriate stimulus has not been applied, the failure in micturition under these circumstances may be explained by supposing that the shock of the spinal injury or some extension of the disease has rendered the lumbar centre unable to act.

The so-called incontinence of urine in children is simply an easily excited and frequently repeated reflex micturition. In cases of cerebral or spinal disease a form of incontinence is frequently met with which seems to be of a different nature. The bladder becoming full, but, owing to a failure in the mechanism of voluntary or reflex micturition, being unable to empty itself by a complete contraction, a continual dribbling of urine takes place through the urethra, the fulness of the bladder being sufficient to overcome the elastic resistance at the neck of the urethra. It is probable, however, that even in these cases the flow is partly caused by obscure, unfelt, intrinsic contractions of the bladder.

CHAPTER V

THE METABOLIC PHENOMENA OF THE BODY.

WE have followed the food through its changes in the alimentary canal, and have seen it enter into the blood, either directly or by the intermediate channel of the lacteals, in the form of peptone (or otherwise modified albumen), sugar (lactic acid), and fats, accompanied by various salts. We have further seen that the waste products which leave the body are urea, carbonic acid, and salts. We have now to attempt to connect together the food and the waste products; to trace out, as far as we are able, the various steps by which the one is transformed into the other, and to inquire into the manner in which the energy set free in this transformation is distributed and made use of.

The master tissues of the body are the muscular and nervous tissues; all the other tissues may be regarded as the servants of these. And we may fairly presume that, besides the digestive and excretory tissues which we have already studied, many parts of the body are engaged either in further elaborating the comparatively raw food which enters the blood, in order that it may be assimilated with the least possible labor by the master tissues, or in so modifying the waste products which arise from the activity of the master tissues that they may be removed from the body as speedily as possible. There can be no doubt that manifold intermediate changes of this kind do take place in the body; but our knowledge of the matter is at present very imperfect. In one or two instances only can we localize these metabolic actions and speak of distinct metabolic tissues. In the majority of cases we can only trace out or infer chemical changes, without being able to say more than that they do take place somewhere; and in consequence, perhaps somewhat loosely, speak of them as taking place in the blood.

SEC. 1.—METABOLIC TISSUES.

The History of Glycogen.

The best known and most carefully studied example of metabolic activity is the formation of glycogen in the hepatic cells.

Claude Bernard, in studying the history of sugar in the economy, was led to compare the relative quantities of sugar in

the portal and hepatic veins, expecting to find that the sugar possibly diminished during the passage of the blood through the liver; he was astonished to discover that, on the contrary, the quantity appeared to be greatly increased. He found, and anyone can make the observation, that when an animal living under ordinary conditions is killed, the hepatic blood after death contains a considerable amount of sugar (grape-sugar), even when there is little or none in the portal blood; moreover, a simple aqueous infusion of the liver is rich in sugar. Not only so, but the sugar continues to be present in the liver when all blood has been washed out of the organ by a stream of water driven through the portal vein, and goes on increasing in amount for some hours after death. Only one interpretation of these facts is possible; so far from the liver destroying or converting the sugar brought to it by the portal vein, it is clearly a source of sugar; the hepatic tissue evidently contains some substance capable of giving rise to the presence of sugar. Bernard further found that when the liver was removed from the body immediately after death, and, after being divided into small pieces, was thrown into boiling water, the infusion or decoction contained very little sugar, and that the small quantity which was present did not increase even when the decoction was allowed to stand for some time. The decoction, however, was peculiarly opalescent, indeed milky in appearance, whereas the decoction of a liver which had been allowed to remain exposed to the warmth for some time after death, before being boiled, and which accordingly contained a large amount of sugar, was quite clear. On adding saliva, or other amylolytic ferment, to the opalescent, sugarless, or nearly sugarless, decoction and exposing it to a gentle warmth ($35°-40°$), the opalescence disappeared; the fluid became clear, and was then found to contain a considerable quantity of sugar. Here, again, the explanation was obvious. The opalescence of the decoction of boiled liver is due to the presence of a body which is capable of being converted by the action of a ferment into sugar, and is therefore of the nature of starch. At the moment of death the liver must contain a considerable quantity of this substance, which after death becomes gradually converted into sugar, either through the action of some amylolytic ferment present in the hepatic cells or in the blood of the hepatic vessels or possibly by some special agency. Hence the *post-mortem* appearance of a continually increasing quantity of sugar. By precipitating the opalescent decoction with alcohol, by boiling the precipitate with alcohol containing potash, whereby the proteid impurities clinging to it were destroyed, and by removing adherent fats by ether, Bernard was able to obtain this sugar-producing or glycogenic substance in a

pure state as a white amorphous powder, with a composition of $C_6H_{10}O_5$, and, therefore, evidently a kind of starch. Its most striking differences from ordinary starch were that it gave a deep red and not a blue color with iodine, and that when dissolved in water it formed a milky fluid. He gave to it the name of *glycogen*.

Since Bernard's discovery glycogen has been recognized as a normal constituent, variable in quantity, of hepatic tissue both in vertebrate and invertebrate animals. That it is present in the hepatic cells, and not simply contained in the hepatic blood, is shown by the fact that it remains in the liver after all blood has been washed out of that organ. It has also been found in muscle, of which indeed it is almost a constant constituent, in the placenta, white corpuscles, testes, brain, and in other parts of the body; the tissues of the embryo at an early stage, especially before the liver has become functionally active, are particularly rich in it.

We have some reasons for thinking that there are several varieties of glycogen, and that the glycogen which exists in muscle is not quite identical with that which occurs in the liver. Indeed there seem to be intermediate stages between glycogen and starch or dextrin. The physiological value of these differences has not yet, however, been clearly determined, and, with this caution, we shall in the discussions which follow, speak of glycogen as a single substance.

Formation and Uses of Glycogen.—The amount of glycogen present in the liver of an animal at any one time is largely dependent on the amount and nature of the food previously taken. When all food is withheld from an animal, the glycogen in the liver diminishes, rapidly at first, but more slowly afterwards. Even after some days' starvation a small quantity is frequently still found, but in rabbits, at all events, the whole may eventually disappear.

If an animal, after having been starved until its liver may be assumed to be free, or almost free from glycogen, be fed on a diet rich in carbohydrates or on one consisting exclusively of carbohydrates, the liver will in a short time be found to contain a very large quantity of glycogen. Obviously the presence of carbohydrates in food leads to an accumulation of glycogen in the liver, and this is true both of starch and of dextrin, and of the various forms of sugar, cane, grape, and milk sugar. The effect may be quite a rapid one, for glycogen has been found in the liver in considerable quantity within a few hours after the introduction of sugar into the alimentary canal of a starving animal.

If an animal similarly starved, be fed on an exclusively meat diet, a certain amount of glycogen is found in the liver. This appears to be especially the case with dogs (probably with other carnivorous animals also), and in his earlier researches Bernard was led to regard the constant presence of glycogen in the livers of dogs fed on meat, as an important indication of the conversion within the body of nitrogenous into non-nitrogenous material. But in the first place, the quantity of glycogen thus stored up in the liver as the result of a meat diet is much less than that which follows upon a carbohydrate diet; and in the second place, ordinary meat, especially horseflesh, on which dogs are ordinarily fed, contains in itself a certain amount either of glycogen or some form of sugar. Moreover, when animals are fed not on meat, but on purified proteid, such as fibrin, casein or albumin, the quantity of glycogen in the liver becomes still smaller, though according to most observers remaining greater than during starvation. We may infer, therefore, that part of the glycogen which appears in the liver after a meat diet is really due to carbohydrate materials present in the meat. Part, however, would appear to be the result of the actual proteid food, and we have similar evidence that gelatine taken as food leads to the formation of some glycogen in the liver. But in this respect these nitrogenous substances fall very far short indeed of carbohydrate material.

With regard to fats, all observers are agreed that these lead to no accumulation of glycogen in the liver; an animal fed on an exclusively fatty diet has no more glycogen in its liver than a starving animal.

Hence of the three great classes of food-stuffs the carbohydrates stand out prominently as the substances which taken as food lead to an accumulation of glycogen in the liver. As far as we know at present, the glycogen which thus appears in the liver as the result of feeding either with any of the various forms of carbohydrates, or with proteids, or with other substances, is of the same kind and presents the same characters; at least we have no evidence to the contrary.

The question naturally arises, What is the use and purpose of this hepatic glycogen? What ultimately becomes of the glycogen thus for a while stored up in the liver?

One view which has been put forward is as follows. We have evidence, as we shall presently learn, that a great deal of the fat of the body is not taken as such in the food, but is constructed anew in the body out of other substances. Both carbohydrates and proteids, taken in excess or under certain circumstances, lead to an accumulation of fat, and we have reason to believe that carbohydrates on the one hand and the carbon-holding

portions of various proteids, may by some process or other be converted into fat.   And it has been suggested that the glycogen in the liver is a phase of a constructive fatty metabolism, that it is material on its way to become fat.

The positive evidence in favor of this view is very scanty ; it is almost limited to the facts that fat, sometimes in very large quantity, is found in the hepatic cells, that while fat itself taken as food leads to no increase in the hepatic glycogen, carbo-hydrates, which are especially fattening, are most active pro-ducers of glycogen, and that the fat present in the hepatic cells seems to be increased by such diets as naturally increase the glycogen in the liver.   No evidence has been offered as to the several steps of the conversion of glycogen into fat, nor indeed has it been suggested what those steps are.   The view indeed is almost exclusively based on the supposed proof that the blood of the hepatic vein contains during life no sugar, or at least not more than does the general blood or even the blood of the portal vein.   From this it is inferred that the glycogen in the liver is not lost to the liver by becoming converted into sugar and so discharged into the hepatic blood, and therefore must be con-verted into some other substance, which substance is presumably fat.   Bernard, both in his earlier and later researches, maintained that the blood of the hepatic vein under normal conditions is richer in sugar than the blood of the portal vein or indeed of any other part of the vascular system ; this he regarded as an indication that the liver is always engaged in discharging a certain quantity of sugar into the hepatic veins ; and his views have been accepted by many observers.   On the other hand, others maintain that the blood in the hepatic vein, if care be taken to keep the animal in a perfectly normal condition, con-tains no more sugar than does the blood of the right auricle or of the portal vein, and indeed that the liver, itself, if examined before *any* post-mortem changes have had time to develop them-selves, is absolutely free from sugar.

Normal hepatic blood was obtained by Pavy, by means of an ingeni-ous catheterization.   He introduced through the jugular vein, into the superior, and so into the inferior vena cava, a long catheter, constructed in such a manner that he could at pleasure plug up the vena cava below the embouchement of the hepatic veins, and draw blood exclusively from the latter, or *vice versâ*.

Now the quantitative determination of sugar in blood by any of the methods as yet suggested is open to many sources of error. And when the quantity of blood which is continually flowing through the liver is taken under consideration, it is obvious that an amount of sugar, which in the specimen of blood taken for

examination fell within the limits of errors of observation, might when multiplied by the whole quantity of blood, and by the number of times the blood passed through the liver in a certain time, reach dimensions quite sufficient to account for the conversion into sugar of the whole of the glycogen present in the liver at any given time. Hence we may safely conclude that the comparative analysis of hepatic and portal blood, if they do not of themselves prove that the liver is either continually or at intervals converting some of its glycogen into sugar and discharging this sugar into the general system, are at least not sufficiently trustworthy to disprove the possibility of such a discharge of sugar being one of the normal functions of the liver.

We may therefore regard the view that glycogen is simply a stage of the formation of fat as not proved; and indeed we shall presently see reason to believe that fat is formed elsewhere.

Another view makes use of the formation of fat for the purposes of analogy only. Seeing that adipose tissue serves as a storehouse of fat which is not wanted by the body at the moment, but may be wanted presently, the question readily presents itself, May not the hepatic glycogen have an analogous function? May we not regard the presence of glycogen in the liver as in a large measure due to the fact that it is deposited there simply as a store of carbohydrate material, being accumulated whenever amylaceous material is abundant in the alimentary canal and being converted into sugar and so drawn upon by the body at large to meet the general demands for carbohydrate material during the intervals when food is not being taken? And we can accept this view without being able to say definitely what becomes of the sugar thus thrown into the hepatic blood. Bernard believed that this sugar underwent an immediate and direct oxidation, but we have already dwelt (p. 417) on the objections to such a view. It is sufficient for us at the present to admit that the sugar is made use of in some way or other.

Now, many considerations lead us to believe that a certain average composition is necessary for that great internal medium the blood, in order that the several tissues may thrive upon it to the best advantage, one element of that composition being a certain percentage of sugar. It would appear that some at least, if not all, of the tissues are continually drawing upon the blood for sugar, and that hence a certain supply must be kept up to meet this demand. On the other hand, an excess of sugar in the blood itself would be injurious to the tissues. And, as a matter of fact, we find the quantity of sugar in blood is small but constant; it remains about the same when food is being taken as in the intervals between meals. If sugar be injected into the jugular

vein in too large quantities or too rapidly, a certain quantity appears in the urine, indicating an effort of the system to throw off the excess and so bring back the blood to its average condition. The maintenance of such a constant percentage of sugar would obviously be provided for, or at least largely assisted by the liver acting as a structure, where the sugar might at once and without much labor be packed away in the form of the less soluble glycogen, at those times when, as during an amylaceous meal, sugar is rapidly passing into the blood, and there is a danger of the blood becoming loaded with far more sugar than is needed for the time being; and it may be incidentally noted that a larger quantity of sugar may be injected into the portal than into the jugular vein without any reappearing in the urine, apparently because a large portion of it is in such a case retained in the liver as glycogen. When, on the other hand, sugar ceases to pass into the blood from the alimentary canal, we may suppose that the average percentage in the blood is maintained by the glycogen previously stored up becoming reconverted into sugar, and slowly discharged into the hepatic blood.

Moreover, this view, that the glycogen of the liver is a reserve fund of carbohydrate material, is strongly supported by the analogy of the migration of starch in the vegetable kingdom. We know that the starch of the leaves of a plant, whether itself having previously passed through a glucose stage or not, is normally converted into sugar, and carried down to the roots or other parts, where it frequently becomes once more changed back again into starch.

A similar argument may be drawn from the relations of glycogen to muscle; that is to say, the glycogen in the muscle may be regarded as a subsidiary store of carbohydrate material laid up for the private use, so to speak, of the muscle. So frequently is glycogen found in muscle, that it may be regarded as an ordinary though not an invariable constituent of that tissue; indeed, it may almost be considered as a constituent of all contractile tissues. The quantity varies very largely both in the different muscles of the same animal and in corresponding muscles of different animals. It disappears readily upon starvation, even before the hepatic glycogen is exhausted; at least this is the case with most muscles. It is said to be increased in quantity when the nerve of the muscle is divided, and the muscle thus brought into a state of quiescence. On the other hand, it diminishes or even disappears when the muscle enters into rigor mortis. Some have maintained that it diminishes during tetanus, but this appears doubtful; and certainly muscles may be fully alive and contractile from which glycogen is wholly absent. From this we may infer, not that glycogen is a necessary chemical factor of

muscular metabolism, but that it can furnish materials for that metabolism, and hence is stored up in the muscle so as to be ready at hand for use.

Accepting, then, the view that the hepatic glycogen is simply store glycogen, waiting to be converted into sugar little by little as the needs of the economy demand, and not glycogen on its way to take part, through the agency of the hepatic protoplasm, in the formation of some more complex compound, such as fat, we have next to deal with the question, What is the exact origin of the hepatic glycogen? By what steps is it formed and what are its immediate antecedents? We have already seen that the presence of glycogen in the liver is especially favored by a carbohydrate diet. Hence, if the use of the glycogen be such as we have supposed, it seems only reasonable to conclude that the glycogen which makes its appearance in the liver after an amylaceous meal arises from a direct conversion of the sugar carried to the liver by the portal vein, the sugar becoming through some action of the hepatic protoplasm dehydrated into starch, by a process the reverse of that by which in the alimentary canal starch is hydrated into sugar through the action of the salivary and pancreatic ferments. Vegetable protoplasm can undoubtedly convert both starch into sugar and sugar into starch; and there are no *à priori* arguments or positive facts which would lead us to suppose that the activity of animal protoplasm cannot accomplish the latter as well as the former of these changes. Again, as we have incidentally mentioned, sugar injected into the jugular vein readily gives rise to sugar in the urine; but a very considerable quantity can be slowly injected into the portal vein without any appearing in the urine. This suggests the idea that the liver, so to speak, catches the sugar as it is passing through the hepatic capillaries, and at once dehydrates it into glycogen.

Upon such a view, the carbohydrate taken as food would be converted in glycogen by the agency of the hepatic cell, without at any time becoming an integral part of the protoplasm of the cell. Such a view may be the true one; but it is open for us to look at the matter in another light. We may conceive of the hepatic cells as being continually engaged in giving rise to carbohydrate material, in the form either of sugar or of some other body, as a product of the metabolism of their own protoplasm; and we may suppose that under certain circumstances, as in the absence of adequate food, the carbohydrate material thus formed is at once discharged into the hepatic blood, for the general use of the body, but that under other circumstances as when an amylaceous meal has been taken, the immediate wants of the economy being covered by the carbohydrates of the meal, the

carbohydrate products of the hepatic metabolism are stored up as glycogen. Under such a view the sugar of the meal is used up somewhere in the body and the glycogen to which it gives rise comes direct from the hepatic protoplasm. An argument against such a view is afforded by the behavior of the substance glycerine. This substance when taken into the alimentary canal, or when injected into the portal vein, gives rise to an increase of glycogen in the liver, but when it is injected into the general venous system no such increase is observed. But if the formation of glycogen were due to the glycerine covering in some way or other the carbohydrate expenditure of the body and thus sparing the products of hepatic metabolism, we should expect to find an increase of glycogen in the latter case as well as in the two former cases. From this not taking place, we infer that glycerine gives rise to glycogen by being in some way or other transformed into glycogen by the agency of the hepatic cell, or at all events by the glycerine producing changes in the hepatic cell. And the small quantity of glycogen which results from proteid food is probably in a similar way the product of the direct action of the proteid on the hepatic protoplasm. From these and similar cases we may conclude that sugar also and the other carbohydrates give rise to glycogen, not by covering the general carbohydrate expenditure, but by producing changes in the liver itself. How far the sugar reaching the hepatic cell by the portal capillaries enters into the upward and downward series of the protoplasm of the cell, whether it is actually built up into the protoplasm before its elements reappear in the course of the destructive metabolism of the complex protoplasm as glycogen, formed so to speak afresh, or whether the protoplasm simply dehydrates the sugar as we just now suggested, while it is still outside itself, we have not at present sufficient evidence to decide. Though the former method seems to entail an unnecessary labor, there may be reasons why it should be adopted.

We have said that glycogen is readily converted by ferments into sugar, and that, after death, a conversion into sugar goes on in most cases with considerable rapidity and energy. An amylolytic ferment may be extracted from the hepatic tissue and it seems probable that the post-mortem appearance of sugar in the liver is due to the uncontrolled action of such a ferment. If this be the case, the question may be asked, How is it possible for the glycogen to remain as glycogen and become stored up in larger quantities in the presence of such a ferment? We can only answer that the solution of this problem is of the same kind as that of the problems, why blood does not clot in the living bloodvessels, why the living muscle does not become rigid, and why the living stomach or pancreas does not digest itself. It

might be added, bearing in mind the history of the fibrin ferment, that even admitting the presence of an amylolytic ferment after death, we have no proof that such a ferment exists in the hepatic cells during life. It is possible that the ferment which can be extracted after death only makes its appearance as the result of post-mortem changes which have taken place in the protoplasm of the hepatic cells. Moreover it is stated that the sugar which makes its appearance in the liver is dextrose, whereas the sugar into which glycogen is converted by the ordinary amylolytic ferments of saliva and pancreatic juice, is, as in the case of starch, largely maltose. This would indicate that the conversion which takes place in the liver is of a peculiar nature ; but the matter requires further investigation.

Diabetes.—Natural diabetes is a disease characterized by the appearance of a large quantity of sugar in the urine. Into the pathology of the various forms of this disease it is impossible to enter here ; but a temporary diabetes, the appearance for a while of a large quantity of sugar in the urine, may be artificially produced in animals in several ways. If the medulla oblongata of a well-fed rabbit be punctured in the region which we have previously described (Fig. 159) (p. 259) as that of the vaso-motor

[FIG. 159.
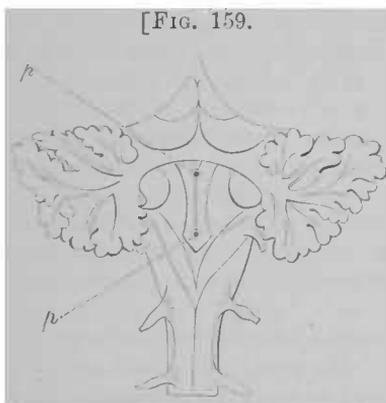
To show the position of the punctures required to produce glycosuria, the lobes of the cerebellum are separated ; below are seen the restiform bodies, the divergence of which circumscribes the apex of the calamus scriptorius and the fourth ventricle. The puncture p′ produces glycosuria, the puncture p glycosuria with polyuria, and a puncture a little higher up than p, albuminuria.]

centre (the area marked out as the " diabetic area " agreeing very closely with that defined as the vaso-motor area), though the animal need not necessarily be in any other way obviously affected by the operation, its urine will be found, in an hour or

even less, to be increased in amount and to contain a considerable quantity of sugar. A little later the quantity of sugar will have reached a maximum, after which it declines, and in a day or two, or even less, the urine will be again perfectly normal. The better fed the animal, or, more exactly, the richer in glycogen the liver at the time of the operation, the greater the amount of sugar. If the animal be previously starved so that the liver contains little or no glycogen, the urine will after the operation contain little of no sugar. It is clear that the urinary sugar of this form of artificial diabetes comes from the glycogen of the liver. The puncture of the medulla causes such a change in the liver that the previously stored-up glycogen disappears, and the blood becomes loaded with sugar, much if not all of which passes away by the urine. In the absence of any proof to the contrary, we may assume that in this form of artificial diabetes the glycogen previously present in the liver becomes converted into sugar, just as we know that it does become so converted by post-mortem changes. The glycogenic function of the liver is, therefore subject to the influence of the nervous system, and in particular to the influence of a region of cerebro-spinal centre which we already know as the vaso-motor centre, or at least of a part of that region. The path of the influence may be traced along the cervical spinal cord (and not along the vagi, though the roots of these nerves lie so close to the diabetic spot), as far down as (in rabbits) the level of the third or fourth dorsal vertebra, or even a little lower, from the spinal cord to the first thoracic ganglion, and thence to the liver by some channel or channels at present undetermined. We cannot at present define clearly the nature of that influence. We cannot say whether the temporary diabetes is a simple effect of a dilatation of the hepatic arteries which accompanies the diabetic puncture or of some direct action of the nerves on the metabolic activity of the hepatic protoplasm, though the latter view seems the more probable one.

Artificial diabetes is also a prominent symptom of urari poisoning. This is not due to the artificial respiration, which is had recourse to in order to keep the urarized animals alive; because, though disturbance of the respiratory functions sufficient to interfere with the hepatic circulation may produce sugar in the urine, artificial respiration may with care be carried on without any sugar making its appearance. Moreover, urari causes diabetes in frogs, although in these animals respiration can be satisfactorily carried on without any pulmonary respiratory movements. The exact way in which this form of diabetes is brought about has not yet been clearly made out.

A very similar diabetes is seen in carbonic oxide poisoning;

and is one of the results of a sufficient dose of morphia or of amyl nitrite.

There can be no doubt that in diabetes, arising from whatever cause, the sugar appears in the urine because the blood contains more sugar than usual. The system can only dispose (either by oxidation, or as seems more probable in other ways) of a certain quantity of sugar in a certain time. Sugar injected into the jugular vein reappears in the urine, whenever the injection becomes so rapid that the percentage of sugar in the blood reaches a certain (low) limit. Sugar in the urine means an excess of sugar in the blood. How in natural diabetes that excess arises, has not at present been clearly made out. It may be that some forms of diabetes resemble the artificial diabetes just described as resulting from puncture of the medulla, and arise from a too rapid conversion of the hepatic glycogen or from carbohydrate material failing to be stored up as glycogen. All forms of diabetes, however, cannot be satisfactorily explained in this way; and it has been suggested, though adequate proof has not yet been supplied, that the sugar of diabetes is of a peculiar nature and accumulates in the blood because it is unable to undergo those changes, whatever they be, which befall the normal sugar of the blood. We must not pursue the subject any further; but there is much to be said in favor of the view that the sources of the excess of sugar in the blood may be various, and, hence, that several distinct varieties of diabetes may exist. In one among many points, the clinical history of diabetes throws light on the possible sources of glycogen. While in many, especially of the less severe cases of diabetes, withdrawal of all amylaceous food is followed by a disappearance of sugar from the urine, in many instances the sugar continues to be discharged even though the diet be perfectly free from carbohydrates; and in many other cases the sugar in the urine is far in excess of the quantity which might be derived from the food. In these cases the sugar must have some non-amylaceous source; from this we infer that glycogen also may have a similar origin. And the fact that the urea is increased (and that too in some cases in ratio with the sugar) in diabetes, suggests that the sugar may arise from proteids which have been split up into a nitrogenous (urea) and a non-nitrogenous moiety, and so points out the way in which proteids may be a source of glycogen.

As a sort of converse of diabetes, we may mention that the administration of arsenic in sufficient doses for an adequate time prevents an accumulation of glycogen in the liver and apparently in the body generally, whatever be the diet used.

The History of Fat.   Adipose Tissues.

Of all the tissues of the body, adipose tissue is the most fluctuating in bulk; within a very short space of time a large amount of adipose tissue may disappear, and within an almost equally short time the quantity present in the body may be several times multiplied.   Histological inquiries teach us that when an animal is fattening the minute drops or specks of fat normally present in certain connective tissue corpuscles (either of a special kind, or certain individuals of the ordinary kind) are seen to increase in number, the protoplasm enlarging at the same time. As these specks increase they coalesce into drops, which by similar coalescence form larger drops, until the protoplasm first ceasing to increase and then diminishing, the original connective-tissue corpuscle is transformed into a fat-cell, with a remnant only of protoplasm gathered about the nucleus and forming an imperfect envelope round the enlarged contents.   When, on the contrary, an animal is fasting, the fat seems in some way or other to escape from the cell, which it may leave as a bag either filled with serous fluid or empty and collapsed around the nucleus. These facts point to the conclusion that the fat of adipose tissue is not simply and mechanically collected in the cell, but is formed by the active agency of the cell, being apparently the result of a breaking up of the protoplasm; when formed, however, it appears to be discharged from the cell in a more or less mechanical manner, as the needs of the economy demand.   And this view is supported by the fact that protoplasm, wherever occurring, both during life and after death (when it could not possibly be supplied with fat from without), is subject to fatty degeneration, in which the fat evidently arises, in large part at least, from the breaking up of proteid compounds.

On the other hand, we have traced the fats taken as food, and found that they pass with comparatively little change from the alimentary canal, chiefly through the intermediate passage of the lacteals, into the blood.   We might infer from this that an excess of fat thus entering the blood would naturally be simply stored up in the available adipose tissue, without any further change, the connective-tissue corpuscles eating the fat brought to them after the fashion of an amœba but not digesting it, simply keeping it in store till it was wanted elsewhere.

Which of these views is the true one, or how far are both these operations carried on in the animal body?   In the first place, it is evident that in an animal fattened on ordinary fattening food, only a small fraction of the fat stored up in the body can possibly come direct from the fat of the food.   Long ago, in opposition

to the views of Dumas and his school, who taught that all construction of organic material, that all actual manufacture of protoplasm or even of its organic constituents, was confined to vegetables and unknown in animals. Liebig showed that the butter present in the milk of a cow was much greater than could be accounted for by the scanty fat present in the grass or other fodder she consumed. He also urged, as an argument in the same direction, that the wax produced by bees is out of all proportion to the fat contained in their food, consisting as this does chiefly of sugar. And Lawes and Gilbert have shown by direct analysis that for every 100 parts of fat in the food of a fattening pig, 472 parts were stored up as fat during the fattening period. It is clear that fat is formed in the body out of something which is not fat.

There are two possible sources of this manufactured fat. In treating of digestion (p. 360), we referred to the possibility of digested carbohydrates becoming by fermentation converted into butyric acid; and we may imagine that when a member of the fatty acid series had thus been formed, higher and more complex members of the same series might be obtained out of it. There can be no doubt indeed that a carbohydrate diet is most efficacious in producing an accumulation of fat in the body : sugar or starch, in some form or other, is always a large constituent of ordinary fattening foods.

Another source of fat is to be found in the proteids. We have seen that the urea of the urine practically represents the whole of the nitrogen which passes through the body. Now in any given quantity of urea the amount of carbon is far less than that found in the quantity of proteid containing the same amount of nitrogen. Thus the percentage composition of the two being respectively,

	Carbon.	Hydrogen.	Oxygen.	Nitrogen.	Sulphur.
Urea .	20.00	6.66	26.67	46.67	1.13
Proteid	53	7.30	23.04	15.53	

100 grammes of urea contain about as much nitrogen as 300 grammes of proteid; but the 300 grammes of proteid contain 139 grammes (159—20) more carbon than do the 100 grammes urea. Hence the 300 grammes of proteid in passing through the body and giving rise to 100 grammes of urea, would leave behind 139 grammes of carbon, in some combination or other; and this surplus of carbon, if the needs of the economy did not demand that it should be immediately converted into carbonic acid and thrown off from the body, might be deposited somewhere in the form of fat. We have already seen, in treating of the action of the pancreatic juice (p. 308), that there is evidence of a fatty

element (viz., leucin, which is amido-caproic acid, and so belongs to the fatty acid series) being thrown off from the complex proteid compound in the very process of digestion.

It is clear that a construction of fat does occur in the body somewhere. What limits can we place on the degree to which this construction is carried? In reference to this point it is worthy of notice that the composition of fat varies in different animals. The fat of a man differs from the fat of a dog, even if both feed on exactly the some food, fatty or otherwise. Were the fat which is taken as food stored up as adipose tissue directly and without change, recourse being had to other sources of food for the construction of fat only in cases where the fat in the food was deficient, we should expect to find that the constitution of the fat of the body would vary greatly with the food. So far from this being the case, direct experiment shows that the fat of the dog is, as far as composition is concerned, almost entirely independent of the food, that the normal constituents of fat make their appearance as usual, though some of them, such as stearin or olein, may wholly be absent in the food, and that abnormal fats such as spermaceti presented as food are not to be found in the fat which is stored up in the body as a consequence of a large supply of that food.

Of course it is quite possible that in such cases as these, though the stearin, or the olein, when absent from the food, was in some way or other constructed anew, yet at the same time those con stituents which were present were simply stored up; but it is also open for us to suppose that all the fat taken as food was in some way or other disposed of, and that all the new fat which made its appearance was constructed anew. And the latter view is supported by the histological facts just mentioned, as well as by other considerations, which we shall presently have to urge. At the present, however, we may be content with the following conclusions: 1. Fat is actually formed in the animal body, and is not merely stored up from the fat of the food. 2. The carbon-elements of the newly formed fat may be supplied either from amylaceous food, or from the carbon surplus of proteid food, or from fats taken as food which are not the natural constituents of the body-fat. 3. The fat stored up appears as fat-granules or drops deposited in the protoplasm of certain cells, and the increase of the fat in the cells is accompanied first by a growth, and subsequently by a decay of the protoplasm; but, as in the analogous case of glycogen, there is no complete evidence to show whether the fat-granules which appear are simply deposited by the protoplasm in a more or less mechanical manner, without their forming an integral portion of it, the chief stages of the manufacture of the fat having been gone through elsewhere, or whether they

arise from a breaking up, a functional metabolism of the proto-
plasm of the fat-cell itself; the latter view is on the whole,
however, the most probable.

The Mammary Gland.

[**Physiological Anatomy of the Mammary Gland.**—The mam-
mary gland is a compound racemose gland, and, like others of
its type, consists of a number of lobes, composed of smaller divi-
sions or lobules; these lobules in turn being made up of smaller
divisions or *vesicles*, which form a cluster on one of the terminal
ducts. (Fig. 160.) They are composed of a basement membrane

FIG. 160.
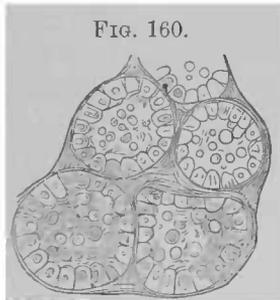
Termination of portion of Milk-duct in a cluster of follicles. From a mercurial injection ;
enlarged four times.

which is lined with glandular epithelium. Each lobule has a
common duct, which, uniting with the ducts from other lobules,
and these reuniting, form about fifteen or twenty larger ducts
which are called the *lactiferous* or *galactophorous* ducts. These
ducts converge as they approach the nipple, at the base of which
they become expanded into saccular dilatations, that act as re-
ceptacles for milk during the period of lactation. From these
receptacles the milk is conveyed to the surface of the nipple
through the final ducts. Near the base of the nipple are numbers
of sebaceous glands which secrete an unctuous fluid, which acts
as a protection to the nipple and parts immediately surrounding
during the act of sucking.

The ducts consist of a fibrous coat, which is composed of fibrous,
elastic, and unstriated muscular tissue. This coat is lined with
a mucous membrane, consisting of a basement membrane with
pavement or spheroidal epithelium.

The gland is invested with a fibrous tissue which penetrates
the substance of the organ between the lobules. This tissue con-
tains the nerves and vessels, with a very large amount of fat.
The capillaries form plexuses around the follicles.]

Since milk is a secretion, and indeed an excretion, the mammary gland ought not to be classed as a metabolic tissue, in the limited meaning we are now attaching to those words. Yet the metabolic phenomena giving rise to the secretion of milk are so marked and distinct, and have so many analogies with the purely metabolic events in adipose tissue, that it will be more convenient to consider the matter here, rather than in any other connection.

Human milk has a specific gravity of from 1.028 to 1.034, and when quite fresh possesses a slightly alkaline reaction. It speedily becomes acid, and cow's milk, even when quite fresh, is sometimes slightly acid, the change of reaction taking place during the stagnation of the milk in the mammary ducts.

The **constituents** of milk are:

1. Proteids, viz., casein,[1] and an albumin, agreeing in its general features with ordinary serum-albumin. The casein may be separated by curdling with rennet (p. 297); it may also be thrown down by the careful addition of acetic acid, but a more complete precipitation is effected by first adding to the milk a slight quantity of acetic acid, and then passing through it a stream of carbonic acid. From the filtrate the serum-albumin, which is present in small and variable quantities, may be obtained by coagulation with heat, or by precipitation with potassium ferrocyanide, etc.

2. Fats. These are, in human milk, palmitin, stearin, and olein. But other fats are also present in small quantities; and the composition of the fats of milk differs in different animals.

3. Milk-sugar, the conversion of which into lactic acid gives rise to many of the features of milk.

4. Extractives, including, according to some observers, urea and salts. The last consists chiefly of potassium phosphate, with calcium phosphate, potassium chloride, small quantities of magnesium phosphate, and traces of iron.

The following is the composition of 1000 parts of

	Human milk.	Cow's milk.
Casein	39.24	48.28
Albumin	—	5.76
Fat	26.66	43.05
Sugar	43.64	40.37
Salts	1.38	5.48
Total solids	110.92	142.94
Water	889.08	857.06

Milk is an emulsion, the fats existing in the form of globules of various but minute size, each protected by a thin envelope of

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[1] Or, if we restrict the word casein to the substance which appears in a solid form in curdling, or which may be precipitated by acids, an antecedent of casein.

casein or albumin. It is this condition of the fat which gives to milk its peculiar white color. The *colostrum* (Fig. 161), or secretion of the mammary gland at the beginning of lactation, differs from milk in being very deficient in casein and proportionately rich in albumin. It is said that the milk at the end of a long lactation again becomes poor in casein and rich in albumin.

[FIG. 161.
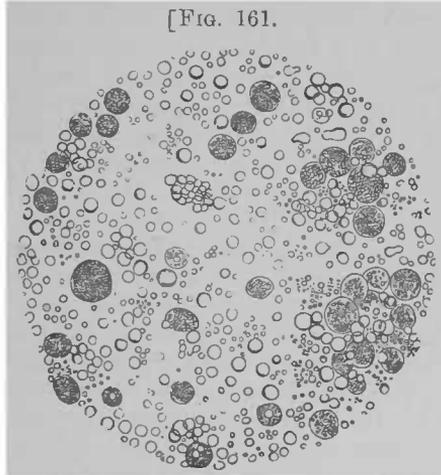
Microscopic appearance of Human Milk, with an intermixture of Colostric Corpuscles.]

Milk, on standing, turns sour and curdles. This is generally due to the milk-sugar becoming converted by a fermentative process into lactic acid, which, in turn, precipitates the casein. Curdling may, however, as we have already seen (p. 297) take place by the action of rennet ferment quite independently of the production of any acid.

Milk, like the other secretions which we have studied, is the result of the activity of certain protoplasmic secreting cells forming the epithelium of the mammary gland. As far as the fat of milk is concerned, the processes taking place in the gland are very instructive, since the fat can be *seen* to be gathered in the epithelium-cell, in the same way as in a fat-cell of the adipose tissue, and to be discharged into the channels of the gland, either by breaking away from the cell, or by a contractile extrusion very similar to that which takes place when an amœba ejects its digested food. All the evidence we possess goes to prove that the fat is formed in the cell through a metabolism of the protoplasm. The microscopic history is thoroughly supported by other facts. Thus the quantity of fat present in milk is largely and directly increased by proteid, but not increased, on the contrary diminished, by fatty food. This is quite intelligible when we

know, as will be shown in a succeeding section, that proteid food increases, and fatty food diminishes, the metabolism of the body; and we have already discussed the manner in which proteid material may give rise to fat. A bitch fed on ment for a given period gave off more fat in her milk than she could possibly have taken in her food, and that too while she was gaining in weight, so that she could not have supplied the mammary gland with fat at the expense of fat previously existing in her body; she apparently obtained it ultimately from the proteids of her food. In the "ripening" of cheese we have a similar conversion of proteids into fat, though this appears to be effected by the agency of certain fungi. We have also indications that the casein is, like fat, formed in the cells of the gland, and not simply separated from the blood. When the action of the cell is imperfect, as at the beginning or end of lactation, the albumin in milk is in excess of the casein; but as long as the cell possesses its proper activity the formation of casein becomes prominent. When milk is kept at 35° C. out of the body the casein is said to be increased at the expense of the albumin, but the substance thus formed out of albumin is probably not real casein but ordinary alkali-albumin, produced by the action of the alkalies of the milk on the albumin. It has been suggested that the casein may be formed by a splitting up of albumin by some fermentative process, and a ferment capable of effecting this is said to have been isolated. That the milk-sugar also is formed in and by the protoplasm of the cell, is indicated by the facts that it is found in no other part of the body, and that its presence in milk is not dependent on carbohydrate food, for it is maintained in abundance in the milk of carnivora when these are fed exclusively on meat, as free as possible from any kind of sugar or glycogen. We thus have evidence in the mammary gland of the formation, by the direct metabolic activity of the secreting cell, of the representatives of the three great classes of food-stuffs, proteids, fats and carbohydrates, out of the comprehensive substance protoplasm. And what we see taking place in the mammary cell is probably a picture of what is going on in all protoplasmic bodies. If the fat of the milk were not ejected from the mammary cell, the mammary gland would become a mass of adipose tissue, especially if, by a slight change in the metabolism, the production of fat were exalted at the expense of the production of casein or milk-sugar. If, again, by a similar slight change the milk-sugar were accumulated rather than the fat or proteid, we should have a result which, by an easy step would bring us to glycogenic tissue. And, lastly, if the proteid accumulation were greater than the fatty, or the saccharine, these being carried off

in some way or other, we should have an image of the nutrition of an ordinary nitrogenous tissue.

That both the secretion and ejection of milk are under the control of the nervous system is shown by common experience, but the exact nervous mechanism has not yet been fully worked out. While erection of the nipple ceases when the spinal nerves which supply the breast are divided, the secretion continues, and is not arrested even when the sympathetic as well as the spinal nerves are cut.

[The fact that many medicines are eliminated in part, by the milk should always be borne in mind. The influence of certain cathartics and mercurials on the child, when given to the mother, is specially noticeable.]

The Spleen.

[**Physiological Anatomy of the Spleen.**—The spleen is a ductless gland. It is covered with a fibro-elastic coat or capsule, which is reflected inwards at the *hilum* as a sheath for the blood-vessels. From the whole of the inner surface of the capsule numerous prolongations called *trabeculæ* are continued into the substance of the organ, and these uniting with similar trabeculæ given off from the sheaths of the vessels, form the framework or *stroma*. The trabeculæ consist of yellow and white elastic tissue containing unstriated muscular fibres, and form by their interlacements numerous irregular spaces, called *loculi*, which contain the splenic *substance* or *pulp*. This pulp is of a reddish-brown color, and of a soft granular consistence; containing blood disks (some of which have undergone retrograde metamorphosis), colorless corpuscles, nuclei, nucleated cells, pigment cells, and extractives. Running through this pulp is an extremely delicate fibrous network containing blood capillaries.

Along the ramifications of the splenic artery are seen numerous ovoid, opaque whitish bodies, which are called the *Malpighian corpuscles* (Fig. 162). They appear upon the walls of the vessels as budding processes, each of them being invested by a capsule which is formed by an expansion of the sheath of the vessel. They are covered with plexuses of capillaries, which send loops into the interior of the corpuscles. The substance of the corpuscles consists of a white semifluid albuminous material containing nuclei, nucleated cells, and granular matter, which are supported in a stroma of fibrillar tissue and capillary loops. The veins arise within the spleen either as continuations of the arterial capillaries, as intercellular passages, or as cæcal pouches. The capacity of the veins is about twice that of the arteries. The nerves are derived from the sympathetic and right pneumogastric.]

The spleen may be wholly removed from an animal without any obvious changes in the economy taking place: the functions

[FIG. 162.
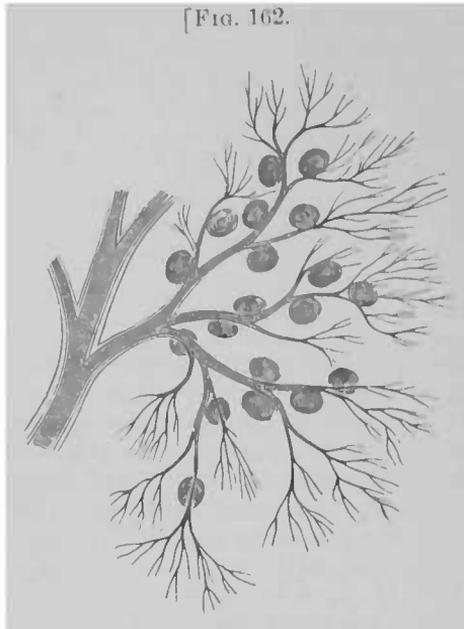
Branch of the Splenic Artery, the ramifications of which are studded with Malpighian Corpuscles.]

of the rest of the body appear to go on unimpaired. We are obliged to assume that some compensating actions take place;

[FIG. 163.
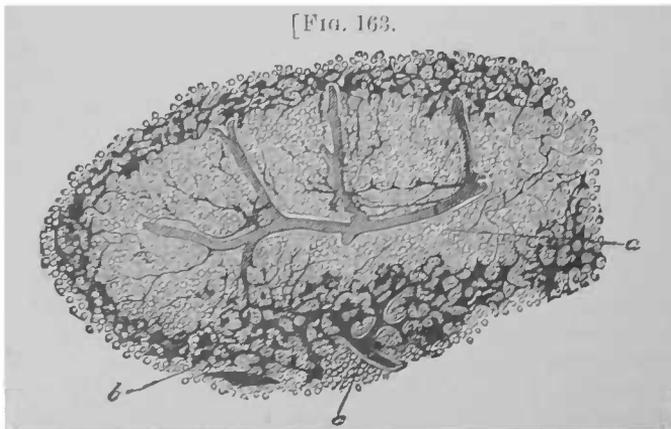
Malpighian Corpuscles from the Spleen of the Hedgehog, with its vascular supply. b, splenic pulp, with the intermediary blood-passages ; c, the rootlets of the vein.]

but what those actions are we do not know, and we are left at present by these experiments almost completely in the dark as to the functions of the spleen. The most that has been observed is a slight increase in the lymphatic glands, and in the activity of the medulla of bones (see p. 58), but even this is doubtful.

After a meal the spleen increases in size, reaching its maximum about five hours after the taking of food ; it remains swollen for some time, and then returns to its normal bulk. In certain diseases, such as in the pyrexia attendant on fevers or inflammations, and more especially in ague, a similar temporary enlargement takes place. In prolonged ague a permanent hypertrophy of the spleen, the so-called ague-cake, occurs.

The turgescence of the spleen seems to be due to a relaxation both of the small arteries and of the muscular bands of the trabeculæ ; to be, in fact, a vaso-motor dilation accompanied by a local inhibition of the tonic contraction of the other plain muscular fibres entering into the structure of the organ, the latter, at all events in some animals, being probably the more important of the two. And the condition of the spleen, like that of other vascular areas, appears to be regulated by the central nervous system, the digestive turgescence being altogether comparable to the flushed condition of the pancreas and of the gastric membrane during their phases of activity.

FIG. 164.
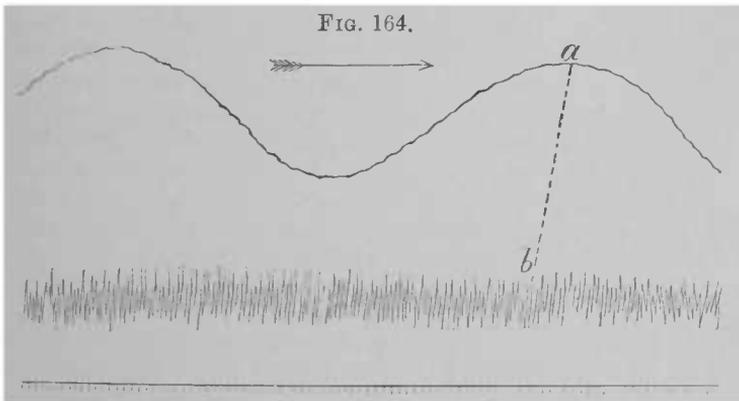
NORMAL SPLEEN CURVE FROM A DOG.

The upper curve is the spleen curve showing the rhythmic contractions and expansions ; the smaller waves are due to the respiratory movements. The lower curve is the blood-pressure curve, and the point a of the spleen curve corresponds in time to the point b of the blood-pressure curve. The marks on the time curve below indicate seconds.

The application of the plethysmographic method to the spleen, carried out in the way which we described in speaking of the kidney (p. 475), has revealed certain interesting phenomena.

A "spleen curve," Fig. 164, taken in the same way as a "kidney curve" brings to light the following facts. The volume of the spleen does not vary, as does that of the kidney, with each pulse wave. The kidney curve, as we have seen, p. 476, gives clear indications of each heart beat, but the spleen curve shows only gentle undulations, obviously due to the respiratory movements. This difference corresponds to the difference in the vascular arrangements of the two organs. In the kidney the small arteries are relatively numerous, and a large portion of the blood in the kidney is contained in them; in the spleen the small arteries are relatively few, and the great bulk of the blood is contained in the capillaries and in the meshes of the peculiar splenic tissue. Consequently the blood-flow through the spleen is of a more even character than that through the kidney, and the effects of variations in the distention of the arteries, and of vaso-motor influences generally are less directly felt.

Besides the respiratory undulations the spleen cure usually shows, as is seen in the figure, large slow variations of volume. Rhythmic contractions and expansions, though not always present, frequently make their appearance, each contraction with its fellow expansion lasting in the cat and dog about a minute, and recurring with great regularity for a long time. There can be little doubt that these variations in volume are due to rhythmic contractions, with intervening relaxations, of the muscular trabeculæ and capsule. In many animals the contractility of the splenic tissue is shown by the white lines of constriction which appear when the electrodes of an induction machine in action are drawn over its surface; and similar lines may be produced by mechanical stimulation with the point of a needle. So that the spleen may be considered as a muscular organ, now expanding to receive a larger quantity of blood and now contracting to drive the blood on to the liver. We have evidence, moreover, that the muscular activity of the spleen is under the dominion of the nervous system. A rapid contraction of the spleen may be brought about in a direct manner by stimulation of the splanchnic or vagus nerves, or in a reflex manner by stimulation of the central ends of a sensory nerve; it may also be caused by stimulation of the medulla oblongata with a galvanic current or by means of asphyxia. Though the matter has not yet been fully worked out, we have already sufficiently clear indications that the flow of blood through the spleen is, through the agency of the nervous system, varied to meet changing needs. At one time a small quantity of blood is passing through the organ, and the blood is at such times probably confined to the well-established capillary passages, the metabolic changes which it undergoes in the transit being comparatively slight. At

another time a larger quantity of blood enters the organ, and then probably is let loose, so to speak, into the splenic pulp, there to undergo more profound changes, and afterwards to be ejected by the rhythmic contractions of the muscular trabeculæ.

Indeed, when the peculiar arrangements of the bloodvessels of the spleen, with their large open venous networks, are borne in mind, it seems in the highest degree probable that metabolic events of great importance (possibly associated in some way with the destruction of metamorphosis of the blood-corpuscles) take place in the spleen, though at present we are unable to follow them. And this view is supported by the somewhat peculiar chemical characters of the spleen-pulp, which, in spite of its containing a very large number of blood-corpuscles, differs markedly in its chemical composition from either blood or serum. Thus a special proteid of the nature of alkali-albumin holding iron in some way peculiarly associated with it seems to be present. The occurrence of this ferruginous proteid, accompanied as it is by several peculiar but at present little understood pigments, rich in carbon, bears out the histological conclusions (see p. 59) concerning the disappearance of the red corpuscles. The inorganic salts of the spleen, or at least those of its ash, are remarkable for the large amount of both soda and phosphates, and the small amount of potash and chlorides which they contain, thus differing from blood-corpuscles on the one hand, and from blood-serum on the other. But perhaps the most striking feature of the spleen-pulp is its richness in the so-called extractives. Of these the most common and plentiful are succinic, formic, acetic, butyric, and lactic acids (these may arise in part from the decomposition of hæmoglobin), inosit, leucin, xanthin, hypoxanthin, and uric acid. Tyrosin apparently is not present in the perfectly fresh spleen, though leucin is: both are found when decomposition has set in. The constant presence of uric acid is remarkable, especially since it has been found even in the spleen of animals, such as the herbivora, whose urine contains none. No less suggestive is the fact that the increase of uric acid in the urine during ague, and during ordinary pyrexia, seems to run parallel to the turgescence, and therefore presumably to the activity, of the spleen. But these facts are at present suggestive only; they point to an active metabolism, associated in some way with digestion, taking place in the spleen; exact information as to the nature of the metabolism is however wanting. The thyroid and thymus bodies, often in description associated with the spleen, though different in structure, the former absolutely so, resemble the spleen somewhat, as far as their extractives are concerned. The thymus contains leucin, xanthin and hypoxanthin, with lactic and succinic acids; uric acid seems to be absent. The extractives of the thyroid are scanty, but apparently of the same nature.

We may now return to the questions which we left unanswered at p. 487. Where is urea formed? What are its immediate antecedents? What are the various chemical links between it and the proteid material of which it is the excretory representative?

We have seen, p. 99, that the muscular tissues contain kreatin, together with smaller quantities of allied nitrogenous crystalline bodies, such as xanthin, hypoxanthin, etc.; and we cannot go far wrong in supposing that these bodies are in some way or other the products of muscular metabolism. We do not know in what quantities they are formed; but since they are such bodies as would readily be carried away from the muscle by the blood-stream, and yet are always to be found in the muscle, we infer that they are continually being formed, and as continually being converted into some other bodies and carried away. And we may further say, that since kreatin exists in muscle to the extent of 0.2 or 0.4 per cent., and since muscle forms so large a portion of the whole body, and must be continually undergoing some nitrogenous metabolism, even if the energy of the muscle (see p. 129) have a non-nitrogenous source, it is at least possible, if not probable, that a considerable amount of kreatin passes within twenty-four hours into the blood, on its way to become transformed by other tissues into urea, or into some stage nearer to urea than itself. The urine, it is true, contains a certain amount (0.9 gramme in twenty-four hours) of kreatinin, into which kreatin is easily converted; but this cannot be considered as the normal form in which the kreatin of the muscles passes out of the body. For the urinary kreatinin is exceedingly variable in quantity, vanishing during starvation, and, though not at all increased by exercise, is largely augmented by a flesh-diet; and kreatin injected into the blood, even in small quantities, reappears as kreatinin in the urine. Without laying too much stress on the last fact, we are led to conclude that the kreatinin or kreatin in urine has an origin quite independent of that which is present in the muscles, being probably derived directly from the food.

Of the metabolism of the nervous tissues we know little; but kreatin is found in the brain, in some cases in not inconsiderable quantity. Moreover, the bodies of the nerve-cells are undoubtedly composed of protoplasm: the axis-cylinders of the nerve-fibres are also protoplasmic in nature, and it is at least possible that much of the peculiar matrix of the cerebral and cerebellar convolutions, and of the gray matter generally, is also in reality protoplasmic. Hence, we may, with a certain amount of reason,

suppose that the nervous, like the muscular tissues, are continually, but to a much less extent, supplying an antecedent to urea in the form of kreatin.

Lastly, the spleen contains a considerable quantity of kreatin, as well as of xanthin, etc.; and these are present also in various glandular organs.

We thus have evidence of a continual formation of kreatin, possibly in large quantities, in various parts of the body. On the other hand, urea is certainly not present in muscle (save in certain exceptional cases), and its presence in nervous tissue is extremely doubtful. It is absent from the spleen (of the occurrence of urea in the liver we shall speak presently), the thymus and thyroid bodies, and from the lymphatic glands, though uric acid, as we have seen, appears to be a normal constituent of the spleen. It seems very tempting to jump at once from these facts to the conclusion that kreatin is the natural antecedent of urea, and that as far as nitrogenous excretion is concerned the labor of the kidney is confined to the simple transformation of kreatin into urea. We have only to suppose that the kreatin passes from these several tissues into the blood, in which it may be found, and while circulating in the blood is seized upon by the renal epithelium and converted into urea. And in support of this view, it has been urged that while ligature of the ureters leads to an accumulation of urea in the various tissues and fluids of the body, kreatin takes the place of urea when the kidneys are wholly extirpated, the explanation given of the different results being that in the former case the kidneys continue to perform their functions, and to manufacture urea out of kreatin, and the urea thus formed is thrown back upon the blood, whereas in the latter case the kreatin-converting organs are absent. Further observations, however, have clearly shown that whether the kidneys be wholly extirpated or the ureter simply ligatured, the result in both cases is the same, an accumulation in the tissues and fluids of urea, or, in the case of birds and snakes, etc., of uric acid. And indeed the ligature of the ureters soon leads to such trouble in the renal epithelium as to arrest their functional activity, so that the distinction between extirpation of the kidney and ligature of the ureters is an illusory one. Hence, though we need not go so far, perhaps, as to say that no part of the urea of urine is furnished by a transformation of kreatin by the kidney itself, it is obvious that we cannot speak of the main mass of urea, which passes from the body, as having such an origin, and as having undergone such a transformation in the kidney. Clearly the great part of the urea of the urine reaches the kidney either as urea existing in the blood, and has simply to be passed through the epithelium cells, the healthy kidneys usually per-

forming their work so well as to leave behind in the blood only such a slight amount of urea as to be with difficulty detected by the means at present at our command, or as some substance which, though not actually urea itself, is so nearly allied as to be capable of being readily transformed into urea, and accumulated as urea in the tissues and fluids, when the excreting power of the kidneys is lost.

The kreatin of muscle and other tissues may, before it reaches the kidney, be a source of this urea or antecedent of urea in the blood, having undergone transformations whose seat and nature are hidden from us, or, as we have suggested, it may not be. There are, however, other possible sources of urea besides the kreatin formed in muscle and elsewhere.   We have seen that one result of the action of the pancreatic juice is the formation of considerable quantities of leucin and tyrosin.   In dealing with the statistics of nutrition, our attention will be drawn to the fact that the introduction of proteid matter into the alimentary canal is followed by a large and rapid excretion of urea, suggesting the idea that a certain part of the total quantity of the urea normally secreted comes from a direct metabolism of the proteids of the food, without these really forming a part of the tissues of the body.   We do not know to what extent normal pancreatic digestion has for its product leucin, and its companion tyrosin ; but if, especially when a meal rich in proteids has been taken, a considerable quantity of leucin is formed, we can perceive an easy and direct source of urea, provided that the metabolism of the body is capable of converting leucin into urea.   That the body can effect this change is shown by the fact that leucin, when introduced into the alimentary canal in even large quantities, does reappear in the urine as urea ; that is, the urine contains no leucin, but its urea is proportionately increased ; and the same is possibly the case with tyrosin, though this is disputed. Now the leucin formed in the alimentary canal is probably carried by the portal blood straight to the liver ; and the liver, unlike other glandular organs, does, even in a perfectly normal state of things, contain urea.   We are thus led to the view that among the numerous metabolic events which occur in the hepatic cells, the formation of urea out of leucin or out of other antecedents may be ranked as one.   And, in support of this view, it may be urged that a large quantity of urea seems to be present in the liver of mammals, and of urates in the liver of birds. Moreover, when a stream of fresh blood is passed several times through the liver of an animal recently killed, the percentage of urea in the blood so used is found to be decidedly increased. This, however, is not conclusive, for the increased quantity in the blood which had been circulated might have been simply

urea, which had been washed out from the liver, where it had previously been staying. Probable, therefore, as this view may seem, it has not as yet been established as a fact. A strong presumption, however, in favor of urea arising through the hepatic metabolism, from leucin as an antecedent, is afforded by the fact that in cases of acute atrophy of the liver, where the hepatic cells lose their functional activity, the urea of the urine is replaced by leucin and tyrosin. And, lastly, it may be remarked that not only are leucin and tyrosin found in nearly all the tissues after death, especially in the glandular tissues, but they also appear with striking readiness in almost all decompositions of proteids, and leucin is also a product of decomposition of gelatiniferous substances.

The view that leucin is transformed into urea lands us, however, in very considerable difficulties. Leucin, as we know, is amidocaproic acid; and, with our present chemical knowledge, we can conceive of no other way in which leucin can be converted into urea than by the complete reduction of the former to the ammonia condition (the caproic acid residue being either elaborated into a fat or oxidized into carbonic acid), and by a reconstruction of the latter out of the ammonia so formed. We have a somewhat parallel case in glycin. This, which is amidoacetic acid, when introduced into the alimentary canal, also reappears as urea; here too a reconstruction of urea out of an ammonia phase must take place. Moreover, when ammonium chloride is given to a dog, a very large portion reappears as urea —i. e., there is an increase in the urea of the urine corresponding to a large portion of the nitrogen contained in the ammonium chloride. And there is a certain amount of evidence into which we cannot enter here, leading to the conception that the immediate antecedent of urea is ammonium carbamate, which by dehydration (and this it is stated may be effected by electrolysis with rapidly alternating currents) is transformed into urea. Or the antecedent which is dehydrated, may be not ammonium carbamate but ammonium carbonate (see Appendix); and, on the other hand, seeing how readily ammonium cyanate is transformed into urea, it may be that the immediate antecedent is some cyanogen compound. Leaving these matters for the present, and indeed we have ventured to call attention to them, chiefly because they serve as a warning not to neglect the possible synthetic operations of the animal body, we may sum up our imperfect knowledge concerning the history of urea as follows. We have evidence, not exactly complete but fairly satisfactory, that a part, at least, of the urea is simply withdrawn from the blood by the renal epithelium. The activity of the protoplasm of the secreting cells must, therefore, as far as this part of the urea is con-

cerned, be confined to absorbing the urea from the renal blood, and to passing it on into the cavities of the renal tubules. The mechanism by which this is effected we cannot at present fathom, but it seems more comparable to a selection of food than to anything else; the cells appear to treat urea much in the same way as they treat sodium sulphindigotate. The antecedents of the urea in the blood are, we may at present suppose, partly the kreatin formed in muscle and elsewhere, partly the leucin and other like bodies formed in the alimentary canal as well as in various tissues. The transformation of these bodies into urea may take place in the liver, and possibly in the spleen, but we have no exact proof of this, nor can we say exactly in what way the transformation is effected. There is no proof of any body existing in the blood capable of effecting this transformation; and we may probably rest assured that in this, as in other metabolic events, the activity exercised in the change comes from some tissue, and cannot be manifested by simple blood plasma.

Lastly, it is possible that the kidney may, besides the simpler duty of withdrawing ready formed urea from the blood, be exercised in transforming various nitrogenous crystalline bodies to serve as part of the supply of urea which passes from it.

Uric Acid.—This, like urea, is a normal constituent of urine, and, like urea, has been found in the blood, and in the liver and spleen; we have already, p. 515, referred to its relations with this latter organ. In some animals, such as birds and most reptiles, it takes the place of urea. In various diseases, the quantity in the urine is increased; and at times, as in gout, uric acid accumulates in the blood, and is deposited in the tissues. By oxidation a molecule of uric acid can be split up into two molecules of urea, and a molecule of mesoxalic acid. It may, therefore, be spoken of as a less oxidized product of proteid metabolism than urea; but there is no evidence whatever to show that the former is a necessary antecedent of the latter; on the contrary, all the facts known go to show that the appearance of uric acid is the result of a metabolism slightly diverging from that leading to urea. And we have no evidence to prove that the cause of the divergence lies in an insufficient supply of oxygen to the organism at large; on the contrary, uric acid occurs in the rapidly breathing birds, as well as in the more torpid reptiles. Nor can the fact that in the frog urea again replaces uric acid, be explained by reference to that animal having so large a cutaneous in addition to its pulmonary respiration. The final causes of the divergence are to be sought rather in the fact that urea is the form adapted to a fluid, and uric acid to a more solid excrement.

Hippuric Acid.—In the urine of herbivora, uric acid is for the most part absent, being replaced by hippuric acid. In the urine of omnivorous man, both acids may be present together. The history of the hippuric acid of urine is very instructive; for though at first sight its presence might appear to indicate that the metabolism of the herbivora is, in some points, fundamentally different from that of carnivora, there can be little doubt that the hippuric acid which appears in the urine of herbivora comes directly from the ingested food. Hippuric acid is a compound of, or rather a result of, the union or conjugation of benzoic acid and glycin; and when benzoic acid is introduced into the stomach of an animal, whether herbivorous or not, it reappears not as benzoic, but as hippuric acid. It evidently meets, somewhere in the body, with glycin; and uniting with this becomes hippuric acid, in which form it passes out by the urine. Nitrobenzoic acid, in a similar way, becomes nitrohippuric acid; and many other bodies of the aromatic class, by a like assumption of glycin, become conjugated in their passage through the body.

The knowledge of the fact that benzoic acid is thus converted into hippuric acid naturally suggested the idea that the food of herbivora might contain either benzoic acid, or some allied body, and that the presence of hippuric acid as a normal constituent of urine might be thus accounted for. And it would appear that all the hippuric acid of herbivorous urine is in reality due to the presence in ordinary fodder (hay) of a particular constituent containing a benzoic residue; when this constituent is withdrawn, the hippuric acid disappears from the urine.

The transformation or conjugation appears to take place chiefly in the kidneys, for when blood containing benzoic acid is driven through the vessels of a fresh, that is of a living, kidney, it is found after the transit to contain hippuric acid. And, indeed, the same change may be effected by simply mixing benzoic acid with portions of fresh and still warm kidney, broken to pieces and as it were mashed up, the mixture being exposed to the temperature of the body. If the kidney be kept some time before the benzoic acid is submitted to its action, the transformation fails, indicating that the change is effected by certain elements, probably by the renal epithelium cells, which retain this power so long only as they remain alive after removal from the body.

A similar transformation of benzoic into hippuric acid is said to take place in some animals, at least, in the liver, benzoic acid injected into the portal vein reappearing as hippuric acid in the blood of the hepatic vein. In both these cases, it is worthy of note, and the observation bears on the formation of urea just discussed, that the change takes place even if no glycin be added

with the benzoic acid. Glycin must, therefore, be present in the kidney or liver, and its presence in the liver is further shown by the formation of glycocholic acid from cholalic acid. But singularly enough, glycin, though a common product of the decomposition of proteid and gelatiniferous substances, has hitherto not been found as such in any part of the living body.

Of the meaning of the appearance in the tissues of such bodies as xanthin, etc., and of the exact nature of the metabolism which they undergo, we know nothing. We cannot say whether they are simply the accidental by-products of nitrogenous metabolism, the result of imperfect chemical machinery; or whether they, though small in quantity, serve some special ends in the economy.

Sec. 3.—The Statistics of Nutrition.

The preceding sections have shown us how wholly impossible it is at present to master the metabolic phenomena of the body by attempting to trace out forwards or backwards the several changes undergone by the individual constituents of the food, the body, or the waste products. Another method is, however, open to us: the statistical method. We may ascertain the total income and the total expenditure of the body during a given period, and by comparing the two may be able to draw conclusions concerning the changes which must have taken place in the body while the income was being converted into the output. Many researches have of late years been carried out by this method; but, valuable as are the results which have been thereby gained, they must be received with caution, since in this method of inquiry a small error in the data may, in the process of calculation and inference, lead to most wrong conclusions. The great use of such inquiries is to suggest ideas, but the views to which they give rise need to be verified in other ways before they can acquire real worth.

Composition of the Animal Body.—The first datum we require is a knowledge of the composition of the body, as far as the relative proportion of the various tissues is concerned. In the human body the proportions by weight of the chief tissues are probably somewhat as follows:

	Adult man. Per cent.	Newborn baby. Per cent.
Skeleton	15.9	17.7
Muscles	41.8	22.9
Thoracic viscera	1.7	3.0
Abdominal viscera	7.2	11.5
Fat	18.2 ⎫	20.0
Skin	6.9 ⎭	
Brain	1.9	15.8

An analysis of a cat has given the following result:

	Per cent.
Muscles and tendons	45.0
Bones	14.7
Skin	12.0
Mesentery and adipose tissue	3.8
Liver	4.8
Blood (escaping at death)	6.0
Other organs and tissues	13.7

One point of importance to be noticed in these analyses is that the skeletal muscles form nearly half the body; and we have already seen (p. 62) that about a quarter of the total blood in the body is contained in them. We infer from this that a large part of the metabolism of the body is carried on in the muscles. Next to the muscles we must place the liver, for, though far less in bulk than them, it is subject to a very active metabolism, as shown by the fact that it alone may hold about a quarter of the whole blood.

The Starving Body.—Before attempting to study the influence of food, it will be useful to ascertain what changes occur in a body when all food is withheld. A cat was found to lose in a hunger-period of thirteen days 734 grammes of solid material, of which 248.8 were fat and 118.2 muscle, the remainder being derived from the other tissues. The percentages of dry solid matter lost by the more important tissues during the period were as follows:

	Per cent.
Adipose tissue	97.0
Spleen	63.1
Liver	56.6
Muscles	30.2
Blood	17 6
Brain and spinal cord	0 0

Thus the loss during starvation fell most heavily on the fat; indeed, nearly the whole of this disappeared. Next to the fat, the glandular organs, the tissues which we have seen to be eminently metabolic, suffered most. Then come the muscles—that is to say, the skeletal muscles, for the loss in the heart was very trifling; obviously this organ, on account of its importance in carrying on the work of the economy, was spared as much as possible; it was, in fact, fed on the rest of the body. The same remark applies to the brain and spinal cord; in order that life might be prolonged as much as possible, these important organs were nourished by material drawn from less noble organs and

tissues. The blood suffered proportionally to the general body-waste, becoming gradually less in bulk, but retaining the same specific gravity; of the total dry proteid constituents of the body, 17.3 per cent. was lost, which agrees very closely with the 17.6 per cent. lost by the blood. It is worthy of remark that the tissues in general became more watery than in health. We might infer from these data the conclusions that metabolism is most active first in the adipose tissue, next in such metabolic tissues as the hepatic cells and spleen-pulp, then in the muscles, and so on; but these conclusions must be guarded by the reflection that because the *loss* of cardiac and nervous tissue was so small, we must not, therefore, infer that their *metabolism* was feeble; they may have undergone rapid metabolism, and yet have been preserved from loss of substance by their drawing upon other tissues for their material.

During this starvation-period, the urine contained in the form of urea (for, as we shall see, the other nitrogenous constituents of urine may for the most part be disregarded) 27.7 grammes of nitrogen. Now, the amount of muscle which was lost during the period contained about 15.2 of nitrogen. Thus, more than half the nitrogen of the output during the starvation-period must have come ultimately from the metabolism of muscular tissue. This is an important fact of which we shall be able to make use hereafter. Bidder and Schmidt came to the conclusion, from their observations on a starving cat, that the quantity of urea excreted per diem, in all but the earlier days of the inanition period, bore a fixed ratio to the body-weight. In the first two or three days of the period, the daily quantity of urea was much in excess of this ratio. They were thus led to distinguish two sources of urea; a quantity arising from the functional activity of the whole body, and therefore bearing a fixed ratio to the body-weight, and continuing until near the close of life; and a quantity arising from the amount of surplus nitrogenous or proteid material which happened to be stored up in the body at the commencement of the period, and which was rapidly got rid of. The latter they regarded as not entering distinctly into the composition of the tissues, but as, so to speak, floating capital, upon which each or any of the tissues could draw. They spoke of its direct metabolism as a *luxus consumption*. More extended observations, however, have shown that though the urea of the first two or three days much exceeds that of the subsequent days of a starvation-period, no such fixed relation of urea to body-weight as that suggested obtains. To the question of a luxus consumption, we shall have again to refer.

The Normal Diet.—What is the proper diet for a given animal under given circumstances, can only be determined when the

laws of nutrition are known. Meanwhile, it is necessary to gain an approximate idea of what may be considered as the normal diet for a body such as that of man under ordinary circumstances. This may be settled either by taking a very large average, or by determining exactly the conditions of a particular case. In the table below are given both the average result obtained by Moleschott from a large number of public diets, and the diet on which an observer (Ranke) found himself in good health, neither losing nor gaining weight.

	Public diet (Moleschott.) Grammes.	Ranke. Grammes.
Proteids	130	100
Fat	84	100
Amyloids	404	240
Salts	30	25
Water	2800	2600

Of these two diets, which agree in many respects, that of Ranke is probably the better one, since in public diets, the cheaper carbohydrates are used to the exclusion of the dearer fats.

Comparison of Income and Output.

Method.—We have now to inquire how the elements of such a diet are distributed in the excreta, in order that, from the manner of the distribution, we may infer the nature of the intermediate stages which take place within the body. By comparing the ingesta with the excreta, we shall learn what elements have been retained in the body, and what elements appear in the excreta which were not present in the food; from these we may infer the changes which the body has undergone through the influence of the food.

In the first place, the real income must be distinguished from the apparent one by the subtraction of the feces. We have seen that by far the greater part of the feces is undigested matter—*i. e.*, food which, though placed in the alimentary canal, has not really entered into the body. The share in the feces taken up by matter which has been excreted from the blood into the alimentary canal, is so small that it may be neglected; certainly with regard to nitrogen, the whole quantity of this element, which is present in the feces, may be regarded as indicating simply undigested nitrogenous matter.

The income, thus corrected, will consist of so much nitrogen, carbon, hydrogen, oxygen, sulphur, phosphorus, saline matters, and water, contained in the proteids, fats, carbohydrates, salts, and water of the food, together with the oxygen absorbed by the lungs, skin, and alimentary canal. The output may be regarded

as consisting of (1) the respiratory products of the lungs, skin, and alimentary canal, consisting chiefly of carbonic acid and water, with small quantities of hydrogen and carburetted hydrogen, these two latter coming exclusively from the alimentary canal ; (2) of perspiration, consisting chiefly of water and salts, for the dubious excretion (see p. 460) of urea by the skin may be neglected and the other organic constituents of sweat amounts to very little; and (3) of the urine, which is assumed to contain all the nitrogen really excreted by the body, besides a large quantity of saline matters, and of water.   Where great accuracy is required the total nitrogen of the urine ought to be determined ; it is maintained, however, that no errors of serious importance arise when the urea alone, as determined by Liebig's method, is taken as the measure of the total quantity of nitrogen in the urine, since, in this method, other nitrogenous bodies besides urea are precipitated, and so contribute to the quantitative result.   It has been, and indeed still is debated whether the body may not suffer loss of nitrogen by other channels than by the urine and feces, whether nitrogen may not leave the body by the skin or, indeed, in a gaseous state by the lungs.   The balance of the conflicting evidence seems, however, in favor of the view that no such loss takes place.   It would appear that though nitrogen, the pivot, so to speak, of the chemical changes of living beings, forms so large a portion of the atmosphere and, moreover, is physically diffused through the bodies of both plants and animals, free nitrogen is of no chemical use to either of them.   It enters into and remains in their bodies as an inert substance, and the nitrogen which leaves a plant or animal, in a gaseous state, is simply a part of the same inert supply and does not come from the breaking up of the nitrogenous substances of the body or of food.

Of these elements of the income and output, the nitrogen, the carbon, and the free oxygen of respiration are by far the most important.   Since water is of use to the body for merely mechanical purposes, and not solely as food in the strict sense of the word, the hydrogen element becomes a dubious one; the sulphur of the proteids, and the phosphorus of the fats, are insignificant in amount; while the saline matters stand on a wholly different footing from the other parts of food, inasmuch as they are not sources of energy, and pass through the body with comparatively little change.   The body-weight must, of course, be carefully ascertained at the beginning and at the end of the period, correction being made where possible for the feces.

It will be seen that the labor of such inquiries is considerable. The urine, which must be carefully kept separate from the feces, requires daily measurement and analysis.   Any loss by the skin,

either in the form of sweat, or, in the case of woolly animals, of hair, must be estimated or accounted for. The food of the period must be, as far as possible, uniform in character, in order that the analyses of specimens may serve faithfully for calculations involving the whole quantity of food taken ; and this is especially the case when the diet is a meat one, since portions of meat differ so much from each other. But the greatest difficulty of all lies in the estimation of the carbonic acid produced and the oxygen consumed. In some of the earlier researches, this factor was neglected, and the variations occurring were simply guessed at, through which very serious errors were introduced. No comparison of income and output can be considered satisfactory unless, at least, the carbonic acid produced be directly measured by means of a respiration chamber. And in order that the comparison should be really complete, the water given off by the skin and lungs must be directly measured also ; but this seems to be more difficult than the determination of the carbonic acid.

In the plan originally adopted by Regnault and Reiset, and followed by some other observers, the animal experimented on is allowed to breathe a limited and measured atmosphere. The carbonic acid, as fast as it is formed, is fixed and removed by a strong solution of caustic potash, and the normal percentage of oxygen in the atmosphere is maintained by a supply of this gas from a gasholder. In this way both the oxygen consumed and the carbonic acid produced are directly determined, while the continual supply of fresh oxygen prevents any evil effects due to breathing a confined portion of air. In order, however, to avoid all possible errors arising from a too restricted atmosphere a different method has been adopted by Pettenkofer and Voit. Their apparatus consists essentially of a large chamber, capable of holding a man comfortably. By means of a steam engine a current of pure air, measured by a gasometer, is drawn through the chamber. Measured portions of the outgoing air are from time to time withdrawn and analyzed, and from the data afforded by these analyses, the amounts of carbonic acid (and other gases) and of water given off by the occupant of the chamber during a given time are determined. The oxygen consumed may also be determined by a comparison of the ingoing and outgoing air ; besides, if the total amounts of carbonic acid and of water given out by the lungs and skin are thus ascertained and the amount of urine and feces known, the quantity of oxygen is determined by a simple calculation. For evidently the difference between the terminal weight plus all the egesta and the initial weight plus all the ingesta can be nothing else than the weight of the oxygen absorbed during the period. This method in turn, however, is also open to objections, since minute errors in the sample determinations acquire by multiplication considerable dimensions. It seems, moreover, undesirable to leave the quantity used of so important an element as oxygen to be determined by indirect calculations.

Let us imagine, then, an experiment of this kind to have been completely carried out, that the animal's initial and terminal weights have been accurately determined, the composition of the

food satisfactorily known to consist of so much proteid, fat, carbo-hydrates, salts, and water, and to contain so much nitrogen and carbon, the weight of the feces and the nitrogen they contain ascertained, the nitrogen of the urine determined, the carbonic acid and water given off by the whole body carefully measured, and the amount of oxygen absorbed calculated—what interpretation can be placed on the result?

Let us suppose that the animal has gained w in weight during the period. Of what does w consist? Is it fat or proteid material which has been laid on, or simply water which has been retained, or some of one and of the other? Let us further suppose that the nitrogen of the urine passed during the period is less, say by x grammes, than the nitrogen in the food taken, of course after deduction of the nitrogen in the feces. This means that x grammes of nitrogen have been retained in the body; and we may with reason infer that they have been retained in the form of proteid material. We may even go further and say that they are retained in the form of flesh—*i. e.*, of muscle. In this inference we are going somewhat beyond our tether, for the nitrogen might be stored up as hepatic, or splenic, or any other form of protoplasm. Indeed, it might be for the while retained in the form of some nitrogenous crystalline body; but this last event is unlikely; and if we use the word " flesh " to mean protoplasm of any kind, contractile or metabolic, or of any other kind, we may without fear of any great error reckon the deficiency of x grammes nitrogen as indicating the storing up of a grammes flesh. There still remain $w-a$ grammes of increase to be accounted for. Let us suppose that the total carbon of the egesta has been found to be y grammes less than that of the ingesta; in other words, that y grammes of carbon have been stored up. Some carbon has been stored up in the flesh with the nitrogen just considered; this we must deduct from y, and we shall then have y' grammes of carbon to account for. Now, there are only two principal forms in which carbon can be stored up in the body: as glycogen or as fat. The former is even in most favorable cases inconsiderable, and we therefore cannot err greatly if we consider the retention of y' grammes carbon as indicating the laying on of b grammes fat. If $a+b$ are found equal to w, then the whole change in the economy is known; if $w-(a+b)$ leaves a residue c, we infer that in addition to the laying on of flesh and fat some water has been retained in the system. If $w-(a+b)$ gives a negative quantity, then water must have been given off at the same time that flesh and fat were laid on. In a similar way the nature of a loss of weight can be ascertained, whether of flesh, or fat, or of water, and to what extent of each. The careful comparison, the debtor and creditor account of income and output, enables us,

with the cautions rendered necessary by the assumptions just now mentioned, to infer the nature and extent of the bodily changes. The results thus gained ought, of course, if an account is kept of the water taken in and given out, to agree with the amount of oxygen consumed, and also to tally with the conclusions arrived at concerning the retention or the reverse of water.

Having thus studied the method and seen its weakness as well as its strength, we may briefly review the results which have been obtained by its means.

Nitrogenous Metabolism.—When a diet of lean meat, as free as possible from fat, is given to a dog, which has previously been deprived of food for some time, and whose body therefore is greatly deficient in flesh, it might be expected that the great mass of food would be at once stored up, and only a small quantity be immediately worked off as an additional quantity of urea, occasioned by the increased labor thrown on the economy by the very presence of the food. This, however, is not the case; the larger portion passes off as urea at once, and only a comparatively small quantity is retained. If the diet be continued—and we are supposing the meals given to be ample ones—the proportion of the nitrogen which is given off in the form of urea goes on increasing until at last a condition is established in which the nitrogen of the egesta exactly equals that of the ingesta. This condition, which is spoken of as nitrogenous equilibrium, is attained in dogs with an exclusively meat diet only when large quantities of food are given, and is not easily maintained for any length of time. The exact quantity of meat required to attain nitrogenous equilibrium varies with the previous condition of the dog; it is frequently seen when 1500 or 1800 grms. of meat are given daily. Thus the most striking effect of a purely nitrogenous diet is largely to increase the nitrogenous metabolism of the body. This result has been explained by supposing that with the meat diet the consumption of oxygen is largely increased; in other words, that the oxidizing activity of the body is directly augmented by a meat diet. This, in turn, may be due in part to the fact that proteid food largely increases the number of the red corpuscles, and so augments the amount of oxygen with which the tissues are supplied; but as we have already urged more than once, the oxidative activity of the tissues is determined by the tissues themselves rather than by the mere abundance of oxygen at their disposal; and, probably, other agencies are at work.

When nitrogenous equilibrium is established, it does not mean that a body-equilibrium is established, that the body-weight

neither increases nor diminishes.   On the contrary, when the meal necessary to balance the nitrogen is a large one, the body may gain in weight, and the increase is proved, both by calculation from the income and output, and by actual examination of the body, to be due to the laying on of fat.   The amount so stored up may be far greater than can possibly be accounted for by any fat still adhering to the meat given as food.   We are, therefore, driven to the conclusion that the proteid food is split into a urea moiety and a fatty moiety, that the urea moiety is at once discharged, and that such of the fat as is not made use of directly by the body is stored up as adipose tissue.   And this disruption of the proteid food at the same time explains why the meat diet so largely and immediately increases the urea of the egesta.   We have already pointed out that possibly this disruptive metabolism of proteids is largely carried on in the alimentary canal itself by the aid of the pancreatic juice; whether or to what extent other organs share in the action we do not at present know.

The characteristic metabolic effects of proteid food are shown not only by these calculations of what is supposed to take place in the body, but also by direct analysis.   Lawes and Gilbert laboriously analyzing the body of a pig, which had been fed on a known diet, and comparing the analysis with that of another pig of the same litter, killed at the time when the first was put on the fixed diet, found that of the dry nitrogenous material of the food only 7.34 per cent. was laid up as dry proteid material during the fattening period, though the amount of proteid food was low; in the sheep the increase was only 4.14 per cent.

It may be worth while to consider briefly here what is exactly meant by the proteid metabolism of which we are speaking.   In the first place, in dealing with the changes taking place in the body we may distinguish between the morphological and physiological destruction and renewal.   We know that an epithelium cell, as notably in the case of the skin, may be bodily cast off and its place filled by a new cell, and probably a similar disappearance of and renewal of histological units takes place in all the tissues of the body to a variable extent.   But, in the adult body, these histological transformations are, in the cases of most of the tissues, slow and infrequent.   A muscle, for instance, may suffer very considerable wasting and recover from that wasting without any loss or renewal of its elementary fibres.   And it is obvious that the metabolism of which we are now speaking does not involve any such shifting of histological units.   On the other hand, we find these histological units, the muscle-fibre or the gland-cell for instance, living on their internal medium the

blood, or rather on the lymph which is the middleman between themselves and the actual blood flowing in the vascular channels. Now, we have previously insisted at length on the view that no oxidative changes on a large scale take place, as was once thought, in the blood. The proteid metabolism which we are now considering or rather the destructive part of that metabolism (and to avoid the introduction of a new word we may venture, in using the word metabolism, to leave the context to explain whether the whole series of changes constructive and destructive, or the constructive changes alone, or the destructive changes alone, are intended) is fundamentally oxidative in character, and we may therefore assume that the large proteid metabolism which we are considering does not go on in the blood. In other words, the metabolism of proteids and the reduction of their nitrogenous residues into urea or into immediate antecedents of urea is carried out by the agency of the elements of the tissues. In a tissue unit, however, such as a muscle-fibre or gland-cell, we must distinguish between the actual living protoplasm or modified protoplasm, the morphological framework, so to speak, and the material or substances solid or in solution, which are lodged in the spaces of the framework, which are not part of the living unit but rather form a sort of internal medium to the unit itself. And we may readily conceive of the living unit affecting changes, and even profound changes, in this its internal medium, without the substances thus changed ever becoming an integral part of the living unit itself. Moreover, we can also conceive of the unit as a whole producing changes in the lymph surrounding it, much in the same way, as, according to some observers, the yeast-cell produces changes in the molecules of sugar which surround it, but which never become part of itself. We may, therefore, in the case of proteids, follow Voit and others in distinguishing between the proteids on the one hand which actually become part of living units and which may be called "tissue-proteids" or "morphotic proteids," and those on the other hand which are found in the internal meshes of the unit or in the surrounding lymph or in the blood, and which since they probably pass readily from one medium to the other, may be spoken of as "circulating proteids." By older physiologists at a time when the energy of bodily movements, of which we shall speak directly, was supposed to come from the direct metabolism of the morphotic proteids of muscle, the increase of urea due to food independent of exertion was regarded as simply arising from proteids metabolized in the blood, and so cast out as useless; hence the phrase, to which we have already referred, of luxus consumption. We now know, however, as will presently be pointed out, that the energy of bodily movements does

not come from the metabolism of the proteids of muscle, and we have already seen that oxidations on a large scale do not take place in the blood. Hence this view of a luxus consumption is no longer tenable. There still remains, however, the difficulty of supposing that every grain of urea which passes from the body after a rich proteid meal is the issue of the metabolism of a quantity of proteid previously existing as an integral part of some tissue unit ; in other words, it seems unlikely that simply as the result of such a meal, the actual living proteid framework of the body should be so largely renewed. Moreover, the contrast between that part of the daily urea which is variable and fluctuating and that part which is more constant has to be explained. Hence has arisen the view that the sources of urea are twofold, corresponding to the metabolism of two distinct categories of the proteids of the body. On the one hand, part of the urea, especially that which appears as the immediate result of food, is supposed to be derived from the metabolism of what we defined above as "circulating proteids," while, on the other hand, a certain (presumably smaller) portion is really due to the metabolism of the "tissue-proteids"—i. e., of the actual living framework of the body.

We must not attempt to discuss this view at length, and indeed our knowledge is inadequate for the purpose. We have not as yet a measure of the rate at which the metabolism of the living unit does or may take place, and the arguments in favor of a metabolism of circulating proteids are, at present, of a very indirect character. Moreover, it is possible that the rapid proteid metabolism indicated by the great increase of urea which follows upon a meal rich in proteids, may be, as we have hinted, merely a destructive digestion of the proteids while they still are retained in the alimentary canal.

We may, however, call attention to a possible analogy between the history of proteids and that of fats and carbohydrates. The uniform composition of the blood, which the body seems ever striving to maintain, probably applies to its proteids as well as to its other constituents. We have seen that a surplus of non-nitrogenous materials in the blood is withdrawn from the circulation and stored up as fat or glycogen, and it is possible that an excess of proteids might similarly be stored up in some tissue or tissues; though from the facts previously mentioned, it is obvious that the power of storage is far less than in the case of fats and carbohydrates. Such a store of proteid matter would represent a sort of circulating proteid, but nevertheless for its final metabolism might have to form an integral part of some living tissue unit.

The Effects of Fatty and of Carbohydrate Food.—Unlike those of proteid food, the effects of fats and carbohydrates cannot be studied alone. When an animal is fed simply on non-nitrogenous food, death soon takes place; the food rapidly ceases to be digested, and starvation ensues. We can, therefore, only study the dietetic effects of these substances when they are taken together with proteid material.

When a small quantity of fat is taken, in company with a fixed moderate quantity of proteid material, the whole of the carbon of the food reappears in the egesta. No fat is stored up; some even of the previously existing fat of the body may be consumed. As the fat of the meal is increased, a point is soon reached at which carbon is retained in the body as fat. So, also, with starch or sugar; when the quantity of this is small, there is no retention of carbon; as soon, however, as it is increased beyond a certain limit, carbon is stored up in the form of fat or, to a smaller extent, as glycogen. Fats and carbohydrates, therefore, differ markedly from proteid food in that they are not so distinctly provocative of metabolism. This is exceedingly well shown in the results of Lawes and Gilbert, for in the pig previously mentioned 472 parts of fat were laid on for every 100 parts of fat taken as such in the food (which consisting of barleymeal, etc., contained a very small amount of actual fat), while of every 100 parts of the total dry non-nitrogenous food, including fat, starch, cellulose, etc., no less than 21.2 parts were retained in the body in the form of fat. No clearer proof than this could be afforded that fat is formed in the body out of something which is not fat.

As one might imagine, the presence of fat or carbohydrates in the food is found to decrease the amount of proteid metabolism necessary to establish nitrogenous equilibrium. For instance, with a diet of 800 grms. meat and 150 grms. fat, the nitrogen in the egesta became equal to that in the ingesta in a dog, in whose case 1800 grms. meat had to be given to produce the same result in the absence of fats or carbohydrates.

On the other hand, it was found, that with a fixed quantity of fatty or carbohydrate food, an increase of the accompanying proteid led not to a storing up of the surplus carbon contained in the extra quantity of proteid, but to an increase in the consumption of carbon. Proteid food increases not only proteid but also non-nitrogenous metabolism. This explains how an excess of proteid food may, by the increase of metabolism, actually reduce the fat of the body.

There can be no doubt, then, that both a proteid diet and a carbohydrate diet may give rise to the formation of fat within the body. And the question which we have already (p. 504)

partly discussed comes again before us. In what way is this fat so formed? Is the sugar, arising during digestion from the carbohydrate, converted by a series of fermentative changes into fat? Or is the sugar directly consumed by the tissues in oxidative changes, by which means the fatty derivatives of the metabolized proteids are sheltered from oxidation and stored up as fat? This is a vexed question which has been hotly debated. Many observers hold strongly to the latter view, and hence contend that all fattening food must contain a supply of proteids adequate to provide, by their decomposition, the carbon of the fat which it is desired to lay up. The balance of evidence, however, seems to be in favor of the view that carbohydrates may be, in some way, directly converted into fat, and that, therefore, fattening foods need not necessarily contain any such definite proportion of proteids.

We have at present no exact information concerning the nutritive differences between fats and carbohydrates, beyond the fact that in the final combustion of the two, while carbohydrates require· sufficient oxygen to combine with their carbon only, there being already sufficient oxygen in the carbohydrate itself to form water with the hydrogen present, fats require in addition oxygen to burn off some of their hydrogen. Hence, in herbivora a larger portion of the oxygen consumed reappears in the carbonic acid of the egesta, than in carnivora, where more of it leaves the body as formed water : the proportions of the oxygen in the carbonic acid expired to the oxygen consumed being on an average 90 per cent. in the former and 60 per cent. in the latter. When a herbivorous animal starves, it feeds on its own fat, and under these circumstances the oxygen proportion in the expired carbonic acid falls to the carnivorous standard. The carbohydrates are notably more digestible than the fats, but on the other hand the fats contain more potential energy in a given weight. As to the dietetic, or rather metabolic, difference between starch and sugar, we know nothing very definite; it has been thought, however, that cane-sugar is rather more fattening than starch.

The Effects of Gelatine Food.—It is a matter of common experience that gelatine will not supply the place of proteids as a constituent of food. Animals fed on gelatine together with fat or carbohydrates die very much in the same way as when they are fed on non-nitrogenous material alone. Nevertheless, it would appear, as might be expected, that the presence of gelatine in food is not without effect. Thus, nitrogenous equilibrium is established at a lower level of real proteid food when gelatine is added. In a dog, moreover, fed on a diet of gelatine and fat

the excess of nitrogen in the excreta over that in the ingesta is less than when the same dog is fed on a diet of fat alone; that is to say, the gelatine has sheltered from metabolism some proteid constituents of the body; and the consumption of fat also seems to be lessened by the presence of gelatine. These facts become intelligible if we suppose that gelatine is rapidly split up into a urea and a fat moiety, in the same way that we have seen a certain quantity of proteid material to be. It is this direct destructive metabolism of proteid matter which gelatine can take up; it seems, however, unable to imitate the other function of proteid matter, and to take part in the formation of living protoplasm. What is the cause of this difference, we cannot at present say.

The Effects of Salts as Food.—All food contains, besides the potential substances which we have just studied, certain saline matters, organic and inorganic, having in themselves little or no latent energy, but yet either absolutely necessary or highly beneficial to the body. These must have important functions in directing the metabolism of the body: the striking distribution of them in the tissues, the preponderance of sodium and chlorides in blood-serum, and of potassium and phosphates in the red corpuscles for instance, must have some meaning; but, at present, we are in the dark concerning it. The element phosphorus seems no less important from a biological point of view than carbon or nitrogen. It is as absolutely essential for the growth of a lowly being like Penicillium as for man himself. We find it probably playing an important part as the conspicuous constituent of lecithin, we find it peculiarly associated with the proteids; but we cannot explain its *rôle*. The element sulphur, again, is only second to phosphorus, and we find it as a constituent of nearly all proteids; but we cannot tell what exactly would happen to the economy if all the sulphur of the food were withdrawn. We know that the various saline matters are essential to health, that when they are not present in proper proportions, nutrition is affected, as is shown by certain forms of scurvy; we are also aware that the properties and reactions of various proteid substances are closely dependent on the presence of certain salts; but beyond this we know very little.

Lastly, water has an effect on metabolism, as shown by the fact that when the water of a diet is increased, the urea is increased to an extent beyond that which can be explained by the increase of fluid increasing the facilities of mere excretion.

SEC. 4.—THE ENERGY OF THE BODY.

Broadly speaking, the animal body is a machine for converting potential into actual energy. The potential energy is supplied by food; this the metabolism of the body converts into the actual energy of heat and mechanical labor. We have in the present section to study what is known of the laws of this conversion, and of the distribution of the energy set free.

The Income of Energy.

Neglecting all subsidiary and unimportant sources of energy, we may say that the income of animal energy consists in the oxidation of food into its waste products, viz., the oxidation of proteids, fats, and carbohydrates into urea, carbonic acid, and water. A principle laid down by the chemist teaches that the potential energy of any body, considered in relation to any chemical change in it, is the same when the final result is the same, whether that result be gained at one leap or by a series of steps; that, for instance, the energy set free by the oxidation of 1 grm. of fat into carbonic acid and water is the same, whatever the changes forward or backward which the fat undergoes before it finally reaches the stage of carbonic acid and water; and similarly, that the energy available for the body in 1 grm. of dry proteid is the energy given out by the complete combustion of that 1 grm., less the energy given out by the complete combustion of that quantity of urea to which the 1 grm. of proteid gives rise in the body. Taking this as our guide, we may easily calculate the total energy of any diet. The following determinations, expressed both in gramme-degree (centigrade) units of heat, and kilogramme metre units of work, may serve as data.

The direct oxidation of the following, dried at 100° C.	gives rise to	
	gram.-deg.	kilo.-met.
1 grm. beef fat	9069	3841
1 grm. butter	7264	3077
1 grm. arrowroot	3912	1657
1 grm. beef muscle purified with ether	5103	2161
1 grm. urea	2206	934

Supposing that all the nitrogen of proteid food goes out as urea, 1 grm. of dry proteid, such as dried beef-muscle, would give rise to about $\frac{1}{3}$ grm. of urea; hence

	gram.-deg.	kilo.-met.
1 grm. proteid	5103	2161
less		
$\frac{1}{3}$ grm. urea	735	311
would give as		
Available energy of proteid	4368	1850

In a normal diet, such as Ranke's, p. 525, would be found:

	gram.-deg.	kilo.-met.
100 grm. proteid	436800	185000
100 grm. fat	906900	384100
240 grm. starch	938880	397680
Total income	2281580	966780

or, in round numbers, one million kilogramme-metres.

The Expenditure.

There are only two ways in which energy is set free from the body—mechanical labor and heat. The body loses energy in producing muscular work, as in locomotion, in all kinds of labor, in the movements of the air, in respiration and speech, and, though to a hardly recognizable extent, in the movements of the air or contiguous bodies by the pulsations of the vascular system. The body loses energy in the form of heat by conduction and radiation, by respiration and perspiration, and by the warming of the urine and feces. All the internal work of the body, all the mechanical labor of the internal muscular mechanisms with their accompanying friction, all the molecular labor of the nervous and other tissues, is converted into heat before it leaves the body. The most intense mental action, unaccompanied by any muscular manifestations, the most energetic action of the heart or of the bowels, with the slight exceptions mentioned above, the busiest activity of the secreting or metabolic tissues, all these end simply in augmenting the expenditure of income in the form of heat.

A normal daily expenditure in the way of mechanical labor can be easily determined by observation. Whether the work take on the form of walking, or of driving a machine, or of any kind of muscular toil, a good day's work may be put down at about 150,000 kilogramme-metres. The normal daily expenditure in the way of heat cannot be so readily determined. Direct calorimetric observations are attended with this difficulty, that the body while within the calorimeter is placed in abnormal conditions, which produce an abnormal metabolism. Hence results arrived at by this method are of little value unless they be accompanied by a comparison of the egesta and ingesta, so that the rate and nature of the metabolism going on may be known. Many attempts have been made to calculate the amount in an indirect manner. As trustworthy as any is the plan of simply subtracting the normal daily mechanical expenditure from the normal daily income. Thus, 150,000 kilogramme-metres subtracted from 1,000,000 kilogramme-metres gives

850,000 kilogramme-metres as the daily expenditure in the form of heat—*i. e.*, between one-fifth and one-sixth of the total income is expended as mechanical labor, the remaining four-fifths or five-sixths leaving the body in the form of heat.

The Sources of Muscular Energy.—Liebig, satisfied with having proved that the animal body was constructive as far as the formation of fat was concerned, still held to the distinction between nitrogenous or plastic and non-nitrogenous or respiratory food.   Put broadly, his view was that all the nitrogenous food went to build up the proteid tissues, the muscular flesh, and other form of protoplasm, and that the nitrogenous egesta arose solely from the functional metabolism of these tissues, while the non-nitrogenous food was used with equal exclusiveness for respiratory or calorific purposes, being either directly oxidized in the blood or, if present in excess, stored up as fatty tissue.   According to him, the two classes of income correspond exactly to the two forms of expenditure.   We have already urged several objections against this view.   We have seen that in the blood itself very little oxidation takes place, that it is the active tissue, and not the passive blood-plasma, which is the seat of oxidation. We have further seen that proteid food may undoubtedly be in Liebig's sense respiratory, and incidentally give rise to the storing up of fat.   One division of Liebig's view is thereby overthrown.   We have now to inquire whether the other division holds good, whether muscle or other protoplasm is fed exclusively on the proteid material of food, and whether muscular energy comes exclusively from the metabolism of the proteid constituents of muscle.   We have already seen (p. 100) that when the muscle itself is examined, we find no proof of nitrogenous waste, but, on the other hand, clear evidence of the production of non-nitrogenous bodies, such as carbonic acid.   And when we ask the question, Does muscular exercise increase the urea given off by the body as a whole? for this, according to Liebig's theory, it certainly ought to do, the evidence we can obtain, though somewhat conflicting, gives on the whole a decidedly negative answer.   Exercise, even severe, appears not necessarily to increase the urea of the urine.

More than this, the experience of Fick and Wislicenus lands us in an absurdity if we suppose the whole energy of muscular work to arise from proteid metabolism.   These observers performed a certain amount of work (an ascent of the Faulhorn) on a non-nitrogenous diet, and estimated the amount of urea passed during the period.   Assuming the urea to represent the oxidation of so much proteid matter, which oxidation represented in turn so much energy set free, they found that whereas

the actual work done amounted to 129.026 and 148.656 kilogram.-kilometres, for each respectively, the total energy available from proteid metabolism during the period was in the case of the first 68.69, and of the second 68.376 kilogram.-kilometres. That is to say, the energy set free by the proteid metabolism of the muscles engaged in the work was at the most far less than that necessary to accomplish the work actually done, besides having to provide for the movements of respiration and circulation. Their muscular energy, therefore, must have had other sources than proteid metabolism.

That on the contrary the production of carbonic acid is at once and largely increased by muscular exercise is beyond all doubt. One hour's hard labor will increase fivefold the quantity of carbonic acid given off within the hour. And in an experiment directed to this point it was found that a man in 24 hours consumed 954 grms. oxygen and produced 1284 grms. carbonic acid when doing work, as against 708 grms. oxygen consumed and 911 grms. carbonic acid produced when remaining at rest, the quantity of urea secreted being in the first case 37 grms., in the second 37.2 grms.

It is evident that the conclusions arrived at by the statistical method entirely corroborate those gained by an examination of muscle itself, viz., that during muscular contraction an explosive decomposition takes place, the non-nitrogenous products of which alone escape from the muscle and from the body, any nitrogenous products which result being retained within the muscle. We must, therefore, reject the second as well as the first division of Liebig's view; not only is the muscle not fed exclusively on proteid material, but also its energy does not arise from an exclusively proteid metabolism.

The Sources and Distribution of Heat.—We have already seen that the conception of the non-nitrogenous portions of food being solely calorifacient or respiratory proves to be unfounded when we attempt to trace the history of the food on its way through the body. The same view is still more strikingly shown to be inadequate, when we study the manner in which the heat of the body is produced. We may, indeed, at once affirm that the heat of the body is generated by the oxidation, not of any particular substances, but of the tissues at large. Wherever metabolism of protoplasm is going on, heat is being set free. In growth and in repair, in the deposition of new material, in the transformation of lifeless pabulum into living tissue, in the constructive metabolism of the body, heat may be undoubtedly to a certain extent absorbed and rendered latent—the energy of the construction may be, in part at least, supplied by the heat present.

But all this, and more than this, viz., the heat present in a potential form in the substances themselves so built up into the tissue, is lost to the tissue during its destructive metabolism; so that the whole metabolism, the whole cycle of changes from the lifeless pabulum through the living tissue back to the lifeless products of vital action, is eminently a source of heat.

Of all the tissues of the body the muscles, not only from their bulk, forming as they do so large a portion of the whole frame, but also from the characters of their metabolism, must be regarded as the chief sources of heat.

In treating (p. 101) of the thermal changes in muscle, we have seen that in the total energy expended in a muscular contraction, the ratio of that which appears as heat to that which appears as external work is variable. If we take what is somewhat below the mean result, and assume that the energy involved in the work done in a muscular contraction is about one-tenth of the total energy expended, the rest going out as heat, then, upon the calculation that the total external work of the body is about one-fifth of the total energy set free in the body, it is clear that the heat given out by the muscles, even at those times only when they are contracting, must form a very large part of the total heat given out by the body. But the skeletal muscles, though frequently, are not continually contracting; they have periods, at times long periods, of rest; and during these periods of rest, metabolism, of a subdued kind it is true, but still a metabolism involving an expenditure of energy is going on. This quiescent metabolism must also give rise to a certain amount of heat; and if we add this amount, which in the present state of our knowledge we cannot exactly gauge, to that given out during the movements of the body, it is very clear, even in the absence of exact data, that the metabolism of the muscles must supply a very large proportion of the total heat of the body. They are par excellence the thermogenic tissues.

Next to the muscles in importance come the various secreting glands. In these the protoplasm, at the periods of secretion at all events, is in a state of metabolic activity, which activity, as elsewhere, must give rise to heat. In the case of the salivary gland of the dog, the temperature of the saliva secreted during stimulation of the chorda has been found to be as much as 1° or 1.5° higher than that of the blood in the carotid artery at the same time, and in all probability the investigation of other secreting glands would lead to similar results. Of all these various glands, the liver deserves special attention on account of its size and large supply of blood, and because it appears to be continually at work. We find, indeed, that the blood in the hepatic veins is the warmest in the body. Thus, in the dog a

temperature of 40.73° C. has been observed in the hepatic vein, while that of the vena cava inferior was 38.35° to 39.58°, and that of the right heart 37.7°. The fact that the blood of the hepatic vein is warmer than that of either the portal vein or the aorta, shows that the increased temperature is not due simply to the liver being far removed from the surface of the body.

The brain too may be regarded as a source of heat, since its temperature is higher than that of the arterial blood with which it is supplied; though from the smaller quantity of blood passing through its vessels it cannot, in this respect, compare with either the liver or the muscles as a source of heat to the body.

The blood itself cannot be regarded as a source of any considerable amount of heat, since, as we have so frequently urged, the oxidations or other metabolic changes taking place in it are comparatively slight. The heat evolved by the indifferent tissues such as bone, cartilage, and connective tissue may be passed over as insignificant; and we cannot even regard the adipose tissue as a seat of the production of heat, since the fat of the fat-cells is in all probability not oxidized *in situ*, but simply carried away from its place of storage to the tissue which stands in need of it, and it is in the tissue that it undergoes the metabolism by which its latent energy is set free. Some amount of heat is also produced by the changes which the food undergoes in the alimentary canal before it really enters the body.

Hence taking a survey of the whole body, we may conclude that since metabolism is going on to greater or less extent everywhere, heat is everywhere being generated; but that, looked at from a quantitative point of view, the muscles and the glandular organs must be regarded as the main sources of the heat of the body, the muscles being in all probability the more important of the two.

But heat, while being thus continually produced, is as continually being lost, by the skin, the lungs, the urine, and the feces. The blood passing from one part of the body to the other, and carrying warmth from the tissues where heat is being rapidly generated, to the tissues or organs where heat is being lost by radiation, conduction, or evaporation, tends to equalize the temperature of the various parts, and thus maintains a " constant bodily temperature."

When the production of heat is not great as compared with the loss there is no great accumulation of heat within the body, the temperature of which consequently is but slightly raised above that of surrounding objects. Thus the temperature of the frog, for instance, is rarely more than 0.04° to 0.05° C. above that of the atmosphere, though in the breeding season the difference may amount to 1°. Such animals, and they comprise all classes

except birds and mammals, are spoken of as cold-blooded.   Exceptions among them are not uncommon.   Some fish, such as the tunny, are warmer than the water in which they live, and in a species of Python (*P. bivittatus*) a difference of as much as 12° C. has been observed.   Hüber found that in a beehive the temperature rose at times as much as to 40° C.   In the so called warm-blooded animals, birds, and mammals, the loss and production of heat are so balanced that the temperature of the body remains constant at, in round numbers, 35° or 40° C., whatever be the temperature of the air.   The temperature of man is about 37.6° C.; in some birds it is as high as 44° C. (Hirundo); and in the wolf it is said to be as low as 35.24° C.

This temperature is with slight variations maintained throughout life.   After death the generation of heat rapidly diminishes, and the body speedily becomes cold; but for some short time immediately following upon systemic death, a rise of temperature may be observed, due to the fact that, while the metabolism of the tissues is still going on, the loss of heat is somewhat checked by the cessation of the circulation.   The onset of pronounced rigor mortis causes a marked accession of heat, and when occurring after certain diseases may give rise to a very considerable elevation of temperature.

This mean bodily temperature of warm-blooded animals is, during health, maintained, with slight variations of which we shall presently speak, within a very narrow margin, a rise or indeed a fall of much more than a degree above or below the limit given above being indicative of some failure in the organism, or of some unusual influence being at work.   It is evident, therefore, that the mechanisms which coördinate the loss with the production of heat must be exceedingly sensitive.   It is obvious, moreover, that these mechanisms may act when the bodily temperature is tending to rise, by either checking the production or by augmenting the loss of heat; and when the bodily temperature is tending to fall, by either increasing the production or by diminishing the loss of heat.   As the regulation of temperature by variations in the loss of heat is better known than regulation by variations in production, it will be best to consider this first.

Regulation by Variations in Loss.—Heat is lost to the body by the warming of the feces and of the urine, by the warming of the expired air, by the evaporation of the water of respiration, by conduction and radiation from the skin, and by the evaporation of the water of perspiration.   It has been calculated that the relative amounts of the loss by these several channels are as follows: In warming the feces and urine about 3, or, according to others, 6 per cent.   By respiration about 20, or, according

to others, about only 9 per cent., leaving 77, or alternatively 85, per cent. for conduction and radiation and evaporation by the skin.

The two chief means of loss, then, which are at all susceptible of any great amount of variation, and which can be used to regulate the temperature of the body, are the skin and the lungs.

The more air passes in and out of the lungs in a given time, the greater will be the loss in warming the expired air, and in evaporating the water of respiration. And in such animals as the dog, which do not perspire freely by the skin, respiration is a most important means of regulating the temperature. The changes which give rise to this loss take place before the inspired air reaches the pulmonary alveoli; both the warming and the evaporation being effected in the nasal and pharyngeal, and to some extent in the bronchial passages. Some observers have maintained that the left side of the heart is warmer than the right, and hence argued that chemical changes leading to a considerable development of heat take place in the pulmonary capillaries. It would appear, however, that the right ventricle, owing to its lying nearer to the liver, the high temperature of which has already been mentioned, is in reality rather hotter than the left. And, indeed, we have no satisfactory evidence of any large amount of heat being produced by any pulmonary metabolism.

The great regulator, however, is undoubtedly the skin. The more blood passes through the skin the greater will be the loss of heat by conduction, radiation, and evaporation. Hence, any action of the vaso-motor mechanism which, by causing dilation of the cutaneous vascular areas, leads to a larger flow of blood through the skin, will tend to cool the body; and, conversely, any vaso-motor action which, by constricting the cutaneous vascular areas, or by dilating the splanchnic vascular areas, causes a smaller flow through the skin, and a larger flow of blood through the abdominal viscera, will tend to heat the body. Besides this, the special nerves of perspiration will act directly as regulators of temperature, increasing the loss of heat when they promote, and lessening the loss when they cease to promote, the secretion of the skin. The working of this heat-regulating mechanism is well seen in the case of exercise. Since every muscular contraction gives rise to heat, exercise must increase for the time being the production of heat; yet the bodily temperature rarely rises so much as a degree centigrade, if at all. By the exercise the respiration is quickened, and the loss of heat by the lungs increased. The circulation of blood is also quickened, and the cutaneous vascular areas becoming dilated, a larger amount of blood passes through the skin. Added to this, the skin perspires freely. Thus, a large amount of heat is lost to the body, suffi-

cient to neutralize the addition caused by the muscular contraction, the increase which the more rapid flow of blood through the abdominal organs might tend to bring about being more than sufficiently counteracted by their smaller supply for the time The sense of warmth which is felt during exercise in consequence of the flushing of the skin, is in itself a token that a regulative cooling is being carried on. In a similar way, the application of external cold or heat, either partially or completely, defeats its own ends. Under the influence of external cold the cutaneous vessels are constricted, and the splanchnic vascular areas dilated, so that the blood is withdrawn from the colder and cooling regions to the hotter and heat-producing organs. This vascular change may be used to explain the fact that stripping naked in a cold atmosphere often gives rise to a distinct increase in the mean temperature of the blood, as indicated by a thermometer placed in the mouth, though possibly the effect may be partly due to an actual increase of the production of heat. Under the influence of external warmth, on the other hand, the cutaneous vessels are dilated, a rapid discharge of heat takes place; and if the circumstances be such that the body can perspire freely, and the perspiration be readily evaporated, the temperature of the body may remain very near to the normal, even in an excessively hot atmosphere. Thus, more than a century ago, Drs. Fordyce and Blagden were able to remain with impunity in a chamber heated even to 127° (260° Fahr.), and with ease in one so hot that it became painful for them to touch the metal buttons of their clothing. It is unnecessary to give any more examples of this regulation of temperature by variations in the loss of heat; they all readily explain themselves.

Regulation by Variations in Production.—It is not, however, solely by variations in the loss of heat that the constant temperature of the warm-blooded animal is maintained. Variations in the amount of heat actually generated in the body constitute an important factor not only in the maintenance of the normal temperature, but also probably in the production of the abnormally high or low temperatures of various diseases. Many considerations have long led physiologists to suspect the existence of a nervous mechanism by which afferent impulses arising in the skin or elsewhere might, through the central nervous system, originate efferent impulses whose effect would be to increase or diminish the metabolism of the muscles or other organs, and thus to increase or diminish the amount of heat generated for the time being in the body. The existence, in fact, of a metabolic or thermogenic nervous mechanism, comparable in many respects to the vaso-motor mechanism, or to the various secreting nervous

mechanisms, seems in itself *à priori* probable. And we have experimental evidence that such a mechanism does really exist.

The warm-blooded animal is distinguished from the cold-blooded animal by the fact that when it is exposed to cold or heat, it does not, like the latter, become colder or hotter, as the case may be, but, within certain limits, maintains its normal temperature. If the maintenance of the temperature of the warm-blooded animal during exposure to cold is assisted by an increased production of heat, and is not due simply to a diminished loss, we ought to find evidence of an increased metabolism during that exposure. We ought to find under these circumstances an increased production of carbonic acid, and an increased consumption of oxygen, since it is to these products, rather than to the nitrogenous factors, on the peculiarities of which as uncertain signs of metabolism we have already insisted, we must look for indications of the rise or fall of metabolic activity. Of these two, the production of carbonic acid and the consumption of oxygen, the latter is the more important and trustworthy measure of metabolism, especially when observations are made for short periods only at a time ; for as we have seen in treating of respiration, the exit of carbonic acid is more closely dependent on the action of the respiratory mechanism than is the income of oxygen, and carbonic acid can be retained in loose combination, and so temporarily stored up by various constituents of the body.

Taking, then, the consumption of oxygen, and though with less confidence the production of carbonic acid, as a measure of metabolic activity, and so of heat-production, Pflüger and his pupils, as well as other observers, have shown that a marked contrast in this respect exists between cold-blooded and warm-blooded animals exposed to changes of temperature. In the cold-blooded animal, cold diminishes and heat increases the metabolic activity of the body ; as the temperature to which the animal is subjected rises or falls, so the consumption of oxygen and production of carbonic acid is increased or lessened. The body of a cold-blooded animal behaves in this respect like a mixture of dead substances in a chemist's retort: heat promotes and cold retards chemical action in both cases. Very different is the behavior of a warm-blooded animal. In this case, within a lower and a higher limit, cold increases and heat diminishes the bodily metabolism, as shown by the increased or diminished consumption of oxygen and production of carbonic acid as the temperature falls or rises. In these animals there is obviously a mechanism of some kind, counteracting and indeed overcoming those more direct effects which alone obtain in cold-blooded animals. And that this mechanism is of a nervous nature, is indicated by the following facts.

When a warm-blooded animal is poisoned by urari, the temperature falls and the metabolism, measured by the consumption of oxygen and the production of carbonic acid, sinks also; and that the latter is the cause, not the effect, of the former is shown by the fact that the metabolism continues to fall though loss of heat be prevented by surrounding the animals with wrappings of cotton-wool. In such a urarized animal, exposure to higher temperatures augments, and exposure to lower temperatures diminishes, metabolism; the urarized warm-blooded animal, in fact, behaves like a cold-blooded animal. Similar, but perhaps not such striking results are gained by division of the medulla oblongata. After this operation the temperature of the body sinks, and the fall, though partly due to increased loss of heat by the skin, caused by the dilated condition of the cutaneous vessels, is also accompanied by diminished metabolism and is, therefore, in part due to diminished production of heat. And when an animal is in this condition, exposure to higher temperatures increases, and exposure to lower temperatures diminishes the bodily metabolism. We can best explain these results by supposing that, under normal conditions, the muscles, which, as we have seen, contribute so largely to the total heat of the body, are placed, by means of their motor nerves and the central nervous system, in some special connection with the skin, so that a lowering of the temperature of the skin leads to an increase, while a heightening of the temperature of the skin leads to a decrease, of the muscular metabolism. Further, though the matter has not yet been fully worked out, the centre of this thermotaxic reflex mechanism appears to be placed above the medulla oblongata, possibly in the region of the pons Varolii. When urari is given, the reflex chain is broken at its muscular end; when the spinal cord is divided, the break is nearer the centre. Whether we should conclude that the working of this reflex mechanism is of such a kind that cold to the skin excites the centre to a heat-producing activity, or of such a kind that warmth to the skin inhibits a previously existing automatic activity of the centre, may be left for the present undetermined.

We may add that the muscular metabolism which thus helps to regulate temperature, need not involve visible muscular contractions, though the heat given out by a muscle will be temporarily increased at every contraction; and that the regulative nervous mechanism may apparently be overborne by an exposure to too great heat or cold. When, for instance, the cold to which the animal is exposed becomes excessive, the reaction of the thermotaxic nervous system is powerless against the depressing direct effects, and the metabolism, together with the temperature, sinks.

Lastly, we have increasing evidence that the phenomena of fever are due, not merely to a derangement of the regulation by loss, though this may be a factor, but also, and indeed chiefly, to an increased production of heat; for in fever, the production of carbonic acid, and the consumption of oxygen, that is to say, the metabolic changes of the tissues, are increased.

We may regard it then as established that such a thermotaxic nervous mechanism does exist, and the importance of such a mechanism in explaining not only the maintenance of the normal temperature, but the abnormal variations of temperature in disease can hardly be exaggerated. Much, however, still requires to be learnt before we can speak with full confidence as to its exact nature, or expound with certainity the details of its work.

By regulative mechanisms of this kind the temperature of the warm-blooded animal is maintained within very narrow limits. In ordinary health the temperature of man varies between 36° and 38°, the narrower limits being 36.25° and 37.5°, when the thermometer is placed in the axilla. In the mouth, the reading of the thermometer is somewhat (0.25° to 1.5°) higher; in the rectum it is still higher (about 0.9°) than in the mouth. The temperature of infants and children is slightly higher, and much more susceptible of variation than that of adults, and after 40 years of age the average maximum temperature (of health) is somewhat lower than before that epoch. A diurnal variation, independent of food or other circumstances, has been observed, the maximum ranging from 9 A.M. to 6 P.M., and the minimum from 11 P.M. to 3 A.M. Meals cause sometimes a slight elevation, sometimes a slight depression, the direction of the influence depending on the nature of the food—alcohol seems always to produce a fall. Exercise and variations of external temperature, within ordinary limits, cause very slight change, on account of the compensating influences which have been discussed above. The rise from even active exercise does not amount to 1° C.; when labor is carried to exhaustion, a depression of temperature may be observed. In travelling from very cold to very hot regions a variation of less than a degree occurs, and the temperature of tropical inhabitants is practicallly the same as of those dwelling in arctic regions.

When external cold or warmth passes certain limits, or when during the application of these agents the regulative mechanisms are interfered with, the temperature of the body may be lowered or raised until death ensues. When the cold or warmth applied is not very great, as in cold and warm baths, it has been noticed that the temperature is more easily raised by warmth than depressed by cold. Death ensues from extreme cold by a depression of the activities of all the tissues, more especially of the

nervous; asphyxia is produced in animals when the fall of temperature is rapid. Puppies can be recovered after the temperature in the rectum has fallen to about 4° or 5° C., and hybernating mammals may be cooled with impunity down to nearly freezing point. When external warmth is brought to bear on a mammal in such a way as to cause a rise of temperature in the body, death ensues when an elevation of about 6° or 7° C. above the normal is reached. The exact cause of the death has not been as yet sufficiently explained. It cannot be due, as has been suggested, to the muscles entering into rigor caloris, for the animals frequently succumb before this takes place. A high temperature makes the heart irregular, and finally stops its beat, but probably other tissues are also injuriously affected, so that death cannot be attributed to the stoppage of the heart alone.

One of the most marked phenomena of starvation is the fall of temperature, which becomes very rapid during the last days of life. Indeed, the low temperature of the body is a powerful factor in bringing about death, for life may be much prolonged by wrapping a starving animal in some bad conductor, so as to economize the bodily heat.

SEC. 5.—THE INFLUENCE OF THE NERVOUS SYSTEM ON NUTRITION.

In the preceding sections we had more than once to refer to the possibility of the nervous system having the power of directly affecting the metabolic actions of the body, apart from any irritable, contractile, or secretory manifestations. Thus the phenomena of diabetes cannot, at present at all events, be satisfactorily explained as a purely vaso-motor effect, and the production of heat is, as we have seen, under the special guidance of the nervous system. In the case of the salivary glands, we meet with the striking fact that when all the nerves of a gland have been divided, the gland enters into a peculiar condition during which it pours forth a continuous, so-called " paralytic " secretion, while ultimately the tissue of the gland degenerates. This result differs, perhaps, from the wasting of a muscle which follows upon severance of its motor nerve, since this may be, partly at all events, explained by the fact that the muscle is no longer functional; and, indeed, if the muscle is rendered functional, if it is directly stimulated for instance from time to time with a galvanic current, the atrophy may be, for a while at least, postponed, though, as we have seen (p. 123), the postponement is probably not indefinite. But the salivary gland, at all events in the case in question, is functional, it does go on secreting; nevertheless, in

the absence of its usual nervous guidance its nutrition becomes profoundly affected. We are not justified in saying that in this case the nutrition of the salivary cell is directly dependent on the nervous system, because all biological studies teach us that the growth, repair, and reproduction of protoplasm may go on quite independently of any nervous system, and the nutrition of the nervous system itself cannot be dependent on the action of that system on itself; but we may go so far as to infer that the nutrition of the salivary cell is in the complex animal body so arranged to meet the constantly recurring influences brought to bear on it by the nervous system, that when those influences are permanently withdrawn, it is thrown out of equilibrium ; its molecular processes, so to speak, run loose, since the bit has been removed from their mouths. And we might expect that similar instances would be met with where nutrition became abnormal after the removal of wonted nervous influences. Such instances, indeed, are not uncommon. And there are many pathological phenomena, inflammation itself to begin with, which seem inexplicable, except when regarded as the result of nervous action. As examples, we might mention the rapid and peculiar degeneration of and loss of contractility in the skeletal muscles in certain affections of the spinal cord, the changes in the muscles being more rapid and profound than in the nerves ; the phenomena of bedsores, especially the so-called acute bedsores of cerebral apoplexy ; some at least of the cases of vesical affections attendant on spinal or cerebral diseases or injuries ; the more rapid atrophy and loss of contractility in muscles which follow upon contusions of nerves as compared with the effects of simple section of nerves ; the occurrence of certain eruptions, such as lichen, zona, ecthyma, etc., in various spinal or cerebral diseases, frequently accompanied, as in maladies affecting the posterior cornua, with intermittent pains, and indeed the general phenomena, and especially the topography of the eruption, of a large number of cutaneous diseases. In all these cases, however, there are many attendant circumstances to be considered before we can feel justified in speaking of any direct influence of the nervous system on nutrition, of any specific action of what have been called " trophic " nerves. Perhaps the instance which has been best worked out is the connection of the nutrition of the eye and face with the fifth or trigeminal nerve. When in a rabbit the trigeminus is divided in the skull there is loss of sensation in those parts of the face of which it is the sensory nerve. Very soon, within twenty-four hours, the cornea becomes cloudy, and this is the precursor of an inflammation which may involve the whole eye and end in its total disorganization. At the same time the nasal chambers of the same side are inflamed, and very

frequently ulcers make their appearance on the lips and gums. Seeing how delicate a structure the eye is, and how carefully it is protected by the mechanisms of the eyelids and tears, it seems reasonable to suppose that the inflammation in question might simply be the result of the irritation caused by dust and contact with foreign bodies to which the eye, no longer guided and protected by sensations, these being destroyed by the section of the nerve, became subject. In the same way the ulcers on the lips and gums might be explained as injuries inflicted by the teeth on those structures in their insensitive condition. And some observers maintain that the inflammation of the eye may be greatly lessened or altogether prevented if the organ be carefully covered up and in all possible ways protected from the irritating influences of foreign bodies. Other observers, however, have failed to prevent the inflammation in spite of every care. This negative result is in itself no strong argument, but the question cannot yet be considered as entirely cleared up.

In a mammal division of both vagi is followed by pneumonia (inflammation of the lungs) ending in death. This has been adduced as an instance of the trophic action on the pulmonary tissues of certain fibres of the vagi, but the real explanation seems to be that owing to a paralysis of the œsophagus and larynx caused by section of the vagi, food accumulating in the pharynx passes into the air-passages and so sets up the pneumonia. In birds death follows sometimes from pneumonia of a similar causation, but more frequently from inanition on account of the food not being able to enter the stomach. The immediate cause of death, however, appears in many cases at all events, both in birds and mammals to be a paralysis of the heart, and the histological changes (acute fatty degeneration) observable in the cardiac muscles are of such a character as to suggest a trophic action of the vagus fibres on the fibres on that tissue.

Other instances of nerves manifesting even a doubtful trophic action as the result of experimental interference are rare, yet there seems to be no reason why the fifth nerve or the vagus should be conspicuous in possessing trophic fibres. When the sciatic nerve of the frog is divided, no nutritive alterations beyond those explicable as the result of loss of function are observed, and indeed the majority of the effects on growth and nutrition resulting from the section of nerves, or from paralysis, can be referred to the absence of the usual functional activity, accompanied in some cases with an altered vascular supply. It must be remembered, however, that functional activity is itself the result of metabolic and therefore nutritional changes, and in cases of inhibition, as, for instance, in the action of the vagus on the heart, we seem to have illustrations of a nerve producing

metabolic changes leading not to the exercise but to the arrest of functional activity.

Taking all things into consideration, we may venture to say that the numerous phenomena of disease, joined to the facts mentioned above, turn the balance of evidence in favor of the view that some more or less direct influence of the nervous system on metabolic actions, and so on nutrition, will be established by future inquiries.

SEC. 6.—DIETETICS.

We may sum up the main results of the previous sections somewhat in the following way. Although the body consists, like the food, of proteids, fats, and carbohydrates, yet the conversion of the one into the other is not direct. Assimilation does not proceed in such a way that the proteids of the food all become the proteids of the body, the fats of the food the fats of the body, and the starch and sugar of the food the glycogen, dextrin, and sugar of the body. We cannot even say that the non-nitrogenous food supplies alone the non-nitrogenous parts of the body, and that the nitrogenous food remains as the sole source of the nitrogenous tissues. We have seen that under all circumstances a certain quantity of proteid food is immediately metabolized, probably while still within the alimentary canal, and that an excess of proteid food may lead to the accumulation of bodily fat. On the other hand, we find that a large proportion of the carbonic acid of the egesta comes from the metabolism taking place in nitrogenous tissues, such as muscle; and we have had proof that the energy set free by muscular contraction may be far greater than could be supplied by the proteid food taken, and that, therefore, the non-nitrogenous factors of the metabolism which set free the energy must have *ultimately* come from non-nitrogenous food. We have abundant evidence that the various food-stuffs become more or less metabolized, and their elements more or less rearranged and mixed, before they appear as constituents of the bodily tissues.

We have seen that the oxidations of the body are, as in the case of muscle, of a peculiar character, and carried on by the tissues themselves. While at present we should be hardly justified in denying that any oxidations at all take place in the blood-plasma, such as do occur must be slight in amount as compared with those going on in the tissues. We might also say that one body only, viz., lactic acid, presents itself as a substance likely to be directly oxidized in the blood itself; and even with regard to this the evidence is as much against as for any such

direct oxidation taking place.   The great mass of the oxidation of the body is of an indirect kind, determined by the activity of the several tissues.   The blood serves as an oxygen carrier for the tissues; and it is not itself the large combustion agent it was once thought to be.   The tendency of all recent inquiries is to show that the body cannot be compared, either as a whole, or in its parts, to a furnace for the direct combustion of combustible food.   On the contrary, we are driven nearer and nearer to the conclusion that all food which has become absorbed into the blood must become tissue before it becomes waste product, and only becomes waste product through a metabolism of the tissue. When we say "become tissue," we must leave it at present wholly undecided how far the constant metabolism which this view demands affects the so-called structural elements of the more highly organized tissues; it is quite open, however, as we have already suggested, for us to imagine that in muscle, for instance, there is a framework of more stable material, giving to the muscular fibre its histological features, and undergoing a comparatively slight and slow metabolism, while the energy given out by muscle is supplied at the expense of more fluctuating molecules which fill up, so to speak, the interstices of the more durable framework, and the metabolism of which alone is large and rapid.

The characteristic feature of proteid food is that it increases the oxidative, metabolic activity of the tissues, leading to a rapid consumption, not only of itself, but of non-nitrogenous food as well.   Where, therefore, a rapid renewal of the tissues is sought for, an excess of proteid food may be desirable.   But it must be borne in mind that by the very nature of its rapid metabolism, proteid food must tend to load the body with the so-called extractives—*i. e.*, with nitrogenous crystalline bodies.   How far these are of use to the body, and what part they play, are at present unknown to us.   That they are of some use, is suggested by the beneficial effects of the *extractum carnis* when taken as food in conjunction with non-nitrogenous material, though it is possible that the dietetic value of this preparation may be due to the small amount of non-crystalline extractives which it contains. That when in excess these nitrogenous products may be highly injurious is indicated by the little we know of the connection between the symptoms of gout and the presence of uric acid.   A large meal of proteid material must tax the system to the utmost in getting rid of or stowing away the nitrogenous crystalline bodies arising through changes either in the alimentary canal or in the liver.

One value of fats and carbohydrates lies in their being sources of energy, more than three-fourths of the normal income of potential energy coming from them (p. 536); and, as we have seen,

they are *ultimate* sources of muscular energy as well as of heat. But their great characteristic is that they do not, like proteid food, excite the metabolic activity of the body. Hence, to a far greater extent than is the case with proteid food, they can be retained and stored up in the body with comparative ease. The digested elements of fatty or carbohydrate food which go to form the protoplasm of adipose tissue, become part and parcel of a substance which can perform its metabolism without any explosive expenditure of energy, and which, therefore, instead of giving rise to bodies demanding immediate excretion from the system, can deposit its metabolic products as apparently little, but, as we have seen in reality, greatly, changed fat. In this way the non-nitrogenous food of to-day is rendered available for future and even distant wants.

In comparing fats with carbohydrates, we can only point to the much greater potential energy of the former than of the latter, weight for weight (see p. 536).

A diet may be chosen either for the simple maintenance of health, or for the sake of muscular energy, or for fattening purposes. For the first purpose there is, we may suppose, a normal diet; and in the case of man, instinct and experience have probably not erred far in choosing some such proportions as those given on p. 525. If, as we have urged, all food becomes tissue before it leaves the body as waste product, the dominant principle of all nutrition, and the ultimate tribunal of all questions of diet, must be the individual character of the tissue, the idiosyncrasy of the body. The same mysterious qualities which cause the same blood-plasma to become here a muscle, and there a secreting cell, convert the same food into the body of a man or of a sheep. All the simpler and more general laws of metabolism are made subservient to more intricate and special laws of protoplasmic construction. We can only speak of a normal diet in the same way that we speak of the average intelligence of man.

In seeking to supply such a normal diet out of ordinary articles of food, we must bear in mind that the nutritive value of any substance, estimated in terms of the potential energy of the proteids, fats, or carbohydrates it contains, must, of course, be corrected by its digestibility. One gramme of cheese has, as far as potential energy is concerned, an exceedingly high value; but the indigestibility of cheese brings its nutritive value to a very low level. Here too the factor of idiosyncrasy makes itself exceedingly felt.

In feeding for fattening purposes the comparatively cheap carbohydrates are, of course, chiefly depended on. If the view mentioned on p. 534 be correct, that the fat really stored up all comes from proteid metabolism, an equivalent of this food-stuff

must always be given.   If, as seems probable, this view is a too hurried generalization, there still remains the possibility that for economical fattening, with the least waste, a certain proportion between the nitrogenous and non-nitrogenous foods must always be maintained.

From what has been previously said it is evident that proteid food is not the only food stuff to be regarded in selecting a diet for muscular labor.   We should, however, equally err in the opposite direction if we selected exclusively non-nitrogenous food on which to do work, since, as we have seen, there is no evidence that the fats or carbohydrates are the *direct*, though they may be in part the *ultimate* source of muscular energy.   Considering how complex a thing strength is, how much it depends on the vigor of parts of the body other than the muscles, a normal diet, calculated to develop equally all parts of the body, is probably the best diet for active labor.   It is possible, however, that an excess of proteid food, by reason of the renewal of tissue caused by its metabolic activity, may be, in such cases, of service.

Lastly, the several saline matters, including the extractives of animal and vegetable food, are no less essential elements of a diet than proteids, fats, or carbohydrates.   Of use, not for the energy they themselves possess, but by reason of their regulating the energy of the food-stuffs more strictly so-called, they are necessary to life—the body in their absence fails to carry out its usual metabolism, and disease if not death follows.

The dietetic superiority of fresh meat and vegetables depends in part on their still retaining these various saline and extractive matters.   A diet from which phosphorus (or even possibly phosphates), or chlorides, or potash, or soda salts are absent, is, as soon as the store of the substance in the body is exhausted, useless for nutritive purposes.   Calcium and magnesia may, to a certain extent, be replaced by bases closely allied to them; but the metabolic *rôle* of phosphorus or of sulphur cannot be taken up by an analogous body; and, as is illustrated by their distribution in the body, the physiological functions of potash and soda are widely different if not antagonistic, closely allied as are these two alkalies when regarded from a chemical point of view. Like medicines and poisons—and, indeed, they are in a manner natural medicines—the action of these bodies depends in part on their dose.   Indispensable as are potash salts to the economy, a large dose of them is injurious; and a dog fed on nothing but Liebig's extract dies sooner than a dog not fed at all, on account of the potash salts of the extract exerting their deleterious influence in the absence of the food whose metabolism their function is to direct.

BOOK III.

THE CENTRAL NERVOUS SYSTEM AND ITS INSTRUMENTS.

CHAPTER I.

[*General Arrangement of the Nervous System.*

THE nervous system consists of two secondary divisions: the *cerebro-spinal* and the *sympathetic* or *ganglionic.*

The cerebro-spinal system embraces a central system, which includes the brain and spinal cord, and a peripheral system, consisting of the cranial and spinal nerves and their ganglia. The central system is known as the cerebro-spinal axis (Fig. 165), and it comprises all the organs presiding over the functions which are characteristic of *animal* life, such as volition, special sensation, etc. The cranial and spinal nerves serve as a means of intercommunication between the central nervous system and the peripheries by conducting impulses to and from the centres.

The brain is composed of the cerebrum and cerebellum and the ganglia forming part of the former; and the medulla oblongata and pons Varolii, by which they are connected to the spinal cord. The spinal cord is that portion of the cerebro-spinal axis which is situated within the spinal canal between the foramen magnum and the second lumbar vertebra. Above, it is continuous with the medulla oblongata; below, it terminates in an extremity of gray matter, which is termed the *filum terminale.*

The cranial nerves arise from the under surface of the cerebrum and medulla oblongata, and make their exit through the foramina in the base of the cranial vault. The spinal nerves arise by two roots, anterior and posterior, from the sides of the spinal cord, and make their exit through the intervertebral foramina. On each posterior root is a ganglion.

The *ganglionic* or *sympathetic* system consists of a double chain

of ganglia, which extends from the base of the brain to the pelvic cavity. Each chain is situated to the front and side of the ver-

FIG. 165.
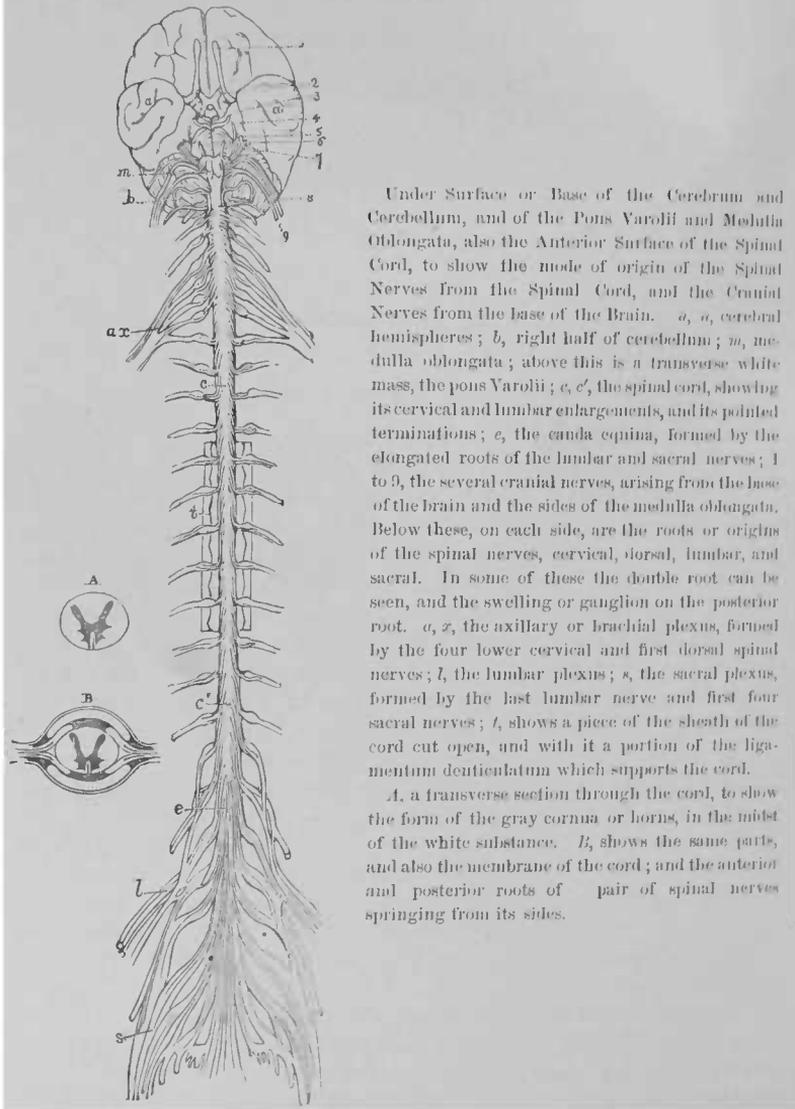
Under Surface or Base of the Cerebrum and Cerebellum, and of the Pons Varolii and Medulla Oblongata, also the Anterior Surface of the Spinal Cord, to show the mode of origin of the Spinal Nerves from the Spinal Cord, and the Cranial Nerves from the base of the Brain. a, a, cerebral hemispheres; b, right half of cerebellum; m, medulla oblongata; above this is a transverse white mass, the pons Varolii; c, c', the spinal cord, showing its cervical and lumbar enlargements, and its pointed terminations; e, the cauda equina, formed by the elongated roots of the lumbar and sacral nerves; 1 to 9, the several cranial nerves, arising from the base of the brain and the sides of the medulla oblongata. Below these, on each side, are the roots or origins of the spinal nerves, cervical, dorsal, lumbar, and sacral. In some of these the double root can be seen, and the swelling or ganglion on the posterior root. a, x, the axillary or brachial plexus, formed by the four lower cervical and first dorsal spinal nerves; l, the lumbar plexus; s, the sacral plexus, formed by the last lumbar nerve and first four sacral nerves; t, shows a piece of the sheath of the cord cut open, and with it a portion of the ligamentum denticulatum which supports the cord.

A, a transverse section through the cord, to show the form of the gray cornua or horns, in the midst of the white substance. B, shows the same parts, and also the membrane of the cord; and the anterior and posterior roots of   pair of spinal nerves springing from its sides.

tebral column. The ganglia are intimately connected with the adjacent ganglia and with the cerebro-spinal axis by means of

nervous cords. The nerves given off from the ganglionic system are principally distributed to the viscera of the thoracic, abdominal, and pelvic cavities, and hence are more intimately connected with the functions of organic life, such as are manifested in growth and nutrition. The ganglionic system has, therefore, been termed the system of *organic* life.

The Physiological Anatomy of the Nerve-tissues.

The nervous system is composed of two elementary nervous structures : the *vesicular* matter, and the *fibrous* matter. The *vesicular* matter is distinguished from the fibrous matter by its characteristic reddish-gray color, its vesicular structure, its softer consistency, and greater vascularity. It consists of an aggregation of vesicles, which are called the ganglionic or nerve corpuscles, and is never found in the nerves. These corpuscles are each composed of a delicate wall, which encloses granular pigmented contents, with an eccentric nucleus, and a variable number of nucleoli.

Fig. 166.
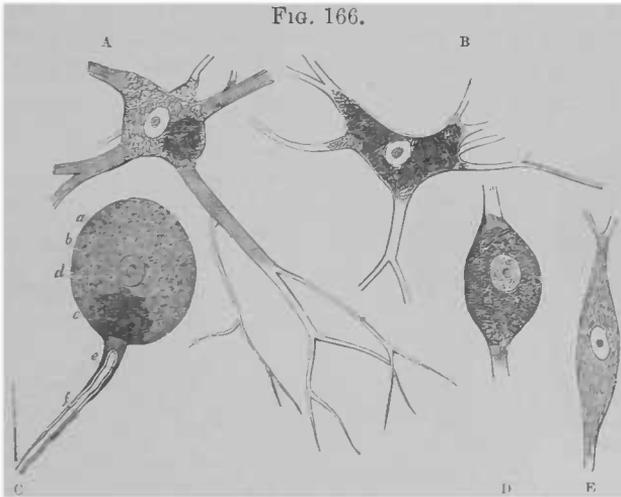
Various forms of Ganglionic Vesicle ; ., B, large stellate cells, with their prolongations, from the anterior horn of the gray matter of the spinal cord ; c, nerve-cell with its connected fibre, from the anastomosis of the facial and auditory nerves in the meatus auditorious internus of the ox ; a, cell-wall ; b, cell contents ; c, pigments ; d, nucleus ; e, prolongation forming the sheath of the fibre ; f, nerve-fibre ; ° nerve-cell from the substantia ferruginea of man ; E, smaller cell from the spinal cord ; magnified 350 diameters.

The nerve-cells are found in aggregated masses, embedded in a granular material, and having intermingled and connected with them some fibrous matter. In this condition they form the ganglia and the great centres of gray matter found in the brain and spinal cord. The vesicular matter alone is supposed to be

capable of generating nerve-force, and of disposing of impressions received from the periphery. The cells are of very irregular and diverse forms (Fig. 166), and generally possess one or more caudate processes or poles; hence they have been termed unipolar, bipolar, and multipolar. The processes intercommunicate with the processes of neighboring cells, or are continuous with the axis-cylinders (Fig. 172) of nerve-fibres. The apolar cells are probably undeveloped cells. The bipolar cells are found in the sympathetic ganglia, and in the ganglia of the posterior roots of the spinal nerves. Dr. Beale and other investigators found in the sympathetic ganglia of the frog very complex pyriform nerve-cells (Fig. 167), which have two fibres arising from their pointed extremity. One of the fibres (a) runs in almost a straight course to the cell; the other fibre (b) arises from the exterior of the cell, frequently as two filaments, which form several spiral turns around the axial fibre (a), and finally emerges from the capsules as a single fibre. Other investigators state that the straight fibre (Fig. 167, B, a) is continued into the nucleus, and that the spiral fibre (b) forms a plexus on the exterior of the cell, and may be traced to the nucleolus. The multipolar cells are found in all the ganglia, but are most numerous in the
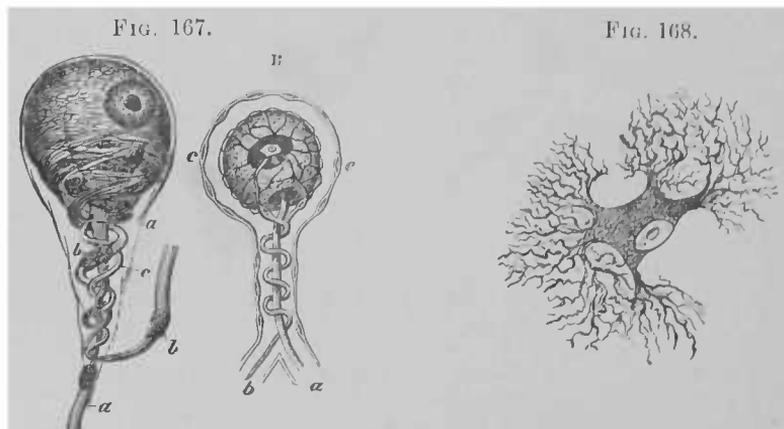
FIG. 167. FIG. 168.

FIG. 167.—Structure of a pyriform ganglionic nerve-cell. A, according to Beale ; B, according to Arnold.

FIG. 168.—Stellate Nerve-cell, from the Nucleus Cervicis Cornu (posterior vesicular column) of a Fœtus of six months. × 420. After BEALE.

gray matter of the cerebro-spinal centres. In the anterior cornua of the spinal cord they possess sometimes as many as twelve processes. The processes of some of the cells divide and subdivide so rapidly into smaller filaments that they form a close radiating plexus in the interstitial vesicular matter adjoining the cell (Fig. 168).

The *white* or *fibrous matter* composes the nerve-fibres forming the cranial and spinal nerves and the white strands of nervous matter which are found in the cerebro-spinal axis. The nerves are composed of bundles of fibres, which are called *funiculi*, and are enclosed in a fibrous sheath, the *perineurium;* the funiculi being separated from each other by an investing fibrous membrane formed by reflections inwards of the perineurium. Each funiculus is formed of a number of bundles of *fibres* or *tubules*, which according to Ranvier, are enclosed in a layer of flat epithelium cells (Fig. 169); this is, however, contradicted by some observers, who deem the cells a lining of lymphatic spaces. If these tubules are separated and individually examined during
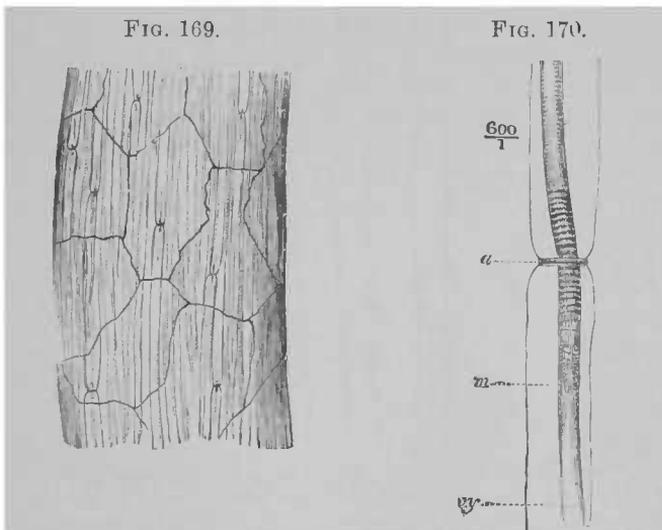
FIG. 169.—Funiculus of a Mouse after impregnation with Nitrate of Silver. Large flat epithelial cells are seen covering its surface. The explanation of the small crosses is seen by reference to the next figure. After RANVIER.

FIG. 170.—Nerve-fibre from the Sciatic Nerve of the Rabbit after the action of Nitrate of Silver. *a*, ring formed by thickened membrane of Schwann ; *m*, white substance of Schwann rendered transparent by glycerin ; *Cy*, axis-cylinder, which just above and below the level of the annular constriction presents the striæ of Frommann.

life they will appear to consist of a simple homogeneous transparent investment, which encloses a soft, transparent, structureless substance. Each tubule has a well-accentuated dark outline (Fig. 171, A). But after removal from the body, the lowered temperature or other influences cause the contents of the tubule to coagulate, and a double contour appears (Fig 171, B), which indicates that the tubules are not of a simple structure, but that they are composed of several elements. These are seen to be an

external or white portion and an internal or gray centre. When these changes are further advanced, or if pressure has been made, they assume a varicose appearance (Fig. 171, C), which is caused by the breaking down of the white matter into small segments or drops, and its collection in certain spots, thereby causing the tubule to swell. Further changes are afterwards observed when the substance of the interior will be seen to be collected in distinct masses. (Fig. 171, D.) The dark outline in B, Fig. 171, indicates the tube-sheath or *neurilemma*, which

FIG. 171.
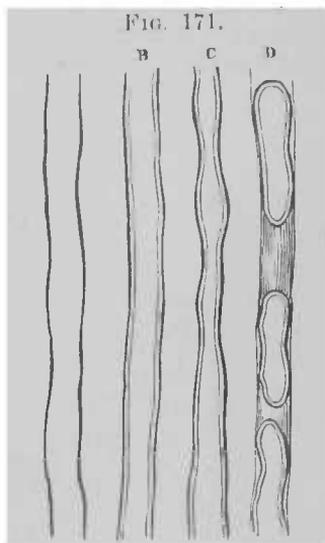
Primitive Nerve-tubules. A, a perfectly fresh tubule with a single dark outline. B, a tubule or fibre with a double contour from commencing post-mortem change. C, the changes further advanced, producing a varicose or beaded appearance. D, a tubule or fibre, the central part of which, in consequence of still further changes, has accumulated in separate portions of the sheath. After WAGNER.

encloses the *medullary substance* or *white substance of Schwann*, the inner boundary of which is indicated by the inner line. In the central portion of the medullary substance, corresponding to the axis, is a gray, flattened, threadlike filament, which is termed the *axis-cylinder*. (Fig. 172.) The fibres thus constructed are called the *medullated* nerve-fibres, in contradistinction to other fibres which possess no medullary substance, and hence are called the *non-medullated* fibres.

At intervals along the course of the tubule, annular constrictions are seen (Fig. 170). These appear to be due to a thickening of the neurilemma at the constricted point. The axis-cylinder passes through these constricted portions uninterruptedly, and at this position is marked by a number of transverse lines

called the striæ of Frommann. Between each of these constricted points a *nucleus* is found, which lies between the white substance of Schwann and the neurilemma. The *axis-cylinder* in the ganglion cells, and in the ultimate termination of the olfactory and optic nerves and some of the sympathetic, have been observed to be composed of a number of extremely attenuated varicose fibres, which are termed the *primitive nerve-fibrils* (Fig. 173).

The *non-medullated* fibres (gelatinous fibres of Remak) differ from the medullated, by the absence of the annular constrictions and of the double contour; by their smaller size, the greater number of nuclei found in their course, and by their grayish color. The non-medullated fibres constitute the entire portion of the olfactory and of some of the sympathetic nerves, and are found in variable quantity with the medullated fibres in the nerves of the cerebro-spinal

FIG. 172.

Diagram of Structure of Nerve-fibre

1, neurilemma; 2, white substance of Schwann; 3, axis-cylinder.

FIG. 173.
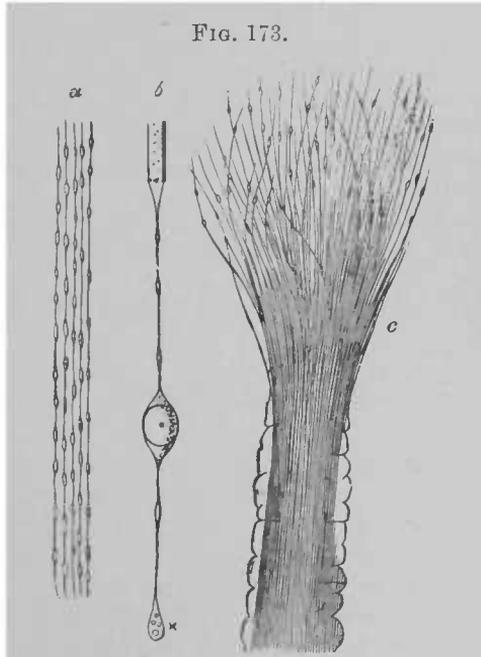
Primitive Nerve-fibrils. *a*, from the nervous fibre-layer of the retina; *b*, from the external granular layer of the retina, showing at *x* a large varicosity resulting from imbibition; *c*, from the olfactory nerve of the pike, showing a thick nerve enclosed in a sheath breaking up into fibrillæ.

system. In the cerebro-spinal nerves, especially at their central and peripheral extremities, other non-medullated fibres are found which are probably nothing more than the axis-cylinders of medullated tubules.

The nerve-fibres serve as a means of intercommunication between the centres or portions of them, and between the centres and peripheries. Each fibre is a continuous one between the periphery and centre, and although they may inosculate, they never form anastomoses. Each fibre, therefore, consists of a central and a peripheral extremity, the central extremity may properly be considered as the *root*; the peripheral extremity as the *peripheral termination*. Fibres which convey impressions from the centre to the periphery are called *efferent* or *motor* fibres; those conveying impressions from the periphery to the centre, *afferent* or *sensory* fibres.

The nerves terminate in *special* and *general* modes. As special modes they terminate in the tactile corpuscles (Fig. 144); the Pacinian corpuscles (Fig. 145); the terminal bulbs of Krause (Fig. 143), and in other terminal organs concerned in special sensation, which will be hereafter noticed. In the voluntary muscles they terminate in the *end-plates*. The mode of termination of the nerves in the involuntary muscles is as yet wrapped in obscurity; recent investigations, however, indicate that the fibres form plexuses, and finally terminate in the nuclei of the cells. In the glands, according to Pflüger, the axis-cylinder is continued into the gland-cell.

The general mode of termination is by the formation of extremely delicate plexuses, the filaments of which cannot be traced to any definite terminal point. The nerve-fibres are devoid of the white substance of Schwann at their ultimate terminations.]

SENSORY NERVES.

In studying the phenomena of motor nerves we are greatly assisted by two facts—First, that the muscular contraction by which we judge of what is going on in the nerve is a comparatively simple thing, one contraction differing from another only by such features as amount, rapidity, and frequency of repetition, and all such differences being capable of exact measurement. Secondly, that when we apply a stimulus directly to the nerve itself, the effects differ in degree only from those which result when the nerve is set in action by natural stimuli, such as the will. When we come, on the other hand, to investigate the phenomena of afferent nerves, our labors are for the time rendered

heavier, but in the end more fruitful, by the facts: First, that we can only judge of what is going on in an afferent nerve by the effects it produces in some central nervous organ, in the way of exciting or modifying reflex action, or modifying automatic action, or affecting consciousness; and we are consequently met on the very threshold of every inquiry by the difficulty of clearly distinguishing the events which belong exclusively to the afferent nerve from those which belong to the central organ. Secondly, that the effects of applying a stimulus to the peripheral end-organ of an afferent nerve are very different from those of applying the same stimulus directly to the nerve-trunk. This may be shown by the simple experience of comparing the sensation caused by the contact of any sharp body with a nerve laid bare by a wound, with that caused by contact of an intact skin with the same body. These differences reveal to us a complexity of impulses, of which the phenomena of motor nerves gave us not so much as a hint; but for the time being they increase the difficulties of our study.

An afferent impulse passing along an afferent nerve may, in certain cases, simply produce a change in our consciousness unaccompanied by any visible bodily movements; in other cases, it may give rise to reflex movements, or modifying existing reflex or automatic actions without causing any change in consciousness; in still other cases, it may bring about both results at the same time. An afferent nerve the stimulation of which gives rise to a sensation, and so leads to a modification of consciousness, may be more closely defined as a "sensory" nerve. There is, however, no distinct proof, having regard to the difficulties just mentioned, that the afferent fibres, which in the body are commonly used to cause or affect reflex action differ at all in kind from those whose function it is to modify consciousness. On the contrary, such evidence as we have goes to show that an appropriate stimulus of the same fibre may give rise to one or other or both events; and that whether the one or the other, or both, events occur depends on the condition of the central organ, and on the relation of its several parts to the afferent nerve. The stimulation of the same nerve (and there are no positive facts which would preclude us from saying "of the same fibre") may under certain circumstances, as for instance when the brain has been removed, simply cause a reflex action, and under other circumstances give rise merely to a sensation. Hence, an afferent nerve is frequently spoken of as a sensory nerve, even under circumstances where there is no evidence of consciousness being affected, because by a slight change of circumstances the same stimulation of the same nerve might give rise to a distinct sen-

sation ; the substitution of the specific for the general term being justified by the convenience of the former.

All the *spinal nerves* are mixed nerves, composed of afferent and efferent, of motor and sensory fibres. When a spinal nerve is divided, stimulation of the peripheral portion causes muscular contraction, of the central portion, a sensation (or a reflex action). At the junction of the nerve with the spinal cord, the sensory fibres are gathered into the posterior, and the motor fibres into the anterior root. The proof of this, which was first made known by Charles Bell and Majendie, their discoveries forming the foundation of modern nervous physiology, is simply as follows.

When the anterior root is divided, the muscles supplied by the nerve cease to be thrown into contractions either by the will, or by reflex action, while the structures to which the nerve is distributed retain their sensibility. During the section of the root, or when the proximal stump, that connected with the spinal cord, is stimulated, no sensory effects are produced. When the distal stump is stimulated, the muscles supplied by the nerve are thrown into contractions. When the posterior root is divided, the muscles supplied by the nerve continue to be thrown into action by an exercise of the will or as part of a reflex action, but the structures to which the nerve is distributed lose the sensibility which they previously possessed. During the section of the root, and when the proximal stump is stimulated, sensory effects are produced. When the distal stump is stimulated no movements are called forth. These facts demonstrate that sensory impulses pass exclusively by the posterior root from the peripheral to the central organs, and that motor impulses pass exclusively by the anterior root from the central to the peripheral organs.

An exception must be made to the above general statement, on account of the so-called recurrent sensibility which is witnessed in conscious mammals, under certain circumstances. It often happens that when the *peripheral* stump of the divided anterior root is stimulated, signs of pain are witnessed. These are not caused by the concurrent muscular contractions or cramp which the stimulation occasions, for they remain if the whole trunk of the nerve be divided some little way below the union of the roots above the origins of the muscular branches, so that no contractions take place. They disappear if the posterior root be also cut, and they are not seen if the mixed nerve-trunk be divided close to the union of the roots. The phenomena are probably due to the fact, that bundles of sensory fibres of the posterior root after running a short distance down the mixed trunk turn back

and run upwards in the anterior root, and by this recurrent course give rise to the recurrent sensibility.

Concerning the *ganglion* on the posterior root, we may say definitely that it is neither a centre of reflex nor of automatic action. Our knowledge concerning its function is almost limited to the fact that it is in some way intimately connected with the nutrition of the nerve. When a mixed nerve-trunk is divided, the peripheral portion degenerates from the point of section downwards towards the periphery. The central portion does not so degenerate, and if the length of nerve removed be not too great, the central portion uniting with the degenerating peripheral portion may grow downwards, and thus regenerate the nerve. This degeneration is observed when the mixed trunk is divided in any part of its course from the periphery to close up to the ganglion. When the posterior root is divided between the ganglion and the spinal cord, the portion attached to the spinal cord degenerates, but that attached to the gangloin remains intact. When the anterior root is divided, the proximal portion in connection with the spinal cord remains intact, but the distal portion between the section and the junction with the other root degenerates; and in the mixed nerve-trunk many degenerated fibres are seen, which if, they be carefully traced out, are found to be motor fibres. If the posterior root be divided carefully between the ganglion and the junction with the anterior root, the posterior root above the section remains intact, but in the mixed nerve-trunk are seen numerous degenerated fibres, which when examined are found to have the distribution of sensory fibres. Lastly, if the posterior ganglion be excised, the whole posterior root degenerates, as do also the sensory fibres of the mixed nerve-trunk. Putting all these facts together, it would seem that the growth of the motor and sensory fibres takes place in opposite directions, and starts from different nutritive or "trophic" centres. The sensory fibres grow away from the ganglion either towards the periphery, or towards the spinal cord. The motor fibres grow outwards from the spinal cord towards the periphery. This difference in their mode of nutrition is frequently of great help in investigating the relative distribution of motor and sensory fibres. When a posterior root is cut beyond the ganglion, or the ganglion excised, all the sensory nerves degenerate, and the sensory fibres, by their altered condition, can readily be traced in the mixed nerve-branches. Conversely, when the anterior roots are cut, the motor fibres alone degenerate, and can be similarly diagnosed in a mixed nerve-tract. When the anterior root is divided some few fibres in it do not, like the rest, degenerate, and when the posterior root is divided, a few fibres in the anterior root are seen to degenerate like those of the posterior

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root; these appear to be the fibres which give to the anterior root its "recurrent sensibility." By the same means in a mixed nerve like the vagus, the fibres which spring from the real vagus root may be distinguished from those proceeding from the spinal accessory, by section of the vagus and spinal accessory roots respectively; and in the mixed vago-sympathetic trunk, met with in many animals, the vagus fibres may be distinguished from the sympathetic, since, after a section of the mixed trunk, the former degenerate from above downwards, whereas the latter degenerate in an upward direction from the inferior cervical ganglion below to the superior cervical ganglion above; for the ganglia of the sympathetic behave in this respect like the spinal ganglia of the posterior roots. This method of diagnosis is often spoken of as the Wallerian method, after A. Waller, to whom we are indebted for the discovery of most of these facts.

In the *cranial nerves* the motor and sensory tracts are far less mixed than in the spinal nerves. The olfactory, optic, and acoustic nerves are purely sensory nerves. The fifth, glosso-pharyngeal, and vagus are mixed nerves; and it is stated that in the dog the afferent and efferent fibres of the vagus are gathered into two bundles so distinct that they may be separated by the knife, the afferent bundle lying to the outside of the efferent bundle. The facial and hypoglossal are for the most part motor (efferent) nerves, but contain sensory (afferent) fibres. The third, fourth, sixth, and spinal accessory are exclusively motor (efferent) nerves. These statements refer to what are commonly looked upon as the trunks of the respective nerves. More exactly speaking, the sensory fibres of the facial come from the fifth, pneumogastric, and glosso-pharyngeal nerves, so that the facial proper is in reality a purely motor nerve. So, likewise, is the hypoglossal, its sensory fibres coming from the fifth, pneumogastric, and three upper cervical nerves. The fifth is a mixed nerve entirely on the plan of a spinal nerve, having distinct motor and sensory roots. The glosso-pharyngeal seems to be essentially a sensory nerve, its motor filaments springing from the fifth and facial nerves. Concerning the vagus, some have maintained that the pneumogastric root proper is entirely sensory (afferent), and that all the efferent functions of the vagus are dependent on the fibres of the spinal accessory which join it. To this point we shall return when we come to consider briefly the special functions of the several nerves.

We have already stated (p. 139) that isolated pieces of motor and of sensory nerves behave exactly alike as far as all the physical manifestations attendant on the passage of a nervous impulse are concerned; the current of action makes its appearance in the same way, and seems to have the same characters in

both kinds of nerves. The same is also true, as far as we know, of nerves within the body.

Moreover, the rate at which nervous impulses travel appears to be about the same in motor and sensory nerves; at least, we have no evidence of any fundamental difference in this respect between the two. We have seen that the velocity of a nervous impulse in the motor nerve of a frog is about 28 metres per second. The velocity of a motor impulse in man, as judged by the difference of the latent period of the contraction of the thumb-muscles, when stimulation is brought to bear on the motor nerve at the wrist, or high up in the arm, is about 33 metres per second. In warm-blooded animals, however, the rate of transmission of motor impulses is very variable, being in particular closely dependent on temperature, and probably also on other circumstances. Thus it may range from as low as 30 m., when the nerve is cooled, to as high as 90 m., when it is warmed. The velocity of a sensory impulse is estimated by measuring the time taken between a stimulus being brought to bear on some sentient surface, as the skin, and the making of a signal by the individual experimented on at the instant that he feels the stimulus. The time taken up in the sensory impulse becoming converted into a sensation after reaching the nervous central organs, in the mental operation of determining to make the signal, and in the effort of making the signal, corresponds in a way to the purely muscular portion of the latent period in the experiment for determining the velocity of a motor impulse. The application of the stimulus and the making of the signal (ex. gr., closing a galvanic circuit) being both recorded on a rapidly travelling surface, the time taken up in the whole operation can be easily measured; and the difference between the time taken when the stimulus is applied to some spot separated from the central nervous system by a short piece of nerve—ex. gr., the top of the thigh, and that taken when a long piece of nerve intervenes—ex. gr., when the stimulus is applied to the toe, will give the time required for the sensory impulse to pass along a piece of sensory nerve as long as the difference of length between the above two nerves; from which the velocity can be calculated. Observations carried on in this way have led to most discordant results, varying from 26 metres to 94 metres, or even more, per second. The difference here is far too great to allow any value to be attached to an average. When it is remembered how complex are all the central nervous operations in these instances, as compared with the changes going on in a muscle during the latent period of its contraction, and how these central operations might vary according as one or other spot of skin was stimulated, quite independently of the length of nerve between the centre and the spot stimu-

lated, these discrepancies will not be wondered at; and it may
fairly be concluded that the velocity of a sensory impulse does
not materially differ from that of a motor impulse.

There are, however, certain phenomena which might at first
sight be interpreted as indicating that afferent and efferent nerve-
fibres behave differently towards stimuli. We have already
(p. 123) stated that, according to most observers, when an ordi-
nary motor nerve, such as a nerve supplying a muscle, is heated,
no indications of the generation of nervous impulses, no con-
traction of the muscle, for instance, are observed. The heat
does not act as a stimulus; it may increase the irritability of
the nerve for the time being, but apparently cannot originate
the explosive discharge which we call an impulse. We have
also seen that during the passage of a constant current along the
nerve of a muscle-nerve preparation no contractions are visible;
no impulses, save in certain particular cases, are generated, so
long as the current is not suddenly varied in strength. But it
has been found that when afferent nerve-fibres, such as those in
the central stump of the divided sciatic or in the central stump
of the vagus, are heated to 45° or 50° events occur, clearly
proving that impulses are generated in the afferent fibres by the
elevation of temperature. In the case of the sciatic the animal
shows sign of pain, the blood-pressure is affected, etc.; and in
the case of the vagus the heart is slowed by reflex inhibitory
impulses passing down the other, intact, vagus, though heating
the peripheral instead of the central stump of the divided vagus
has no effect whatever on the heart. Similarly when the same
nerves or other nerves containing afferent fibres are submitted
to the action of the constant current, there are like evidences of
the continued generation of nervous impulses during the whole
time of the passage of the current, even though it be kept as
uniform in strength as possible. On the other hand, many
chemical substances which act as powerful stimuli to motor
nerves are ineffectual towards afferent fibres. These results,
however, until the contrary is proved by further inquiries into
the phenomena attending the generation and transmission of
nervous impulses, may be taken as indicating not so much that
the afferent and efferent fibres are themselves acted upon in a
different way by heat or by the constant current as that the
molecular disturbances generated in both cases have different
effects according as they impinge upon a central or a peripheral
mechanism. We can readily imagine that molecular disturbances
which would be impotent to stir the sluggish muscular substance
to a contraction, and thus, so to speak, be lost upon the muscle,
might produce a very great effect on the more sensitive and
mobile material of the central nervous system. We may for the
present, therefore, conclude that there is no distinct proof of an

absolute difference between afferent and efferent fibres, but we must at the same time be cautious not to consider the grosser phenomena, presented by a muscle-nerve preparation, as a satisfactory test of all the changes which may take place in a nerve-fibre. The necessity of this caution will be almost immediately illustrated from another point of view.

The apparent identity in function between afferent and efferent fibres, taken into consideration with the facts just mentioned concerning the regeneration of nerves, suggests the inquiry whether by a change of the peripheral or central organs a motor nerve can be converted into a sensory nerve, or *vice versa*. Experiments made with a view of obtaining a functional union between purely motor and sensory nerves have, in the hands of most observers, failed. And, though an apparent union between the central portion of a divided lingual (sensory) nerve and the peripheral portion of a divided hypoglossal (motor) nerve has been accomplished, with the result that stimulation of the lingual trunk produced movements in the tongue, the case breaks down upon examination. In the first place, though the nerves appeared to have united, there was no actual union between the lingual and hypoglossal fibres, but degeneration of the latter, and a growth downward of the former ; in the second place, the movements of the tongue when the lingual trunk was stimulated appear to have been brought about by stimulation not of the sensory, true lingual, fibres, but of motor (chorda tympani) fibres running in the lingual trunk.

We have already seen (p. 139) that a sensory nerve in its simplest form may be regarded as a strand of eminently irritable protoplasm, forming a link between a superficial cell which alone is subject to extrinsic stimuli, and a central (reflex or automatic) cell which receives stimuli, chiefly in the form of nervous impulses proceeding from the former along the connecting strand. In the earliest stages of the development of a sensory nervous system, the superficial sensory cell is susceptible of stimuli of all kinds, provided they are sufficiently strong; and probably all the impulses which it transmits to the central cell resemble each other very closely, differing only in degree. It is obvious, however, that the economy would gain by a further division of labor, by a differentiation of the simple uniform superficial cell into a number of cells, each of which was more susceptible to particular stimuli than its fellows. Thus one cell, or rather one group of cells, would become eminently susceptible to the influence of light : in them the impact of rays of light would give rise to nervous impulses more readily than in the other groups ; another group would develop a sensitiveness to waves of sound, and so on. In this way, the primary homogeneous bodily surface would

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be differentiated into a series of *sense-organs*, disposed and arranged among ectodermic cells, the purpose of the latter being simply protective, and, therefore, not demanding the existence of any direct connection with the central nervous system. Similar but less highly marked differentiations would be established in the endings of the afferent nerves connecting the central nervous system with the internal surfaces and parts of the body.

Moreover, it is obvious that the sensory impulses transmitted to the central nervous system by these differentiated sense-organs will probably be themselves largely differentiated. Just as the impulses which pass along a motor nerve differ according to the nature of the stimulus which is applied to the nerve (whether, for instance, the stimulus be a single induction-shock, or several shocks repeated slowly, or several shocks repeated rapidly, and so on, the effect on the muscle being in each case a different one), so also, and even to a much greater degree, do the impulses generated by light in a visual sense-organ in all probability differ from those generated by simple pressure in a tactile sense-organ.

And since these various sensory impulses have much work to perform on arriving at the central nervous system, in the way of influencing the multitudinous molecular operations going on in the central cells, and of affecting consciousness, this differentiation of sensory organs and sensory impulses will naturally he accompanied by a corresponding differentiation of those central cells which the impulses first reach on arriving at the central organ. Those cells, for instance, of the central nervous system which first receive the particular nervous impulses coming from the visual sense-organs, will be set apart for the task of so modifying and preparing those impulses as to adapt them in the best possible way for the work which they have to do. Hence, each *peripheral* sense-organ will be united by means of its nerve with a corresponding *central* sense-organ, the former being able to affect various parts of the central nervous system only through the medium of the latter. And we have evidence, at least as far as relates to all the central nervous operations in which consciousness is concerned, that such central sense-organs do really exist. For of the total characters which belong to an affection of consciousness by means of any of the sense-organs—*i. e.*, which belong to any special sensations—we find that while some are gained during the rise of the sensory impulses in the peripheral sense-organ, others first appear in the central sense-organ in the course of the changes through which the sensory impulses give rise to a sensation. Thus a stimulus of any kind applied to the optic nerve along any part of its course, if it is able to start any impulses at all, gives rise to a sensation of light and precisely

the same stimulus applied to the acoustic nerve along any part of its course gives rise to a sensation of sound; and so on. All the evidence we possess goes against the view that a piece of optic nerve, deprived of both its peripheral and central endings, differs in function from a similarly isolated piece of acoustic nerve; such facts as are within our knowledge go to show that the disturbances generated in a piece of optic nerve by a galvanic current are the same as those generated in a piece of acoustic nerve. We are, therefore, driven to the conclusion that the difference which appears when the central endings are intact, arises in the central organs.

In all these differentiated sensory mechanisms, or special senses as they are called, we have then to deal with two elements; the peripheral sense-organ, in which we have to study how the special physical agent gives rise to special sensory impulses; and the central sense-organs, in which our study is confined to the manner in which these special impulses modify the operations of the central nervous system. Inasmuch as in a normal body the peripheral organ remains in connection with the central organ, and our study of the special senses is carried on chiefly by subjective observations in which we make use of our own consciousness, it frequently becomes very difficult to distinguish in any given sensation the peripheral from the central element. The two become more distinct, the more complex the sense and the more highly organized the sense-organs. For this reason, it will be most convenient to commence our study of the special senses with the sense of vision.

THE eyeball is of a spheroidal shape. It consists of two segments of different-sized spheres. The larger segment is situated posteriorly, and constitutes about five-sixths of the walls of the eyeball. From its free margin projects the smaller segment,

FIG. 174.
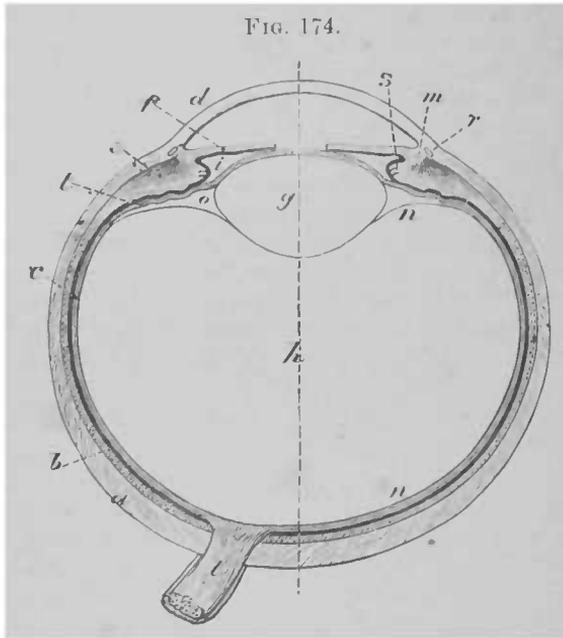
DIAGRAM OF A HORIZONTAL SECTION OF THE EYEBALL

a, outer or sclerotic coat ; *d*, the cornea : *b*, middle or choroidal coat ; *m*, ciliary ligament ; *s*, ciliary process ; *e*, ciliary muscle, and *f*, iris ; *c*, inner coat of retina, continuous with the optic nerve behind, with a dark layer outside it ; *g*, lens ; *t*, suspensory ligament of the lens ; *h*, vitreous body ; *n*, hyaloid membrane ; *i*, posterior chamber ; *o*, canal of Petit ; *r*, sinus circularis iridis ; *l*, optic nerve. The dotted line through the centre is the longitudinal axis of the ball.

which is that of a smaller sphere. The posterior segment is composed of a whitish, opaque, firm wall, consisting of three coats or *tunics*—the *sclerotic*, the *choroid*, and *retina*. The anterior segment is continuous with the sclerotic coat. (Fig. 174.)

It is a transparent, elastic, convex organ, called the *cornea*. The cornéa consists of three layers—an anterior and posterior elastic lamina, having between them a layer which is the proper tissue of the organ. This middle layer is composed of about sixty superimposed laminæ of fusiform fibrous cells. In the interstices between the laminæ are found tubular spaces, which contain a transparent fluid. The anterior and posterior elastic laminæ are structureless and highly elastic. When separated from the proper corneal tissue they have a great tendency to curl up. This fact suggests that these two laminæ are active agents in the retention of a proper curvature of the cornea. The cornea is

FIG. 175.
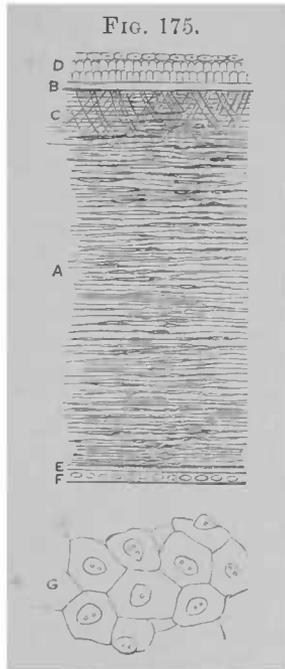
VERTICAL SECTION OF THE CORNEA

A, proper tissue of the cornea ; *B*, anterior elastic lamina of cornea, with *D*, the conjunctival epithelium on it ; *C*, oblique fibres from it to the layers of the cornea ; *E*, posterior elastic lamina, with *F* epithelium on it of the membrane of Demours ; *G*, surface view of the epithelium of the membrane of Demours.

covered on its anterior surface by the conjunctival mucous membrane, which consists of three or four layers of pavement epithelium cells; the deeper layers of cells are oblong, and placed perpendicularly. (Fig. 175.) The conjunctiva at this point has no perceptible basement membrane. The posterior surface of the cornea is covered by a transparent serous membrane, which

consists of a simple layer of polygonal pavement epithelium cells resting on an elastic membrane. This is called the membrane of Demours. The cornea has no bloodvessels, and therefore derives its nutriment by diffusion.

The *sclerotic coat* is so named on account of the firmness of its texture and hardness. It forms the outer tunic of the posterior segment. It is whitish, opaque, smooth, excepting at the points of attachment of the muscles of the eyeball. It is composed of white fibrous tissue, arranged more or less in bundles, which interlace each other in various directions. Anteriorly the interlacements are in a general transverse direction; posteriorly the direction is longitudinal. This coat also contains yellow elastic fibres and fusiform nucleated cells. It is continuous anteriorly with the cornea, and posteriorly with the perineurium of the optic nerve. At the internal border of the junction with the cornea is a venous sinus called the *sinus circularis iridis* or *canal of Schlemm*. The optic nerve pierces it about 2.6 mm. internal to the antero-posterior axis of the eyeball. At this point the coat is perforated by minute openings for the passage of the nerve-filaments. One of these openings, which is relatively large, gives passage to the *arteria centralis retinæ*. Surrounding this point of entrance of the optic nerve are many small openings for the passage of the ciliary nerves and vessels. The internal surface of the sclera contains some pigment-granules. It is separated from the *choroid* coat by a delicate flocculent cellular tissue, called the *lamina fusca*.

The *choroid coat* is a vascular membrane containing some pigment-granules. The external portion is composed principally of bloodvessels and nerves. Between the vessels are found numerous stellate pigment-cells, which form a fibrous network. The internal surface, where it is adjoined to the pigment layer of the retina, also contains pigment-cells. Posteriorly it is pierced by the optic nerve; anteriorly it is continuous with the ciliary processes, and is separated from the sclerotic coat by the *ciliary muscle*.

The *ciliary processes* are arranged in the form of a ring. They consist of about sixty to eighty somewhat conical-shaped bodies, situated with their bases internally. (Fig. 176.) They are placed posterior to the *iris*, and are attached by their thickened or internal extremities to the *suspensory ligament* of the lens.

The *ciliary muscle* arises from the point of junction of the sclerotic coat and the cornea. It consists of two portions—a radiating or meridional, and a circular layer. The radiating fasciculi are situated externally, and have a meridional direction. (Fig. 177.) From this layer numerous fasciculi interlace between the fasciculi of the circular layer, which occupies an

internal position to the radiating layer. The ciliary muscle is inserted into the external surface of the anterior portion of the choroid coat, the fibres extending somewhat posterior to the

FIG. 176.
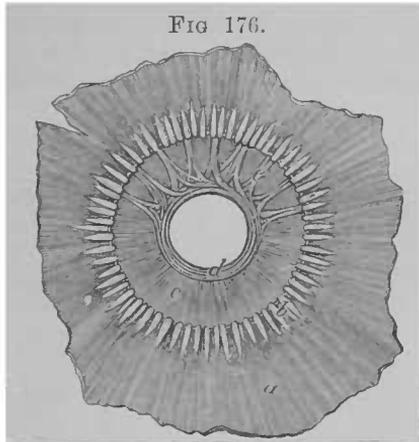
INNER VIEW OF THE FRONT OF THE CHOROID COAT WITH ITS CILIARY PROCESSES, AND THE BACK OF THE IRIS.

a, anterior piece of the choroid coat; *b*, ciliary processes; *c*, iris; *d*, sphincter of the pupil; *e*, bundles of fibres of the dilator of the pupil.

anterior margin of the retina. This muscle is a very important factor in the mechanism of accommodation.

FIG. 177.
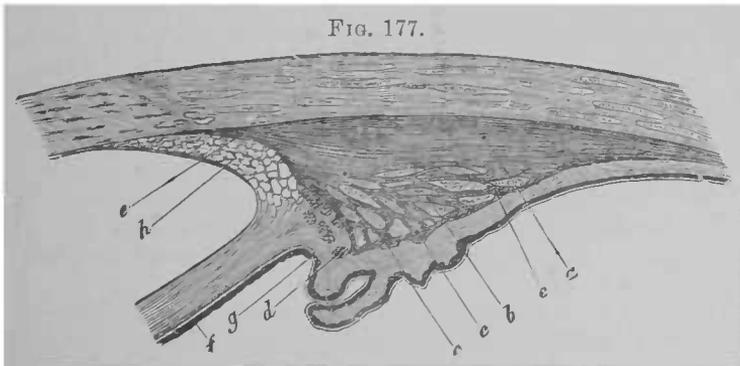
SECTION OF THE CILIARY REGION OF THE EYE IN MAN.

a, meridional muscular fasciculi of the musculus ciliaris; *b*, deeper-seated radiating fasciculi; *c, c, c*, annular plexus; *d*, annular muscle of Müller; *f*, muscular lamina on the posterior surface of the iris; *g*, muscular plexus at the ciliary border of the iris; *e*, annular tendon of the musculus ciliaris; *h*, ligamentum pectinatum.

The *iris* is a fibro-muscular curtain which is suspended between the cornea and the crystalline lens. It is attached by its cir-

cumference to the internal wall of the sinus c. iridis. In its
centre is a round perforation called the pupil, which is susceptible
of considerable variations in size. This membrane is composed
of a fibro-connective tissue having a general radiating direction
from the papillary border. Within this tissue are found pigment-
cells and unstriated muscular tissue. The muscular tissue
element consists of *radiating* and *circular* fasciculi. (Fig. 178.)

FIG. 178.
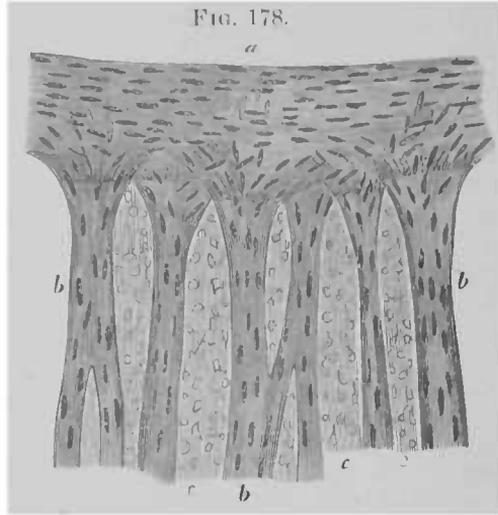
MUSCULAR STRUCTURE OF THE IRIS OF A WHITE RABBIT.

a, sphincter of the pupil ; *b, b,* radiating fasciculi of dilator muscle ; *c, c,* connecting tissue
with its corpuscles.

The *circular* fasciculi form a sphincter at the pupillary margin;
the radiating fasciculi radiate from the sphincter to the circum-
ference. At the circumference of the iris the membrane lining
the anterior chamber forms fibrous processes, which are termed
the *ligamentum iridis pectinatum.* The posterior surface is covered
with a pigmentary layer, which is a continuation of the pigment
layer of the retina.

The *retina* or third coat consists of two portions : the pig-
mentary membrane and terminal elements of the optic nerve.
The *pigmentary membrane* or *external* layer, which has been
called the system of the *uvea,* covers the whole of the internal
surface of the ciliary processes, the iris, and the choroid. It
consists of a single layer of hexagonal nucleated pigment-cells
(Fig. 179) of a dark-brown color. From the internal surface of
this membrane delicate fibres are continued between the cellular
elements of the nervous layer. It is frequently dissected with
the choroid coat, and spoken of as one of its laminæ. The color

of the iris in different individuals is dependent upon the density of the fibro-connective tissue anterior to the *uvea*, and to the amount of pigment-granules in it. In persons with dark eyes the pigment in this tissue is relatively more abundant.

The *internal* or *nervous* layer of the retina is composed essentially of the terminal nerve elements of the optic nerve. Ex-
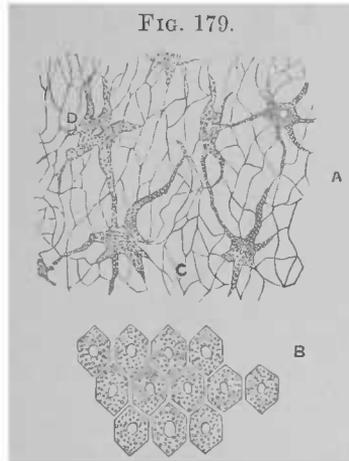
FIG. 179.

PIGMENT-CELLS OF THE EYEBALL. (KOLLIKER.)

A, ramified pigment-cells of the choroid coat; B, front view of the hexagonal cells of the pigmentary membrane.

ternally it is covered with the pigmentary layer; internally, it is lined by a homogeneous transparent structure called the *hyaloid membrane*. The structure of the retina is one of great complexity. It consists of nine distinct layers, seven of which are layers of nerve elements. All of these layers are bound together and supported by a connective tissue which contains bloodvessels. This layer extends from the entrance of the optic nerve to a point where the annular fasciculi of the ciliary muscle are found; at this point the nervous elements cease to exist, and the layer has an irregular dentated margin called the *ora serrata*. Beyond this, the nervous layer is continued as a mere fibrous extenuation.

The optic nerve pierces the sclerotic and the choroid coats, and the pigmentary membrane of the retina, when it rapidly divides into vast numbers of fibres, which consist alone of the axis-cylinders or their ultimate fibrillæ. This layer of fibres is continuous over nearly the whole of the internal surface, and is called the *second* or *optic nerve-fibre layer*. On its internal surface, between it and the hyaloid membrane, is a delicate structure called the *first* layer, or *membrana limitans interna*. The *third* or *ganglion layer* is composed of multipolar ganglion cells, similar

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to those found in the cerebral substance. In the posterior portion
of the retina these ganglion cells are in several layers; at the
macula lutea there are as many as eight, and at the anterior

Fig. 180.   Fig. 181.   Fig. 182.
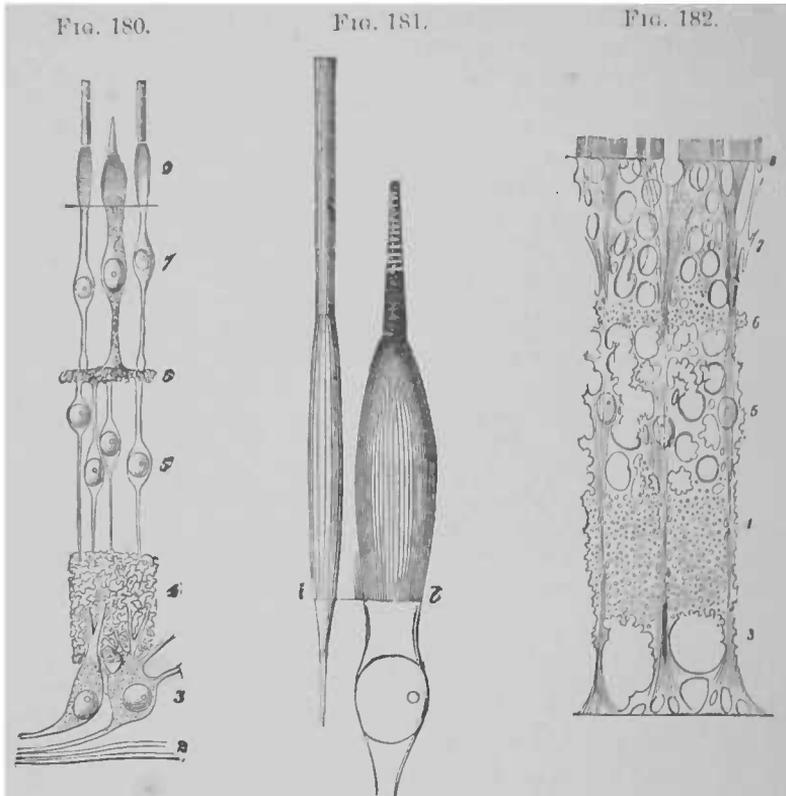
FIG. 180.—Diagrammatic Representation of the Connections of the Nerve-fibres in the
Retina. 1, membrana limitans interna; 2, optic nerve-fibre layer; 3, layer of ganglion cells;
4, internal granulated or molecular layer; 5, internal granule-layer; 6, external granulated
or molecular layer; 7, external granule-layer; 8, membrana limitans exterior; 9, bacillary
layer, or layer of rods and cones.

FIG. 181.—Rod and Cone from the Retina of Man preserved in a two per cent solution of
perosmic acid to show the fine fibres of the surface, and the different lengths of the internal
segment. The outer segment of the cone is broken up into disks, which, however, are still
adherent to one another; at the base of the cone are seen a few fine hairs ($\times$ 1000 diameters)

FIG. 182.—Diagrammatic Representation of the Connective Tissue of the Retina as seen
near the Ora Serrata. The numbers correspond to those of the several layers of the retina
shown in Fig. 180.

portion of the retina there is but a single layer. From each of
these cells fibres are continued to the *fifth* or *internal granule-*
layer, which consists of granular cells with nuclei. Between

the third and fifth layers is a layer of vesicular matter containing nerve-fibrils of extreme minuteness. This layer is the *fourth* or internal *granulated* or *molecular layer*. The *sixth* or *external granulated* or *molecular layer* consists of parallel interlaced fibres, containing nuclei and smooth cells. The *seventh* or *external granule layer* is very similar to the *fifth*. The *eighth* layer consists of a delicate membrane of connective tissue, called the *membrana limitans externa*. The *ninth* or *bacillary layer*, or *layer of rods* and *cones*, or *Jacob's membrane*, is composed of two elements, the *rods* and *cones*. The rods are cylindrical bodies, each ending externally in a truncated, flattened extremity, and internally as an attenuated fibre, which probably communicates with the deeper layer of ganglion cells. The *cones*, as their names indicate, are conical-shaped bodies. Each consists of two portions, a conical body having projecting from its apex a rod-like segment, which appears in all respects like the rods. This segment is called the cone rod. The terminal extremities of the cone rods do not extend as far externally as the extremities of the rods. The rods and cones have been demonstrated to consist of two segments or limbs, which are composed of filaments, granular matter, and nuclei.

The optic nerve, where it pierces the coats of the eye, projects somewhat beyond the surface of the retina, as a *papilla;* here the essential nerve-elements of the retina are absent, and luminous rays are unperceived ; hence it is called the *blind spot*. About 2.6 mm. external to the point of entrance of the optic nerve, and in the exact centre of the retinal surface corresponding to the antero-posterior axis of the eye, is the "yellow spot of Sömmerring" or *macula lutea*. (Fig. 183.) It is an elliptical-shaped spot, having its long diameter transverse. In the centre of the macula lutea is a depression called the *fovea centralis*. At this point the nervous layer of the retina is very much modified in composition of the different layers. At the macula lutea the nervous layer is much thicker than at any other part of the membrane. The ganglion (*third*) and the external granulated (*sixth*) are the most thickened. The ganglion layer consists of six or eight laminæ of cells. The rods of the ninth layer are absent, and are replaced by cones. In the *fovea centralis* the internal granulated (*fourth*), the internal granule (*fifth*), and the optic nerve-fibre (*second*), are wanting. The ganglion cell (*third*), the external granulated (*sixth*), and the external granule (*seventh*) layers are increased in thickness. The ganglion layer of cells in the fovea consists of three laminæ. In all portions of the nervous layer the rods greatly predominate in number over the cones, excepting in the macula lutea, where they are entirely absent. The retina is much thicker posteriorly, becoming thinner

as it extends forwards; the nervous layer gradually disappearing in the anterior portion of the membrane.

The interior of the eyeball is divided into two portions by the crystalline lens and its suspensory ligament. The anterior portion contains the *aqueous humor*, the posterior contains the *vitreous body*.

The *crystalline lens* measures about 7 mm. in transverse diameter, and about 4 mm. antero-posterior diameter. It is a
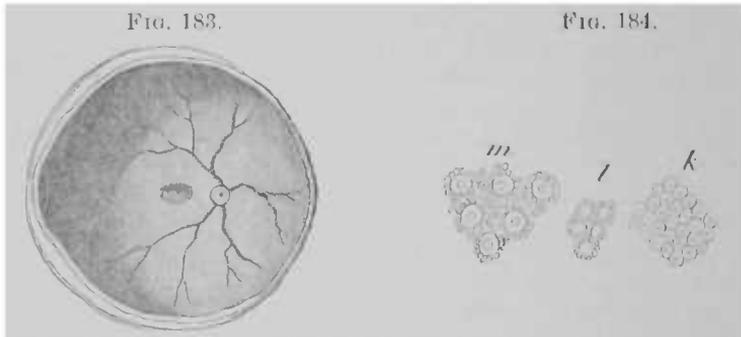
Fig. 183.—Objects on the Inner Surface of the Retina. In the centre of the ball is the yellow limbus luteus, here represented by shading, and in its middle the dark spot. To the inner side is the nerve, with its accompanying artery. After Sömmerring.

Fig. 184.—Magnified Vertical Section of the Retina (altered from Kölliker). *k*, microscopic appearance of the outer surface of the retina over the yellow spot, where there are only cones; *l*, appearance of the retina near the yellow spot—a single circle of rods surrounding each cone; *m*, appearance of the middle of the retina, a large number of rods surrounding each one. In all three figures the larger rings represent the cones, and the smaller ones the rods seen endwise. After Ellis.

transparent biconvex body, somewhat flattened anteriorly. It consists of a number of segments which radiate from the centre, similar to the segments of an orange. These segments are composed of superimposed laminæ of varying density. The most superficial are soft and gelatinous; the deeper are relatively hard, so that they form a kernel or *nucleus*. The laminæ are made up of parallel fibres, with an undulating course, the convexities and concavities of the adjoining fibres fitting accurately into each other. The lens is covered with a capsule consisting of a transparent, elastic, fragile membrane, which has a tendency to curl up, with its external surface innermost.

The *suspensory ligament* of the lens is formed by a continuation of the hyaloid membrane which lines the vitreous body. The *hyaloid membrane* is a delicate transparent structure situated between the vitreous body and membrana limitans interna of the retina. It is continued in front to the *ora serrata*, where it divides into two layers. The posterior is attached to the posterior por-

tion of the capsule of the lens; the anterior portion gradually becomes thicker as it extends forwards behind the ciliary processes, and is attached to the anterior surface of the capsule. This thickened portion of the membrane, which is corrugated where it has attached the ciliary processes, is called the *zone of Zinn.* These two layers constitute the suspensory ligament. Between them is a triangular canal, with its base corresponding to the crystalline lens. This is called the canal of Petit.

FIG. 185.
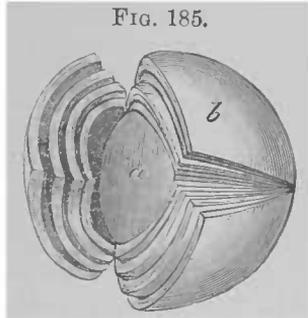
A REPRESENTATION OF THE LAMINÆ IN A HARDENED LENS.
a, the nucleus; *b*, superficial laminæ.

The *vitreous body* is contained within the cavity formed by the hyaloid membrane and the posterior surface of the lens. It consists of a clear colorless albuminous fluid, having an extremely delicate interlacement of fibres extending in all directions through it. These fibres are not discernible in the adult, but can readily be seen in the fœtus.

The *aqueous humor* is contained within the space formed by the posterior surface of the cornea, and the anterior surface of the lens. The space, which is divided into two chambers by the iris, is filled with a clear, colorless, limpid fluid containing saline and proteid substances in solution. This fluid constitutes the *aqueous humor.*

The anterior external portion of the eyeball, comprising the surface of the cornea and about 6 or 8 mm. of the sclerotic coat, is covered by the conjunctival mucous membrane.]

SIGHT.

A ray of light falling on the retina gives rise to what we call a sensation of light; but in order that distinct vision of any object may be gained, an image of the object must be formed on the retina, and the better defined the image the more distinct

will be the vision. Hence in studying the physiology of vision,
our first duty is to examine into the arrangements by which the
formation of a satisfactory image on the retina is effected; these
we may call briefly the dioptric mechanisms. We shall then
have to inquire into the laws according to which rays of light
impinging on the retina give rise to sensory impulses, and those
according to which the impulses thus generated give rise in turn
to sensations. Here we shall come upon the difficulty of dis-
tinguishing between the unconscious or physical and the con-
scious or psychical factors. And we shall find our difficulties
increased by the fact, that in appealing to our own consciousness
we are apt to fall into error by confounding primary and direct
sensations with states of consciousness which are produced by
the weaving of these primary sensations with other operations of
the central nervous system, or, in familiar language, by con-
founding what we see with what we think we see. These two
things we will briefly distinguish as visual sensations and visual
judgments; and we shall find that both in vision with one eye,
but more especially in binocular vision, visual judgments form a
very large part of what we frequently speak of as our sight.

SEC. 1.—DIOPTRIC MECHANISMS.

The Formation of the Image.

The eye is a camera, consisting of a series of lenses and media
arranged in a dark chamber, the iris serving as a diaphragm;
and the object of the apparatus is to form on the retina a distinct
image of external objects. That a distinct image is formed on
the retina, may be ascertained by removing the sclerotic from
the back of an eye, and looking at the hinder surface of the
transparent retina while rays of light proceeding from any ex-
ternal object are allowed to fall on the cornea.

A dioptric apparatus in its simplest form consists of two
media separated by a (spherical) surface; and the optical pro-
perties of such an apparatus depend upon (1) the curvature of
the surface, (2) the relative refractive power of the media. The
eye consists of several media, bounded by surfaces which are
approximately spherical but of different curvature. The sur-
faces are all centred on a line called the *optic axis*, which meets
the retina at a point somewhere above and to the inner (nasal)
side of the fovea centralis. In passing from the outer surface
of the cornea to the retina the rays of light traverse in suc-
cession the cornea, the aqueous humor, the lens, and the vitreous
humor. Refraction takes place at all the surfaces bounding

these several media, but particularly at the anterior surface of the cornea, and at both the anterior and posterior surfaces of the lens. Since the anterior and posterior surfaces of the cornea are parallel, or very nearly so, the rays of light would suffer little or no change of direction in passing through the cornea, if it were bounded on both sides by the same medium. The direction of the rays of light in the aqueous humor would therefore remain the same if the cornea were made exceedingly thin, if in fact its two surfaces were made into one, forming a single anterior surface to the aqueous humor; or, which comes to the same thing in the end, since the refractive power of the substance of the cornea is almost exactly the same as that of the aqueous humor, the refraction at the posterior surface of the cornea may be neglected altogether. Thus the two surfaces of the cornea are practically reduced to one. The lens varies in density in different parts, the refractive power of the central portions being greater than that of the external layers; but the refractive power of the whole may, without any serious error, be assumed to be uniform. The refractive power of the vitreous humor is almost exactly the same as that of the aqueous humor.

Thus the apparently complicated natural eye may be simplified into a "diagrammatic eye," in which the refracting surfaces are reduced to three, viz., (1) the anterior surface of the cornea, (2) the anterior surface of the lens separating the lens from the aqueous humor, and (3) the posterior surface of the lens separating the lens from the vitreous humor. The media will similarly be reduced to two; the substance of the lens, and the aqueous or vitreous humor. This "diagrammatic eye" is of great use in the various calculations which become necessary in studying physiological optics; for the magnitudes which are derived by calculation from it represent the corresponding magnitudes in an average natural eye with sufficient accuracy to serve for all practical purposes. The values adopted by Listing for the constants of this "diagrammatic eye," and to him we are indebted for the introduction of it, are as follows:

	Millimetres.
Radius of curvature of cornea	8
Radius of curvature of anterior surface of lens	10
Radius of curvature of posterior surface of lens	6
Refractive index of aqueous or vitreous humor	$\frac{103}{77}$
Mean refractive index of lens	$\frac{16}{11}$
Distance from anterior surface of cornea to anterior surface of lens	4
Thickness of lens	4

The calculated position of the *principal posterior focus*—*i. e.*, the point at which all rays falling on the cornea parallel to the optic axis are brought to a focus, is in the diagrammatic eye 14.6470

mm. behind the posterior surface of the lens, or 22.6470 mm. behind the anterior surface of the cornea. That is to say, the fovea centralis must occupy this position in order that a distinct image of a distant object may be formed upon it. It must be understood that these values refer to the eye when at rest —*i. e.*, when it is not undergoing any strain of accommodation.

Accommodation.

When an object, a lens, and a screen to receive the image, are so arranged in reference to each other, that the image falls upon the screen in exact focus, the rays of light proceeding from each luminous point of the object are brought into focus on the screen in a point of the image corresponding to the point of the object. If the object be then removed further away from the lens, the rays proceeding in a pencil from each luminous point will be brought to a focus at a point in front of the screen, and, subsequently diverging, will fall upon the screen as a circular patch composed of a series of circles, the so-called *diffusion circles*, arranged concentrically round the principal ray of the pencil. If the object be removed, not further, but nearer, the lens, the pencil of rays will meet the screen before they have been brought to focus in a point, and consequently will in this case also give rise to diffusion circles. When an object is placed before the eye, so that the image falls into exact focus on the retina, and the pencils of rays proceeding from each luminous point of the object are brought into focus in points on the retina, the sensation called forth is that of a distinct image. When, on the contrary, the object is too far away, so that the focus lies in front of the retina, or too near, so that the focus lies behind the retina, and the pencils fall on the retina, not as points, but as systems of diffusion circles, the sensation produced is that of an indistinct and blurred image. In order that objects both near and distant may be seen with equal distinctness by the same dioptric apparatus, the focal arrangements of the apparatus must be *accommodated* to the distance of the object, either by changing the refractive power of the lens, or by altering the distance between the lens and the screen.

That the eye does possess such a power of accommodation, is shown by every-day experience. If two needles be fixed upright some two feet or so apart, into a long piece of wood, and the wood be held before the eye, so that the needles are nearly in a line, it will be found that if attention be directed to the far needle, the near one appears blurred and indistinct, and that, conversely, when the near one is distinct, the far one appears blurred. By an effort of the will we can at pleasure make either

the far one or the near one distinct, but not both at the same time. When the eye is arranged so that the far needle appears distinct, the image of that needle falls exactly on the retina, and each pencil from each luminous point of the needle unites in a point upon the retina; but when this is the case, the focus of the near needle lies *behind* the retina, and each pencil from each luminous point of this needle falls upon the retina in a series of diffusion circles. Similarly, when the eye is arranged so that the near needle is distinct, the image of that needle falls upon the retina in such a way that each pencil of rays from each luminous point of the needle unites in a point on the retina, while each pencil from each luminous point of the far needle unites at a point *in front of* the retina, and then diverging again falls on the retina, in a series of diffusion circles. If the near needle be gradually brought nearer and nearer to the eye, it will be found that greater and greater effort is required to see it distinctly, and at last a point is reached at which no effort can make the image of the needle appear anything but blurred. The distance of this point from the eye marks *the limit* of accommodation for near objects. Similarly, if the person be short-sighted, the far needle may be moved away from the eye, until a point is reached at which it ceases to be seen distinctly, and appears blurred. In the one case, the eye, with all its power, is unable to bring the image of the needle sufficiently forward to fall on the retina : the focus lies permanently behind the retina. In the other, the eye cannot bring the image sufficiently backward to fall on the retina : the focus lies permanently in front of the retina. In both cases the pencils of rays from the needles strike the retina in diffusion circles.

The same phenomena may be shown with greater nicety by what is called Scheiner's Experiment. If two smooth holes be pricked in a card, at a distance from each other less than the diameter of the pupil, and the card be held up before one eye, with the holes horizontal, and a needle placed vertically be looked at through the holes, the following facts may be observed : When attention is directed to the needle itself, the image of the needle appears single. Whenever the gaze is directed to a more distant object, so that the eye is no longer accommodated for the needle, the image appears double, and at the same time blurred. It also appears double and blurred when the eye is accommodated for a distance nearer than that of the needle. When only one needle is seen, and the eye therefore is properly accommodated for the distance of the needle, no effect is produced by blocking up one hole of the card, except that the whole field of vision seems dimmer. When, however, the image is double on account of the eye being accommodated for a distance greater than that

of the needle, blocking the left-hand hole causes a disappearance
of the right-hand or opposite image, and blocking the right-hand
hole causes the left-hand image to disappear. When the eye is
accommodated for a distance nearer than that of the needle,
blocking either hole causes the image on the same side to vanish.
The following diagram will explain how these results are brought
about:

Let a (Fig. 186) be a luminous point in the needle, and ae, af
the extreme right-hand and left-hand rays of the pencil of rays

FIG. 186.
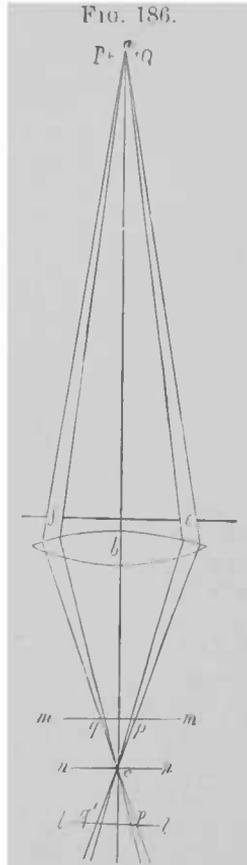
DIAGRAM OF SCHEINER'S EXPERIMENT.

proceeding from it, and passing respectively through the right-
hand e, and left-hand f, holes in the card. (The figure is sup-
posed to be a horizontal section of the eye.) When the eye is
accommodated for a, the rays e and f meet together in the point

c, the retina occupying the position of the plane nn; the luminous point appears as one point, and the needle will appear as one needle. When the eye is accommodated for a distance beyond a, the retina may be considered to lie,[1] no longer at nn, but nearer the lens, at mm for example; the rays ae will cut this plane at p, and the rays af at q; hence the luminous point will no longer appear single, but will be seen as two points, or rather as two systems of diffusion circles, and the single needle will appear as two blurred needles. The rays passing through the right-hand hole e, will cut the retina at p—*i. e.*, on the right-hand side of the optic axis; but, as we shall see in speaking of the judgments pertaining to vision, the image on the right-hand side of the retina is *referred by the mind* to an object on the left-hand side of the person; hence the affection of the retina at p, produced by the rays ae falling on it there, gives rise to an image of the spot a at P, and similarly the left-hand spot q corresponds to the right-hand Q. Blocking the left-hand hole, therefore, causes a disappearance of the right-hand image, and *vice versâ*. Similarly, when the eye is accommodated for a distance nearer than the needle, the retina may be supposed to be removed to ll, and the right-hand ae and left-hand af rays, after uniting at c, will diverge again and strike the retina at p' and q'. The blocking of the hole e will now cause the disappearance of the image q' on the left-hand side of the retina, and this will be referred by the mind to the right-hand side, so that Q will seem to vanish.

If the needle be brought gradually nearer and nearer to the eye, a point will be reached within which the image is always double. This point marks with considerable exactitude the near limit of accommodation. With short-sighted persons, if the needle be removed further and further away, a point is reached beyond which the image is always double; this marks the far limit of accommodation.

The experiment may also be performed with the needle placed horizontally, in which case the holes in the card should be vertical.

The adjustment of the eye for near or far distances may be assisted by using two needles, one near and one far. In this case one needle should be vertical, and the other horizontal, and the card turned round so that the holes lie horizontally or vertically according to whether the vertical or horizontal needle is being made to appear double.

In what may be regarded as the normal eye, the so-called *em-*

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[1] Of course, in the actual eye, as we shall see, accommodation is effected by a change in the lens, and not by an alteration in the position of the retina; but for convenience sake we may here suppose the retina to be moved.

metropic eye (Figs. 187 and 188), the near limit of accommoda-
tion is about 10 or 12 cm., and the far limit may be put for
practical purposes at an infinite distance. The range of dis-
tinct vision," therefore, for the emmetropic eye is very great. In

[FIG. 187.

A
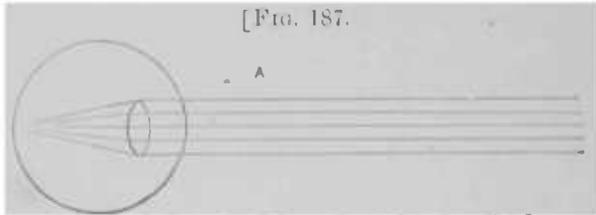
Emmetropic Eye. Parallel rays focussed on the retina.]

the *myopic* (Fig. 189), or short-sighted eye, the near limit is
brought much closer (5 or 6 cm.) to the cornea; and the far
limit is at a variable but not very great distance, so that the
rays of light proceeding from an object not many feet away are

[FIG. 188.

B
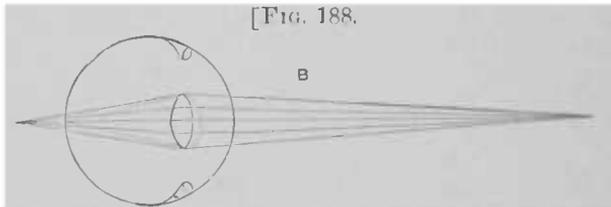
Emmetropic Eye. The dotted lines showing how accommodation for the diverging rays of near objects is effected.]

brought to a focus, not on the retina, but in the vitreous humor.
The range of distinct vision is, therefore, in the myopic eye very
limited. In the *hypermetropic* (Fig. 190), or long-sighted eye,
the rays of light coming from even an infinite distance are, in

[FIG. 189.

D
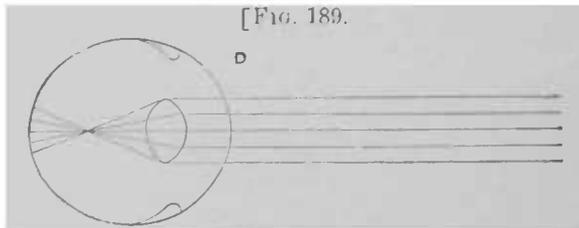
Myopic Eye.]

the passive state of the eye, brought to a focus beyond the retina.
The near limit of accommodation is at some distance off, and a
far limit of accommodation does not exist. The *presbyopic* eye,
or the long sight of old people, resembles the hypermetropic eye

in the distance of the near point of accommodation, but differs
from it inasmuch as the former is an essentially defective condi-
tion of the accommodation mechanism, whereas in the latter the
power of accommodation may be good, and yet, from the internal
arrangements of the eye, be unable to bring the image of a near
object on to the retina. When a normal eye becomes presbyopic,

[Fig 190.
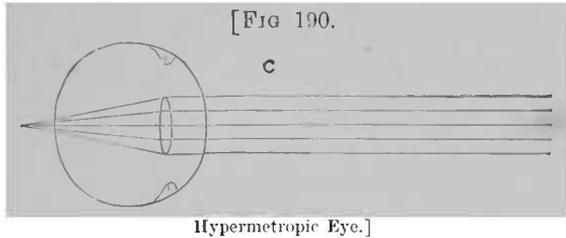
Hypermetropic Eye.]

the far limit may remain the same, but since the power of ac-
commodating for near objects is weakened or lost, the change is
distinctly a reduction of the range of distinct vision. In the
normal emmetropic eye, when no effort of accommodation is
made, the principal focus of the eye lies on the retina, in the
myopic eye in front of it, and in the hypermetropic eye behind it.

Mechanism of Accommodation.—In directing our attention
from a far to a very near object we are conscious of a distinct
effort, and feel that some change has taken place in the eye;
when we turn from a very near to a far object, if we are con-
scious of any change in the eye, it is one of a different kind.
The former is the sense of an active accommodation for near
objects; the latter, when it is felt, is the sense of relaxation after
exertion.

Since the far limit of an emmetropic eye is at an infinite dis-
tance no such thing as active accommodation for far distances
need exist. The only change that will take place in the eye in
turning from near to far objects will be a mere passive undoing
of the accommodation previously made for the near object. And
that no such active accommodation for far distances takes place
is shown by the facts—that the eye, when opened after being
closed for some time, is found not in the medium state but ad-
justed for distance; that when the accommodation mechanism of
the eye is paralyzed by atropin or nervous disease, the accom-
modation for distant objects is unaffected, and that we are con-
scious of no effort in turning from moderately distant to far
distant objects. The sense of effort often spoken of by myopic
persons as being felt when they attempt to see things at or

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beyond the far limit of their range seems to arise from a movement of the eyelids, and not from any internal changes taking place in the eye.

What then are the changes which take place in the eye, when we accommodate for near objects? It might be thought, and indeed once was thought, that the curvature of the cornea was changed, becoming more convex, with a shorter radius of curvature, for near objects. Young, however, showed that accommodation took place as usual when the eye (and head) is immersed in water. Since the refractive powers of aqueous humor and water are very nearly alike, the cornea, with its parallel surfaces, placed between these two fluids, can have little or no effect on the direction of the rays passing through it when the eye is immersed in water. And accurate measurements of the dimensions of an image on the cornea have shown that these undergo no change during accommodation, and that, therefore, the curvature of the cornea is not altered. Nor is there any change in the form of the bulb: for any variation in this would necessarily produce an alteration in the curvature of the cornea, and pressure on the bulb would act injuriously by rendering the retina anæmic, and so less sensitive. In fact, there are only two changes of importance which can be ascertained to take place in the eye during accommodation for near objects.

One is that the pupil contracts. When we look at near objects, the pupil becomes small; when we turn to distant objects, it dilates. This, however, cannot have more than an indirect influence on the formation of the image; the chief use of the contraction of the pupil in accommodation for near objects is to cut off the more divergent circumferential rays of light.

The other and really efficient change is that the anterior surface of the lens becomes more convex. If a light be held before the eye, three reflected images may, with care and under proper precautions, be seen by a bystander; one a very bright one, caused by the anterior surface of the cornea, a second less bright, by the anterior surface of the lens, and a third very dim, by the posterior surface of the lens; when the images are those of an object, such as a candle, in which a top and bottom can be recognized, the two former images are seen to be erect, but the third inverted. When the eye is accommodated for near objects, no change is observed in either the first or the third of these images; but the second, that from the anterior surface of the lens, is seen to become distinctly smaller, showing that the surface has become more convex. When, on the contrary, vision is directed from near to far objects, the image from the anterior surface of the lens grows larger, indicating that the convexity of the surface has diminished, while no change takes place in the

curvature either of the cornea or of the posterior surface of the lens. And accurate measurements of the size of the image from the anterior surface of the lens have shown that the variations in curvature which do take place, are sufficient to account for the power of accommodation which the eye possesses.

The observation of these reflected images is facilitated by the simple instrument introduced by Helmholtz, and called a Phakoscope. It consists of a small dark chamber, with apertures for the observed and observing eyes; a needle is fixed at a short distance in front of the former, to serve as a near object, for which accommodation has to be made, and a lamp or candle is so disposed as to throw an image on each of the three surfaces of the observed eye. Since the distance between two images is more readily appreciated than is a simple change of size of a single image, two prisms are employed so as to throw a double image of the lamp on each of the three surfaces. When the anterior surface of the lens becomes more convex the two images reflected from that surface approach each other, when it becomes less convex they retire from each other.

These observations leave no doubt that the essential change by which accommodation is effected, is an alteration of the convexity of the anterior surface of the lens. And that the lens is the agent of accommodation, is further shown by the fact that after removal of the lens, as in the operation for cataract, the power of accommodation is lost. In the cases which have been recorded, where eyes from which the lens had been removed seemed still to possess some accommodation, we must suppose that no real accommodation took place, but that the pupil contracted when a near object was looked at, and so assisted in making vision more distinct.

This increase of the convexity of the lens has been supposed to be due to a compression of the circumference of the lens by a contraction of the iris; but this is disproved by the fact that accommodation may take place in eyes from which the iris is congenitally absent. It has also been attributed to vaso-motor changes, to increased fulness of the vessels of the iris or ciliary processes, surrounding the lens; but this also is disproved by the fact that accommodation may be effected, after death in an eye which is practically bloodless, by stimulating the ciliary ganglion or ciliary nerves with an interrupted current or by other means. The real nature of the mechanism seems to be as follows.

The lens when examined after removal from the eye is found to be a body of considerable elasticity. When the curvature of the anterior surface of the lens is determined, as may be done by appropriate means, in its natural position in the eye at rest, and then again determined after the lens has been removed from the eye, the anterior surface is found to be more convex in the latter than in the former case. There seems to be, in the eye in its

natural condition, some agency at work, keeping the anterior surface of the lens somewhat flattened. The suspensory ligament, attached to the choroid and ciliary processes behind, and passing over the front of the lens, is just such a structure as would produce this effect. In the natural position of the choroid this ligament is tense, and tends to flatten the front of the lens. When the choroid is pulled forward, the ligament becomes slack, and the lens bulges out forward. Further, the ciliary muscle attached, on the one hand, to a fairly fixed region, the junction of the sclerotic and cornea, and, on the other, to the looser and more movable choroid, would naturally, when thrown into contraction, **pull** forward the choroid and so slacken the suspensory ligament, and hence permit the elastic lens to bulge out forwards. And we have experimental evidence, carried out on lower animals, that stimulation of the ciliary ganglion, or of its so-called radix brevis, does lead, on the one hand, to a contraction of the ciliary muscle and pulling forward of the choroid, and, on the other hand, to an increased curvature of the anterior surface of the lens. Hence, we may conclude that accommodation for near objects consists essentially in a contraction of the ciliary muscle, which, by pulling forward the choroid coat and the ciliary process, slackens the suspensory ligament, and allows the lens to bulge forward by virtue of its elasticity, and so to increase the convexity of its anterior surface.

Accommodation is, in most cases, a voluntary act; since, however, the change in the lens is always accompanied by movements in the iris, it will be convenient to consider the latter, before we discuss the nervous mechanism of the whole act.

Movements of the Pupil.—Though by making the efforts required for accommodation we can, at pleasure, contract or dilate the pupil, it is not in our power to bring the will to act directly on the iris by itself. This fact alone indicates that the nervous mechanism of the pupil is of a peculiar character, and such, indeed, we find it to be. The pupil is *contracted* (1) when the retina (or optic nerve) is stimulated, as when light falls on the retina, the brighter the light the greater being the contraction; (2) when we accommodate for near objects. The pupil is also contracted when the eyeball is turned inwards, when the aqueous humor is deficient, in the early stages of poisoning by chloroform, alcohol, etc.; in nearly all stages of poisoning by morphia, physostigmin, and some other drugs, and in deep slumber. The pupil is *dilated* (1) when stimulation of the retina (or optic nerve) is diminished or arrested, as in passing from a bright into a dim light or into darkness; (2) when the eye is adjusted for far objects. Dilation also occurs when there is an excess of

aqueous humor, during dyspnœa, during violent muscular efforts, as the result of a stimulation of sensory nerves, as an effect of emotions, in the later stages of poisoning by chloroform, etc., and in all stages of poisoning by atropin and some other drugs.

Contraction of the pupil is caused by contraction of the circular fibres or sphincter of the iris. Dilation is caused by contraction of the radial fibres of the iris; for though the existence of radial fibres has been denied by many observers, the preponderance of evidence is clearly in favor of their being really present

Considering how vascular the iris is, it does not seem unreasonable to interpret some of the variations in the condition of the pupil as the results of simple vascular turgescence, or of depletion, brought about by vaso-motor action or otherwise, the small or contracted pupil corresponding to the dilated and filled, and the large or dilated pupil to the constricted and emptied condition of the bloodvessels. Thus, slight oscillations of the pupil may be observed synchronous with the heart-beat, and others synchronous with the respiratory movements. But the variations in the pupil seem too marked to be merely the effects of vascular changes, and, indeed, that constriction of the pupil cannot be wholly the result of turgescence, nor dilatation wholly the result of depletion of the vessels of the iris, is shown by the facts that both these events may be witnessed in a perfectly bloodless eye, and that the movements of the pupil when brought about by agents which also affect the bloodvessels, begin some time before the changes in the calibre of the bloodvessels, and, indeed, may be over before these have arrived at their maximum. Moreover, the fibres of the sympathetic, which as we shall see are concerned in causing dilation of the pupil, run a somewhat different course from those which govern the bloodvessels of the eye. We may therefore adhere to the view that the main changes of the pupil in the direction of narrowing and widening are brought about by contractions of the plain muscular fibres in the iris.

Muscular contractions leading to changes of the pupil may be observed in the eye removed from the body, and indeed in the extirpated iris. The plain muscular fibres of the iris, like other plain muscular fibres, are remarkably sensitive to variations in temperature. Besides this there seems to be in certain animals at least a connection within the eye between the iris and retina of such a kind, that light falling into an extirpated eye will lead to a narrowing of the pupil. Putting aside however such exceptional events, we may lay down the broad principle that contraction of the pupil, brought about by light falling on the retina, is a reflex act, of which the optic is the afferent nerve,

the third or oculo-motor the efferent nerve, and the centre some portion of the brain lying below the corpora quadrigemina in the front part of the floor of the aqueduct of Sylvius. This is proved by the following facts. When the optic nerve is divided, the falling of light on the retina no longer causes a contraction of the pupil. When the third nerve is divided, stimulation of the retina or of the optic nerve no longer causes contraction; but direct stimulation of the peripheral portion of the divided third nerve causes extreme contraction of the pupil. If the region of the brain spoken of above as a centre be carefully stimulated, contraction of the pupil will take place even in the absence of light and after division of the optic nerve. After removal of the same centre stimulation of the retina is ineffectual in narrowing the pupil. But if the centre and its connections with the optic nerve and third nerve be left intact and in thoroughly sound condition, contractions of the pupil will occur as a result of light falling on the retina, though all other nervous parts be removed.

The nervous centre is not a double centre with two completely independent halves, one for each eye; there is a certain amount of functional communion between the two sides, so that when one retina is stimulated both pupils contract. It might be imagined that this cerebral centre acted as a tonic centre, whose action was simply increased, not originated, by the stimulation of the retina; but this is di roved by the fact that, if the optic nerve be divided, subsequent section of the third nerve produces no further dilation.

In considering the movements of the pupil, he   we have to deal not only with a narrowing of the pupil u.   ught about, in a reflex way by contraction of the circular sphincter fibres, and with the absence of such a narrowing, but also with active dilation due to a contraction of the radial dilator fibres, and this renders the whole matter much more complex than might be supposed to be the case from the simple statement just made.

The iris is supplied in common with the ciliary muscle and choroid, by the short ciliary nerves (Fig. 191, *s. c.*) coming from the ophthalmic or lenticular (ciliary) ganglion (*l. c.*) which is connected by its roots with the third nerve (*r. b.*), the cervical sympathetic nerve (*sym.*), and with the nasal branch of the ophthalmic division of the fifth nerve (*r. l.*). The short ciliary nerves are, moreover, accompanied by the long ciliary nerves (*l. c.*) coming from the same nasal branch of the ophthalmic division of the fifth nerve. What are the uses of these several nerves in relation to the pupil?

If the cervical sympathetic in the neck be divided, all other

portions of the nervous mechanism being intact, a contraction of the pupil (not always very well marked) takes place, and if the peripheral portion (*i. e.*, the upper portion still connected with the head) be stimulated, a well-developed dilation is the result. The sympathetic has, it will be observed, an effect on the iris, the

FIG. 191.
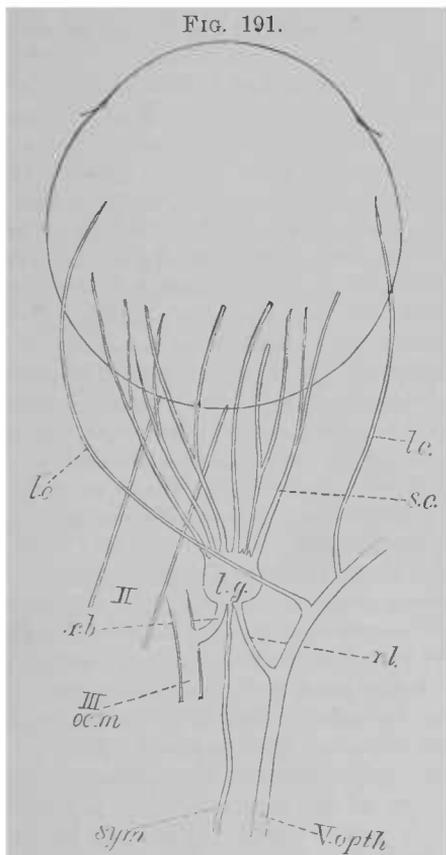
DIAGRAMMATIC REPRESENTATION OF THE NERVES GOVERNING THE PUPIL

II. Optic nerve. *l. g.* lenticular ganglion. *r. b.* its short root from *III*. *oc. m.* third or oculo-motor nerve. *sym.* its sympathetic root. *r. l.* its long root from *V. opthm.* the nasal branch of the ophthalmic division of the fifth nerve. *s. c.* the short ciliary nerves from the lenticular ganglion. *l. c.* the long ciliary nerve from the nasal branch of the ophthalmic division of the fifth nerve.

opposite of that which it exercised on the bloodvessels ; when it is stimulated the pupils are dilated while the bloodvessels are constricted. The dilating influence of the sympathetic may, as in the case of the vaso-motor action of the same nerve, be traced back down the neck to the upper thoracic ganglion and thence

along the rami communicantes and roots of the lower cervical and first dorsal or first two dorsal spinal nerves, to a region in the lower cervical and upper dorsal cord (called by some authors the *centrum ciliospinale inferius*), and thence up through the medulla oblongata to a centre, which appears to be placed in the floor of the front part of the aqueduct of Sylvius not far from and apparently on either side of the centre for contraction of the pupil.

The dilation of the pupil which is witnessed in dyspnœa, and that which results from stimulation of sensory nerves and from emotions, appears to be brought about by the action of the sympathetic, the venous blood, or the sensory impulses or the emotional impulses so affecting the dilating centre as to augment the dilating impulses proceeding from it along the sympathetic. The existence of the subordinate centre in the cervical or dorsal cord, spoken of just now, is supposed to be indicated by the fact that after division of the medulla oblongata, and consequent severance of the efferent paths from the centre in the aqueduct of Sylvius, dilation of the pupil may still be brought about, in some animals at least, by dyspnœa or by adequate stimulation of sensory nerves. A question is raised here in fact somewhat similar to that raised in connection with the medullary respiratory centre (p. 420); and here as there we may probably conclude that the independent action of such a spinal centre is of subordinate importance.

The pupil then seems to be under the dominion of two antagonistic mechanisms: one a contracting mechanism, reflex in nature, the third nerve serving as the efferent, and the optic as the afferent tract; the other a dilating mechanism, apparently tonic in nature, but subject to augmentation from various causes, and of this the cervical sympathetic is the efferent channel. Hence, when the third or optic nerve is divided, not only does contraction of the pupil cease to be manifest, but active dilation occurs, on account of the tonic dilating influence of the sympathetic being left free to work. When, on the other hand, the sympathetic is divided, this tonic dilating influence falls away, and contraction results. When the optic or third nerve is stimulated, the dilating effect of the sympathetic is overcome, and contraction results; and when the sympathetic is stimulated, any contracting influence of the third nerve which may be present is overcome, and dilation ensues.

But there are considerations which show that the matter is still more complex than this. A small quantity of atropin introduced into the eye or into the system causes a dilation of the pupil. This might be attributed to a paralysis of the third nerve, and indeed it is found that after atropin has produced its

effects the falling of light on the retina no longer causes contraction of the pupil. A difficulty however is introduced by the fact that when the third nerve is divided, and when therefore the contracting effects of stimulation of the retina are placed entirely on one side, and there is nothing to prevent the sympathetic producing its dilating effects to the utmost, dilation is still further increased by atropin. When physostigmin is introduced into the eye or system, contraction of the pupil is caused, whether the third nerve be divided or not; and when the dose is sufficiently strong the contraction is so great that it cannot be overcome by stimulation of the sympathetic. The dilation which is caused by a sufficient dose of atropin may be greater than that which can ordinarily be produced by stimulation of the sympathetic, and the contraction caused by a sufficient dose of physostigmin may be greater than that which is ordinarily produced in a reflex manner by stimulation of the optic nerve, or even than that produced by direct stimulation of the third nerve. Evidently these drugs act either directly on the plain muscular fibres of the iris or on some local mechanism, the one in such a way as to cause dilation, the other in such a way as to cause contraction. Such a local mechanism cannot however lie in the ophthalmic ganglion, for both drugs continue to produce these effects in a most marked degree after the ganglion has been excised. We must suppose therefore that the mechanism if it exists is situated in the iris itself or in the choroid, where indeed ganglionic nerve-cells are abundant. The movements of the iris in the extirpated eye, spoken of just now, may perhaps be attributed to the same local mechanism. Further it is stated that with stimulation of the sympathetic, the latent period—*i. e.*, the period intervening between the beginning of stimulation and the beginning of the movement of the iris, is much greater than with stimulation of the third nerve, indicating that the former acts through a local mechanism but the latter more directly on the muscular fibres. The whole question however of this local mechanism, and of the exact mode of action of the various drugs and of the changes in the body which lead to contraction or dilation respectively of the pupil, needs fuller discussion than we can afford to give to it here. We may add that the local action of atropin in contrast to any action on the cerebral centre is well illustrated by applying atropin to one eye locally. The pupil of that eye dilates widely; in consequence more light falls on the retina, and this so affects the cerebral centre, which as we have seen is not strictly unilateral but in communion with its fellow, that increased constricting impulses pass from both centres, and these, though ineffectual in the atropinized eye, lead in the untouched eye to an increased narrowing of the pupil.

The share of the fifth nerve in the work of the iris seems to be in part a sensory one: the iris is sensitive, and the sensory impulses which are generated in it pass from it along the fibres of the fifth nerve. Moreover, the fifth is peculiarly related to the dilating effects of the sympathetic: for, though the ophthalmic ganglion does receive fibres directly from the cavernous plexus of the sympathetic, the dilating action of the sympathetic would seem to be carried out, not by these fibres, but by fibres joining the fifth nerve, and passing to the iris, not by the ganglion, but by the ophthalmic branch and the long ciliary nerves. The vaso-motor fibres of the sympathetic, and those which dilate the iris, after running together in the main cervical sympathetic chain, part company higher up, the latter passing to the Gasserian ganglion, and thus reaching the nasal branch of the ophthalmic division of the fifth nerve. Some observers maintain that, in addition to these dilating fibres of the sympathetic joined to it, the fifth contains fibres of its own which also are able to dilate the pupil.

We may sum up the nervous mechanism of the pupil, then, somewhat as follows: The salient and most frequently repeated event, the contraction of the pupil, upon exposure to light, is a reflex act, the centre of which is placed in the brain; and the correlative widening of the pupil upon diminution of light is due to the tonic action of the sympathetic making itself felt upon the waning of its antagonist. The contraction of the pupil in the earlier stages of the action of alcohol and chloroform and in slumber is probably due to an increased action of the contracting centre, but the narrow pupil caused by such drugs as morphia and physostigmin is due, chiefly at least, to a local action. The dilating effects of such drugs as atropin are also largely due to a local action, but in the widened pupil of the later stages of alcohol poisoning and of dyspnœa we can probably trace the effects of an exhaustion of the cerebral contracting centre, assisted, possibly, by an increased activity of the dilating centre.

There remains a word to be said concerning the contraction of the pupil which takes place when the eye is accommodated for near objects, and when the pupil is turned inwards (the two being closely allied, since the eyes converge to see near objects), and the return to the more dilated condition when the eye returns to rest and regains the accommodation for far objects. These are instances of what are called "associated movements." Two movements are thus spoken of as "associated" when the special central nervous mechanism employed in carrying out the one act is so connected by nervous ties of some kind or other with that employed in carrying out the other, that when we set the one mechanism in action we unintentionally set the other in

action also. The ciliary muscles which bring about accommodation are governed in this action by fibres which may be traced, through the ciliary nerves and lenticular ganglion, along the third or oculo-motor nerve, to a centre which lies (in dogs) in the hind part of the floor of the third ventricle, and which is especially connected with the most anterior bundles of the roots of the third nerve. This centre is under the command of our will: when we wish to accommodate for near objects we throw it into action, and it, when in action, calls also into action by "association" the centre for the contraction of the pupil; when the action of the accommodation centre ceases and the eye falls back to the condition of rest, in which it is accommodated for far objects, the action of the pupil-contracting centre ceases also, and the pupil therefore widens.

The mechanism of accommodation may also be affected in a local manner. And the drugs which have a special action on the pupil, such as atropin and calabar bean, also affect the mechanism of accommodation. Atropin paralyzes it, so that the eye remains adjusted for far objects; and physostigmin throws the eye into a condition of forced accommodation for near objects. This double action has been explained by the supposition that while atropin paralyzes, physostigmin throws into tonic or tetanic contraction, on the one hand the circular muscles of the iris and on the other the ciliary muscles; but the phenomena, on inquiry, appear too complicated to be explained in so simple a manner.

We can accommodate at will; but few persons can effect the necessary change in the eye unless they direct their attention to some near or far object, as the case may be, and thus assist their will by visual sensations. By practice, however, the aid of external objects may be dispensed with; and it is when this is achieved that the pupil may seem to be made to dilate or contract at pleasure, accommodation being effected without the eye being turned to any particular object.

Imperfections in the Dioptric Apparatus.

The emmetropic eye may be taken as the normal eye. The myopic and hypermetropic eyes may be considered as imperfect eyes, though the former possesses certain advantages over the normal eye. An eye might be myopic from too great a convexity of the cornea, or of the anterior surface of the lens, or from permanent spasm of the accommodation-mechanism, or from too great a length of the long axis of the eyeball. The last appears to be the usual cause. Similarly, most hypermetropic eyes possess too short a bulb. Moreover, in the strongly marked

myopic eye there is frequently hypertrophy of the longitudinal (meridional) fibres of the ciliary muscle, often spoken of exclusively as the ciliary muscle, and atrophy or absence of the circular fibres; in the hypermetropic eye, on the other hand, the circular fibres are well developed and the meridional fibres scanty. The presbyopic eye is, as we have seen, an eye normally constituted, in which the power of accommodation has been lost or is failing through increasing weakness of the ciliary muscle or a loss of elasticity in the lens, or through the parts becoming rigid.

Spherical Aberration.—In a spherical lens the rays which impinge on the circumference are brought to a focus sooner than those which pass nearer the centre, and the rays proceeding from a luminous point are no longer brought to a single focus at one point, but form a number of foci at different distances. Hence, when rays are allowed to fall on the whole of the lens, the image formed on a screen placed in the focus of the more central rays is blurred by the diffusion-circles caused by the circumferential rays which have been brought to a premature focus. In an ordinary optical instrument spherical aberration is obviated by a diaphragm which shuts off the more circumferential rays. In the eye the iris is an adjustable diaphragm; and when the pupil contracts in near vision the more divergent rays proceeding from a near object, which tend to fall on the circumferential parts of the lens, are cut off. As, however, the refractive power of the lens does not increase regularly and progressively from the centre to the circumference, but varies most irregularly, the purpose of the narrowing of the pupil cannot be simply to obviate spherical aberration; and, indeed, the other optical imperfections of the eye are so great, that such spherical aberrations as are caused by the lens produce no obvious effect on vision.

Astigmatism.—We have hitherto treated the eye as if its dioptric surfaces were all parts of perfect spherical surfaces. In reality this is rarely the case, either with the lens or with the cornea. Slight deviations do not produce any marked effect, but there is one deviation, known as regular astigmatism, which, present to a certain extent in most eyes, very largely developed in some, frequently leads to very imperfect vision. This defect is due to the dioptric surface being not spherical but more convex along one meridian than another, more convex, for instance, along the vertical than along the horizontal meridian. When this is the case, the rays proceeding from a luminous point are not brought to a single focus at a point, but possess two linear

foci, one nearer than the normal focus and corresponding to the more convex surface, the other further than the normal and corresponding to the less convex surface. If the vertical meridians of the surface be more convex than the horizontal, then the nearer linear focus will be horizontal and the further linear focus will be vertical, and *vice versa*. (This can be shown much more effectually on a model than in a diagram in which we are limited to two dimensions.) Now, in order to see a vertical line distinctly, it is much more important that the rays which diverge from the line in a series of horizontal planes should be brought to a focus properly than those which diverge in the vertical plane of the line itself; and, similarly, in order to see a horizontal line distinctly, it is much more important that the rays which diverge from the line in a series of vertical planes should be brought to a focus properly than those which diverge in the horizontal plane of the line itself. Hence, a horizontal line held before an astigmatic dioptric surface, most convex in the vertical meridians, will give rise to the image of a horizontal line at the nearer focus, the vertical rays diverging from the line being here brought to a linear horizontal focus. Similarly, a vertical line held before the same surface will give rise to an image of a vertical line at the further focus, the horizontal rays diverging from the vertical line being here brought to a linear vertical focus. In other words, with a dioptric surface most convex in the vertical meridians, horizontal lines are brought to a focus sooner than are vertical lines.

Most eyes are thus more or less astigmatic, and generally with a greater convexity along the vertical meridians. If a set of horizontal or vertical lines be looked at, or if the near point of accommodation be determined by Scheiner's experiment (p. 585), for the needle placed first horizontally and then vertically, the horizontal lines or needle will be distinctly visible at a shorter distance from the eye than the vertical lines or needle. Similarly, the vertical line must be further from the eye than a horizontal one, if both are to be seen distinctly at the same time. The cause of astigmatism is, in the great majority of cases, the unequal curvature of the cornea; but sometimes the fault lies in the lens, as was the case with Young.

When the curvature of the cornea or lens differs not in two meridians only but in several, irregular astigmatism is the result. A certain amount of irregular astigmatism exists in most lenses, thus causing the image of a bright point, such as a star, to be not a circle but a radiate figure.

Chromatic Aberration.—The different rays of the spectrum are of different refrangibility, those towards the violet end of the

spectrum being brought to a focus sooner than those near the red end. This in optical instruments is oviated by using compound lenses made up of various kinds of glass. In the eye we have no evidence that the lens is so constituted as to correct this fault; still, the total dispersive power of the instrument is so small, that such amount of chromatic aberration as does exist attracts little notice. Nevertheless, some slight aberration may be detected by careful observation. When the spectrum is observed at some distance, the violet end will not be seen in focus at the same time as the red. If a luminous point be looked at through a narrow orifice covered by a piece of violet glass, which while shutting out the yellow and green allows the red and blue rays to pass through, there will be seen alternately an image having a blue centre with a red fringe, or a red centre with a blue fringe, according as the image of the point looked at is thrown on one side or other of the true focus. Thus, supposing f (Fig. 192) to be

FIG. 192.

DIAGRAM ILLUSTRATING CHROMATIC ABERRATION.

hh is the dioptric surface, hv represents the blue, and hr the red rays; V is the focal plane of the blue, R of the red rays.
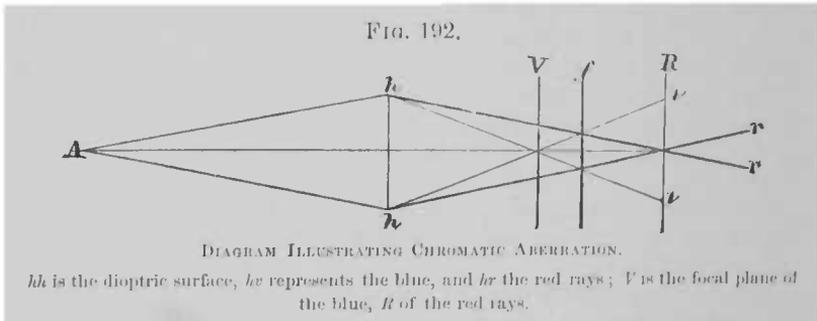
the plane of the mean focus of A, the violet rays will be brought to a focus in the plane V, and the red rays in the plane R. If the rays be supposed to fall on the retina between V and f, the diverging or blue rays will form a centre surrounded by the still converging red rays; whereas, if the rays fall on the retina between f and R, the converging red rays will form a centre with the still diverging blue rays forming a fringe round them. If the rays fall on the retina at f, the two kinds of rays will be mixed together; as will be seen from the figure, the circumferential still converging red ray hr as it cuts the plane of the retina is, in ordinary vision, accompanied by the diverging violet ray hv, and thus by a sort of compensation, we see together even the rays which differ most in refraction.

Entoptic Phenomena.—The various media of the eye are not uniformly transparent; the rays of light in passing through them undergo local absorption and refraction, and thus various shadows are thrown on the retina, of which we become conscious as im-

perfections in the field of vision, especially when the eye is directed to a uniformly illuminated surface. These are spoken of as entoptic phenomena, and are very varied, many forms having been described.

The most common are those caused by the presence of floating bodies in the vitreous humor, the so-called *muscæ volitantes*. These are readily seen when the eye is turned towards a uniform surface, and are frequently very troublesome in looking through a microscope. They are especially obvious when divergent rays fall upon the eye. They assume the form of rows and groups of beads, of single beads, of streaks, patches, and granules, and may be recognized by their almost continual movement, especially when the head or eye is moved up and down. When an attempt is made to fix the vision upon them, they immediately float away. Tears on the cornea, temporary unevenness on the anterior surface of the cornea after the eyelid has been pressed on it, and imperfections in the lens or its capsule, also give rise to visual images. Not unfrequently a radiate figure corresponding to the arrangement of the fibres of the lens makes its appearance.

Imperfections in the margin of the pupil appear in the shadow of the iris which bounds the field of vision; and the movements of the iris in one eye may be rendered visible by looking at a bright point or luminous surface through a pinhole in a card placed close in the front of the eye, in the anterior focus in fact, and then alternately closing and opening the other eye; the field of the first may be observed to contract when light enters, and to expand when the light is shut off from the second. The media of the eye are fluorescent, a condition which favors the perception of the ultra-violet rays. If a white sheet or white cloud be looked at in daylight through a Nicol's prism, a somewhat bright double cone or double tuft, with the apices touching, of a faint blue color, is seen in the centre of the field of vision, crossed by a similar double cone of a somewhat yellow darker color. These are spoken of as Haidinger's brushes; they rotate as the prism is rotated, and are supposed to be due to the unequal absorption of the polarized light in the yellow spot. The prism must be frequently rotated, as when the prism remains at rest the phenomena fade. Lastly, the optical arrangements have a further imperfection in that the dioptric surfaces are not truly centred on the optic axis.

Sec. 2.—Visual Sensations.

Light falling on the retina excites *sensory impulses*, and these passing up the optic nerve to certain parts of the brain, produce changes in certain cerebral structures, and thus give rise to what

we call a *sensation*. In a sensation we ought to be able to distinguish between the events through which the impact of the rays of light on the retina is enabled to generate sensory impulses, and the events, or rather series of events, through which these sensory impulses (or, judging by the analogy of motor nerves, we have no reason to think that they undergo any fundamental changes in passing along the optic nerve), by the agency of the cerebral arrangements, develop into a sensation. Such an analysis, however, is, at present at least, in most particulars, quite beyond our power; and we must therefore treat of the sensations as a whole, distinguishing between the peripheral and central phenomena, on the rare occasions when we are able to do so.

The Origin of Visual Impulses.

Of primary importance to the understanding of the way in which luminous undulations give rise to those nervous changes which pass along the optic nerve as visual impulses, is the fact that the rays of light produce their effect by acting not on the optic nerve itself but on its terminal organs (see p. 571). They pass through the anterior layers of the retina apparently without inducing any effect; it is not till they have reached the region of the rods and cones that they set up the changes concerned in the generation of visual impulses and the impulses here generated travel back to the layer of fibres in the anterior surface of the retina and thence pass along the optic nerve. That the optic fibres are themselves insensible to light and that visual impulses begin in the region of rods and cones is shown by the phenomena of the blind spot and of Purkinje's figures respectively.

Blind Spot.—There is one part of the retina on which rays of light falling give rise to no sensations; this is the entrance of the optic nerve, and the corresponding area in the field of vision is called the blind spot. If the visual axis of one eye, the right for instance, the other being closed, be fixed on a black spot in a white sheet of paper, and a small black object, such as the point of a quill pen dipped in ink, be moved gradually sideways over the paper away to the outside of the field of vision, at a certain distance the black point of the quill will disappear from view. On continuing the movement still further outward the point will again come into view and continue in sight until it is lost in the periphery of the field of vision. If the pen be used to make a mark on the paper at the moment when it is lost to view, and at the moment when it comes into sight again; and if similar marks be made along the other meridians as well

as the horizontal, an irregular outline will be drawn circumscribing an area of the field of vision within which rays of light produce no visual sensation. (Fig. 193.) This is the blind spot.

[FIG. 193.

Fix the visual axis of the right eye on the black spot, keeping the left eye closed. Hold the page about five inches from the eye, and both the spot and cross will be seen. If now, while the right eye is steadily fixed on the spot, the page is moved slowly outwards, the cross will disappear entirely, and again reappear if the movement is continued.]

The dimensions of the figure drawn vary, of course, with the distance of the paper from the eye. If this distance be known, the size as well as the position of the area of the retina corresponding to the blind spot may be calculated from the diagrammatic eye (p. 583). The position exactly coincides with the entrance of the optic nerve, and the dimensions (about 1.5 mm. diameter) also correspond. While drawing the outline as above directed the indications of the large branches of the retinal vessels as they diverge from the entrance of the nerve can frequently be recognized. The existence of the blind spot is also shown by the fact that an image of light, sufficiently small, thrown upon the optic nerve by means of the ophthalmoscope, gives rise to no sensations.

The existence of the blind spot proves that the optic fibres themselves are insensible to light; it is only through the agency of the retinal expansion that these can be stimulated by luminous vibrations.

Purkinje's Figures.—If one enters a dark room with a candle, and while looking at a plain (not parti-colored) wall, moves the candle up and down, holding it on a level with the eyes by the side of the head, there will appear in the field of vision of the eye of the same side, projected on the wall, an image of the retinal vessels, quite similar to that seen on looking into an eye with the ophthalmoscope. The field of vision is illuminated with a glare, and on this the branched retinal vessels appear as shadows. In this mode of experimenting the light enters the eye through the cornea, and an image of the candle is formed on the nasal side of the retina; and it is the light emanating from this image which throws shadows of the retinal vessels on to the rest of the retina. A far better method is for a second person to concentrate the rays of light, with a lens of low power, on to the outside of the sclerotic just behind the cornea; the light in this case emanates from the illuminated spot on the sclerotic and passing straight through the vitreous humor throws a direct shadow of the vessels on to the retina. Thus the rays passing through the

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sclerotic at *b*, Fig. 194, in the direction *bv*, will throw a shadow of the vessel ν on the retina at β; this will appear as a dark line at B in the glare of the field of vision. This proves that the structures in which visual impulses originate must lie behind the retinal vessels, otherwise the shadows of these could not be perceived.

If the light be moved from *b* to *a*, the shadow on the retina will move from β to α, and the dark line in the field of vision will move from B to A. If the distance BA be measured when
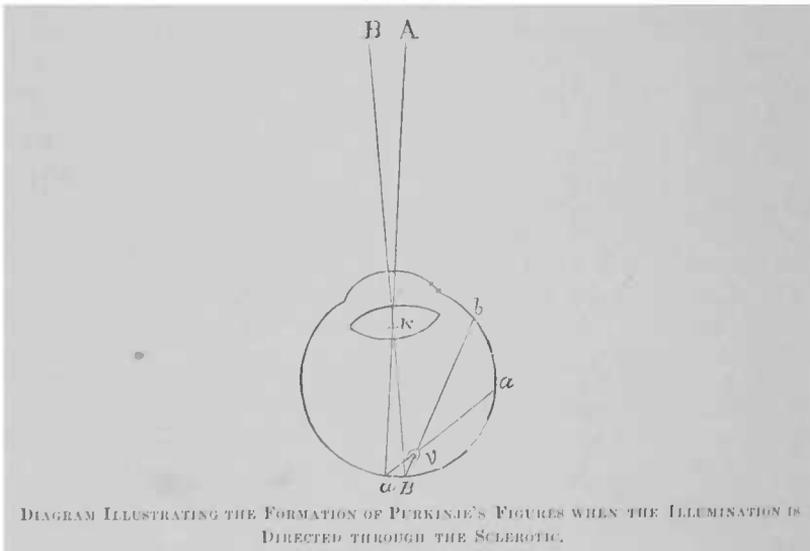
DIAGRAM ILLUSTRATING THE FORMATION OF PURKINJE'S FIGURES WHEN THE ILLUMINATION IS DIRECTED THROUGH THE SCLEROTIC.

the whole image is projected at a known distance, *k*B from the eye, *k* being the optical centre,[1] then, knowing the distance *k*β in the diagrammatic eye, the distance βα can be calculated. But, if the distance βα be thus estimated, and the distance *ba* be directly measured, the distances βv, αv, *b*v, *a*v can be calculated, and if the appearance in the field of vision is really caused by the shadow of ν falling on β, these distances ought to correspond to the distances of the retinal vessels ν from the sclerotic *b* on the one hand, and from that part of the retina β where visual

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[1] For the properties of the optical centre, we must refer the reader to the various treatises on optics. The optical centre of a lens is the point through which all the principal rays of the various pencils of rays falling on the lens pass. The diagrammatic eye of Listing (p. 583) has two optical centres, but these may, without serious error, be further reduced for practical purposes to one lying in the lens near its posterior surface, at about 15 mm. distance from the retina.

impressions begin, on the other. H. Müller found that the distance $\beta\nu$ thus calculated corresponded to the distance of the retinal vessels from the layer of rods and cones. Thus Purkinje's figures prove, in the first place, that the sensory impulses which form the commencement of visual sensations originate in some part of the retina behind the retinal vessels—*i. e.*, somewhere between them and the choroid coat; and H. Müller's calculations go far to show that they originate at the most posterior or external part of the retina, viz., the layer of rods and cones. It must be admitted, however, that H. Müller's results were not sufficiently exact to allow any great stress to be placed on this argument.

In the second method of experimenting, the image always moves in the same direction as the light, as it obviously must do. In the first method, where the light enters through the cornea, the image moves in the same direction as the light when the light is moved from right to left, provided the movement does not extend beyond the middle of the cornea, but in the opposite direction to the light when the latter is moved up and down. In Fig. 195, which represents a horizontal section of an eye, if a

FIG. 195.

DIAGRAM ILLUSTRATING THE FORMATION OF PURKINJE'S FIGURES WHEN THE ILLUMINATION IS DIRECTED THROUGH THE CORNEA.
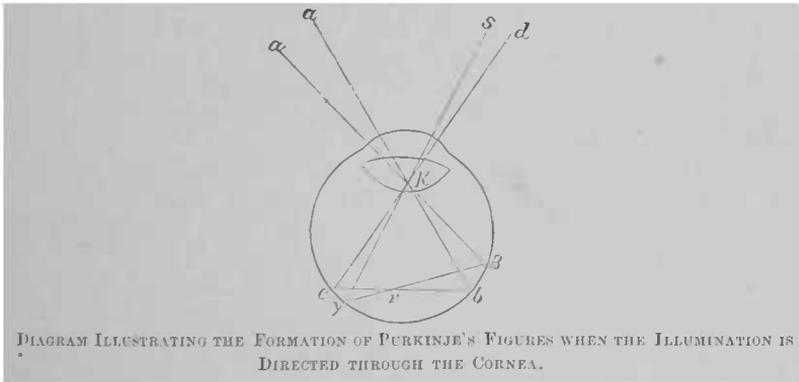
be moved to a, b will move to β, the shadow on the retina c to γ, and the image d to δ. If, on the other hand, a be supposed to move about the plane of the paper, b will move below, in consequence c will move above, and d will appear to move below—*i. e.*, d will sink as a rises.

It is desirable in these cases to move the light to and fro, especially in the first method, as the retina soon becomes tired, and the image fades away. Some observers can recognize in the axis of vision a faint shadow corresponding to the edge of the depression of the fovea centralis.

The retinal vessels may also be rendered visible by looking

through a small orifice such as a pinhole in a card placed close to the eye, at a bright field such as the sky, and moving the orifice very rapidly from side to side, or up and down. If the movement be from side to side, the vessels which run vertical will be seen; if up and down, the horizontal vessels. The fine capillary vessels are seen more easily in this way than by Purkinje's method. The same appearances may also be produced by looking through a microscope from which the objective has been removed and the eye-piece only left (or in which, at least, there is no object distinctly in focus in the field), and moving the head rapidly from side to side or backward and forward. Or the microscope itself may be moved; a circular movement of the field will then bring both the vertically and horizontally directed vessels into view at the same time.

The Photochemistry of the Retina.—In seeking to understand how it is that rays of light falling upon the region of the rods and cones can give rise to sensory visual impulses in the optic nerve, we may adopt one or other of two views. On the one hand, we may suppose that the vibrations of the ether are able, through the means of the retinal apparatus of the rods and cones for example, to give rise in some way or other to molecular vibrations, which are the beginning of the nervous impulses in the optic nerve. No satisfactory explanation of how such a change can be brought about has been offered, and, indeed, the difficulties of such a conception are very great. On the other hand, we may more naturally turn to a chemical explanation. We are familiar with the fact that rays of light are able to bring about the decomposition of very many chemical substances; and we accordingly speak of these substances as being sensitive to light. All the facts dwelt on in this book illustrate the great complexity and corresponding instability of the composition of protoplasm. And we might reasonably suppose that protoplasm itself would be sensitive to light; that is to say, that rays of light falling on even undifferentiated protoplasm might set up a decomposition of that protoplasm and so inaugurate a molecular disturbance; in other words, that light might act as a direct stimulus to protoplasm. As a matter of fact, however, such evidence as we at present possess, goes to show that native undifferentiated protoplasm is, as a rule, not sensitive to light (that is, to those particular waves which when they fall on our retina give rise in us to the sensation of light), though in the case of some lowly organisms, whose protoplasm exhibits very little differentiation and in particular contains no pigment, a sensitiveness to light has been observed. Nor can we be surprised at this indifference of protoplasm when we reflect that what we

may call pure protoplasm is remarkable for its transparency, that is to say, the rays of light pass through it with the slightest possible absorption. But in order that light may produce chemical effects, it must be absorbed; it must be spent in doing the chemical work. Accordingly the first step towards the formation of an organ of vision is the differentiation of a portion of protoplasm into a pigment at once capable of absorbing light, and sensitive to light—i. e., undergoing decomposition upon exposure to light. An organism, a portion of whose protoplasm had thus become differentiated into such a pigment, would be able to react towards light. The light falling on the organism would be in part absorbed by the pigment, and the rays thus absorbed would produce a chemical action and set free chemical substances which before were not present. We have only to suppose that the chemical substances are of such a nature as to act as a stimulus to the protoplasm of other parts of the organism (and we have manifold evidence of the exquisite sensitiveness of protoplasm in general to chemical stimuli), in order to see how rays of light falling on the organism might excite movements in it, or modify movements which were being carried on, or might otherwise affect the organisms in whole or in part.

Such considerations as the foregoing may be applied to even the complex organ of vision of the higher animals. If we suppose that the actual terminations of the optic nerve are surrounded by substances sensitive to light, then it becomes easy to imagine how light falling on these sensitive substances should set free chemical bodies possessed of the property of acting as stimuli to the actual nerve-endings and thus give rise to visual impulses in the optic fibres. We say "easy to imagine," but we are, at present, far from being able to give definite proofs that such an explanation of the origin of visual impulses is the true one, probable and enticing as it may appear.

One of the most striking features in the structure of the retina is the abundance of black pigment in the retinal, or, as it is sometimes called, choroidal, epithelium. It is difficult to suppose that the sole function of this pigment is to absorb the superfluous rays of light, and that the rays thus absorbed are put to no use but simply wasted. And, indeed, it has been shown that the pigment is sensitive to light; but the changes in it induced by light are excessively slow. Moreover, its presence cannot be of fundamental importance, since vision is not only possible but fairly distinct with albinos in which this pigment is absent.

Then again, in the vast majority of vertebrate animals, the outer limbs of the rods are suffused with a purplish-red pigment, the so-called visual purple, which is so eminently sensitive to light that images of external objects may, by appropriate means, be

photographed in it on the retina. When the eye of a frog or of a rabbit is examined in an ordinary way, with full exposure to light, the retina appears colorless. But if the eye be kept in the dark for some time before it is examined, the retina, if removed rapidly, will be found to be of a beautiful purplish-red color. Upon exposure to light the color changes to yellow and then fades away, leaving, however, the retina, not only white but more opaque than it was before. Upon examination with the microscope it is found that the purple color is confined exclusively to the rods and to the outer limbs of the rods, the inner limbs being wholly devoid of it.

The color of the rods is due to the presence of a distinct pigment, the "visual purple," diffused through the substance of the outer limbs; and this may be extracted from the rods by dissolving these in an aqueous solution of bile salts. A clear purple solution is thus obtained, which is capable of being bleached by the action of light, and in its general features and behavior is similar to the pigment as it naturally exists in the retina.

Visual purple is found, as we have said, exclusively in the outer limbs of the rods; it has never yet been found in the cones, and it is accordingly absent from the retinas (such as those of snakes) which are composed of cones only, and from the macula lutea and fovea centralis of the retinas of man and the ape. The intensity of the coloration varies in different animals, and the retinas even of some animals possessing rods (bat, dove, hen) seem to be wholly devoid of the visual purple; it is generally well marked in retinas in which the outer limbs of the rods are well developed. Its absence or presence is not dependent on nocturnal habits, since the intense color of the retina of the owl is in strong contrast to the absence of color in the bat. It has been found in the retina of the embryo.

The visual purple is bleached not only by white but also by monochromatic light. Of the various prismatic rays, the most active are the greenish-yellow rays, those to the blue side of these coming next, the least active being the red. Now it is precisely the greenish-yellow rays which are most readily absorbed by the color itself. A natural colored retina or a solution of visual purple gives a diffuse spectrum without any defined absorption bands, and according to the amount of coloring material through which the light passes, absorption is seen either to be limited to the greenish-yellow part of the spectrum or to spread thence towards the blue and, to a much less extent, towards the red. Thus the various prismatic rays produce a photochemical effect on the visual purple in proportion as they are absorbed by it. Under the action of light, the visual purple, whether in solution, or in its natural condition in the rods, passes through a purplish-

orange to a yellow, and finally becomes colorless; and we appear to be justified in speaking of a "visual yellow" and "visual white" as products of the photochemical changes undergone by the visual purple.

For the restoration of the visual purple, after it has been destroyed by light, the maintenance of the circulation of the blood through the tissues of the eye is not essential. The choroidal epithelium has by itself, provided that it still retains its tissue life, the power of regenerating the purple. If a portion of the retina of an excised eye be raised from its epithelial bed, bleached, and then carefully restored to its natural position, the purple will return if the eye be kept in the dark. The choroidal epithelium may, in fact, be spoken of as a "purpurogenous" membrane.

If the image of some bright object, such as a lamp or a window, be thrown on to the retina, either of an eye in its natural position or of one recently excised, care having been taken to keep the retina for some time previous away from any rays of light, the portion of the retina on which the rays have fallen will be found to be bleached, the rest of the retina remaining purple. In fact, an "optogram" of external objects may thus be obtained; and, if the retina be removed and treated with a four per cent. solution of potash alum before the choroidal epithelium has had time to obliterate the bleaching effects, the retina may remain permanently in that condition; the photochemical effect may, as the photographers say, be "fixed."

It seemed very tempting, especially upon the first discovery of it, to suppose that this visual purple is directly concerned in vision. If we suppose that visual purple itself is inert towards the endings of the optic nerve, but that either visual yellow or visual white—*i. e.*, some product of the action of light on visual purple, may act as a stimulus to those endings, the way seems opened to understanding how rays of light can give rise to sensory impulses in the optic nerve. Unfortunately, visual purple is absent from the cones, and from the fovea centralis which, as we shall see, is the region of distinct vision; it is further entirely wanting in some animals which undoubtedly see very well; and, lastly, animals, such as frogs, naturally possessing the pigment, continue to see very well and even apparently to see colors when their visual purple has been absolutely bleached, as it may be by prolonged exposure of the eyes to strong light. We cannot, therefore, at present at least, explain the origin of visual impulses by the help of visual purple. At the same time its history suggests that some substances, sensitive like it to light, but unlike it, colorless, and therefore escaping observation, may exist, and by photochemical changes be the means of exciting the optic

nerves. And, as we shall see later on, one theory of color vision is based on the assumption that vision is carried on in some way or other by changes in what may be called visual substances present in the retina, these substances being used up and regenerated as vision is going on.

But even admitting as probable the existence of these sensitive visual substances, the changes in which lead to stimulation of the real endings of the retinal nervous mechanisms, we cannot at present state anything definite concerning those nerve-endings or the manner of their stimulation. It may be that even the outer limbs of the rods and cones, in spite of the apparent break of continuity between the outer and inner limbs, are really nervous in nature. It may be, on the other hand, that the outer limbs are either purely dioptric in function, or are associated with the sensitive visual substances in such a way that the purely nervous structures must be considered as extending no further, at least, than the inner limbs. We cannot as yet make any definite statement in the one direction or the other.

In connection with the origin of visual impulses we may perhaps call attention to the remarkable changes which the cells of the retinal pigment epithelium undergo under the influence of light. When an eye has been shut off from all light for some little time, the pigment is concentrated in the bodies of the cells, and the remarkable filamentous processes of the cells, with the pigment granules or crystals which they carry, extend a slight distance only between the limbs of the rods and cones (about one-third down the length of the outer limbs of the rods). Under the influence of light these processes loaded with pigment thrust themselves a much longer way down towards the external limiting membrane; in consequence a considerable quantity of pigment is found massed between the outer and even the inner limbs of the rods and cones; indeed the outer limbs of the rods swelling, at the same time, become jammed as it were between the masses of pigment, causing the epithelial layer to adhere very closely to the layer of rods and cones.

The retina and optic nerve like other nervous structures develop electric currents which may be spoken of as currents of rest and currents of action. They may be shown by placing one electrode on the retina of a bisected eye, or on the cornea of a whole one, and the other on the optic nerve, or hind part of the eyeball or even on some distant part of the body. They are also manifested by the isolated retina itself. The phenomena appear somewhat complicated by the appearance now of positive, now of negative variations; but this fact comes out clearly that the incidence of light on the irritable retina develops an electric change, the magnitude of which is to a certain extent propor-

tionate to the intensity of the light acting as a stimulus. The changes accordingly diminish and cease to appear as the retina gradually loses its irritability after death. We may add that these electric phenomena appear to be quite independent of the condition of the visual purple.

Simple Sensations.

Relations of the Sensation to the Stimulus.—If we put aside for the present all questions of color, we may say that light, viewed as a stimulus affecting the retina, varies in intensity—that is, in the energy of the luminous vibrations as manifested by their amplitude; and in duration—that is, in the length of time a succession of waves continues to fall upon the retina. The effect of the light will also depend on the extent of retinal surface exposed to the luminous vibrations at the same time. Taking a luminous point, in order to eliminate the latter circumstance, we may make the following statements.

The sensation has a duration much greater than that of the stimulus, and, in this respect, is comparable to a muscular contraction caused by such a stimulus as a single induction shock. The sensation of a flash of light, for instance, lasts for a much longer time than that during which luminous vibrations are falling on the retina. Hence, when two stimuli, such as two flashes of light, follow each other at a sufficiently short interval, the two sensations are fused into one; and a luminous point moving rapidly round in a circle gives rise to the sensation of a continuous circle of light. This again is quite comparable to muscular tetanus. The interval at which fusion takes place, that is, the interval between successive stimuli which must be exceeded in order that successive distinct sensations may be produced, varies according to the intensity of the light, being shorter with the stronger light; with a faint light it is about $\frac{1}{10}$ sec., with a strong light $\frac{1}{30}$ or $\frac{1}{50}$ sec. This may be shown by rotating rapidly before the eye a disk arranged with alternate black and white sectors of equal width. With a faint illumination, the flickering indicative of the successive sensations from the white sectors not being completely fused, ceases when the rotation becomes so rapid that each pair of black and white sectors takes only $\frac{1}{10}$ sec. in passing before the eye. When a brighter illumination is used the rapidity must be increased before the flickering disappears. That part of the sensation which is recognized as lasting after the cessation of the stimulus is frequently spoken of as the "after-image."

Though the duration of the after-image is longer with the stronger light (that caused by looking even momentarily at the

sun lasting for some time), the commencement of the decline of the sensation begins relatively earlier, hence the greater difficulty in the complete fusion of successive sensations with the stronger light. The interval at which fusion takes place differs with different colors, being shortest with yellow, intermediate with red, and longest with blue.

The duration of a stimulus necessary to call forth a sensation is exceedingly short; thus, the shortest possible flash, such as that of an electric spark, gives rise to a sensation of light.

Objects in motion, when illuminated by a single electric spark, appear motionless, the stimulus of the light reflected from them ceasing before they can make an appreciable change in their position. When a moving body is illuminated by several rapid flashes in succession, several distinct images corresponding to the positions of the body during the several flashes are generated — the images of the body corresponding to the several flashes fall on different parts of the retina.

The intensity of the sensation varies with the luminous intensity of the object; a wax candle appears brighter than a rush-light. The ratio, however, of the sensation to the stimulus is not a simple one. If the luminosity of an object be gradually increased from a very feeble stage to a very bright one, it will be found that, though the corresponding sensations likewise gradually increase, the increments of the sensations due to increments of the luminosity gradually diminish; and at last an increase of the luminosity produces no appreciable increase of sensation; a light, when it reaches a certain brightness, appears so bright that we cannot tell when it becomes any brighter. Hence, it is much easier to distinguish a slight difference of brightness between two feeble lights than the same difference between two bright lights; we can easily tell the difference between a rush-light and a wax candle; but two suns, or even two bright lamps, one of which differed from the other merely by just the number of luminous rays which a wax candle emits in addition to those sent forth by a rushlight, would appear to us to have exactly the same brightness. In a darkened room an object placed before a candle will throw what we consider a deep shadow on a sheet of paper, or any white surface. If, however, sunlight be allowed to fall on the paper at the same time from the opposite side, the shadow is no longer visible. The difference between the total light reflected from that part of the paper where the shadow was, and which is illuminated by the sun alone, and that reflected from the rest of the paper which is illuminated by the candle as well as by the sun, remains the same; yet we can no longer appreciate that difference.

On the other hand, if using two rushlights we throw two

shadows on a white surface and move one rushlight away until the shadow caused by it ceases to be visible; and, having noted the distance to which it had to be moved, repeat the same experiment with two wax candles; we shall find that the wax candle has to be moved just as far as the rushlight.   In fact, it is found by careful observation, that within tolerably wide limits, the smallest difference of light which we can appreciate by visual sensations is a constant fraction (about $\frac{1}{100}$th) of the total luminosity employed.   The same law holds good with regard to the other senses as well.   The smallest difference in length we can detect between two lines, one an inch long and the other a little less than an inch, is the same fraction of an inch, that the smallest difference in length we can detect between a line a foot long and one a little less than a foot, is of a foot.   Put in a more general form, then, the law, which is often called Weber's law,[1] is as follows: When a stimulus is continually increased, the increase of stimulus necessary to call forth the smallest appreciable increase of sensation always bears the same proportion to the whole stimulus.

Distinction and Fusion of Sensations.—When light falls on a large portion of the retina, the total sensation produced is greater in *amount* than when a small portion only of the retina is affected; a large piece of white paper produces a greater total effect on our consciousness than a small one; though, if the surfaces be uniformly and equally illuminated, the *intensity* of the sensation is in each case the same; the small piece of paper appears as bright or as "white" as the large one.   If the images of two luminous objects fall on the retina at sufficient distances apart, the consequent sensations are distinct, and the intensity of each sensation will depend solely upon the luminosity of the corresponding object.   If, however, the two objects are made to approach each other, a point will be reached at which the two sensations are fused into one.   When this occurs, the intensity of the total sensation produced will be greater than that of either of the sensations caused by the single objects.   A number of luminous points scattered over a wide surface would appear each to have a certain brightness; each would give rise to a sensation of a certain intensity.   If they were all gathered into one spot, that spot would appear far brighter than any of the previous points; the intensity of the sensation would be greater.   We may therefore suppose the retina to be divided into areas corresponding to sensational units.   If the images from two luminous objects fall

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[1] From which Fechner, by an assumption, obtained a mathematical expression or formula, which is sometimes incorrectly spoken of as Fechner's law.

on separate visual areas, if we may so call them, two distinct sensations will be produced; if, on the contrary, they both fall on the same visual area, one sensation only will be produced. Where the sensations are separate, the intensity of the one (with exceptions hereafter to be mentioned) is not affected by the presence of the other; but where they become fused, the intensity of the united sensations is greater than either of, though not equal to the sum of, the single sensations. The existence of these sensational units is the basis of distinct vision. When we speak of the smallest size visible or distinguishable, we are referring to the dimensions of the retinal areas corresponding to these sensational units. The retinal area must be carefully distinguished from the sensational unit, for the sensation is, as we have seen, a process whose arena stretches from the retina to certain parts of the brain, and the circumscription of the sensational unit, though it must begin as a retinal area, must also be continued as a cerebral area in the brain, the latter corresponding to, and being, as it were, the projection of, the former. With most people two stars appear as a single star when the distance between them subtends an angle of less than 60 seconds; and the best eyes generally fail to distinguish two parallel white streaks when the distance between the two, measured from the middle of each, subtends an angle of less than 73 seconds. Some, however, can distinguish objects 50 seconds distant from each other. An angle of 73 seconds in an object corresponds in the diagrammatic eye (see p. 583) to the length of 5.36μ in the retinal image,[1] and one of 50 seconds to 3.65μ.

In the human eye 50 cones may be counted along a line of 200μ in length drawn through the centre of the yellow spot; this would give 4μ for the distance between the centres of two adjoining cones in the yellow spot, the average diameter of a cone at its widest part being 3μ and there being slight intervals between neighboring cones. Hence if we take the centre of a cone as the centre of an anatomical retinal area, those anatomical areas correspond very fairly to the physiological visual areas as determined above. That is to say, if two points of the retinal image are less than 4μ apart, they may both lie within the area of a single cone; and it is just when they are less than about 4μ apart that they cease to give rise to two distinct sensations. It must be remembered, however, that the fusion or distinction of the sensations is ultimately determined by the brain and not by the retina. Two points of the retinal image less than 4μ apart might lie both within the area of a single cone; but the reason why, under such circumstances, they give

[1] By μ is meant one-thousandth of a millimetre.

rise to one sensation only is not because one cone-fibre only is stimulated. Two points of a retinal image might lie, one on the area of one cone and another on the area of an adjoining cone, and still be less than 4 μ apart; in such a case two cone-fibres would be stimulated, and yet only one sensation would be produced. So also in the less sensitive peripheral parts of the retina two points of the retinal image might stimulate two cones a considerable distance apart, and yet give rise to one sensation only.

In the case where the two points lie entirely within the area of a single cone, it is exceedingly probable that, even if the adjacent cones or cone-fibres in the retina are not at the same time stimulated, impulses radiate from the cerebral ending of the excited cone into the neighboring cerebral endings of the neighboring cones; in other words, the sensation-area in the brain does not exactly correspond to and is not sharply defined like the retinal area, but gradually fades away into neighboring sensation-areas. We may imagine two points of the retinal image so far apart that even the extreme margins of their respective cerebral sensation-areas do not touch each other in the least; in such a case there can be no doubt about the two points giving rise to two sensations. We might, however, imagine a second case where two points were just so far apart that their respective sensation-areas should coalesce at their margins, and yet that, in passing from the centre of one sensation-area to the centre of the other, we should find on examination a considerable fall of sensation at the juncture of the two areas; and in a third case we might imagine the two centres to be so close to each other that in passing from one to the other no appreciable diminution of sensation could be discovered. In the last case there would be but one sensation, in the second there might still be two sensations if the marginal fall were great enough, even though the areas partially coalesced. Thus, though the mosaic of rods and cones is the basis of distinct vision, the distinction or fusion of two visual impulses is ultimately determined by the disposition and condition of the cerebral centres. Hence the possibility of increasing by exercise the faculty of distinguishing two sensations, since by use the cerebral sensation-areas become more and more differentiated. This however is even more strikingly shown in touch than in sight.

Color Sensations.

When we allow sunlight reflected from a cloud or sheet of paper to fall into the eye, we have a sensation which we call a sensation of white light. When we look at the same light through a prism, and allow different parts of the spectrum to

fall in succession into the eye, we have sensations which we call
respectively sensations of red, orange, yellow, green, blue, violet,
etc., light. In other words, rays of light falling on the retina
give rise to different sensations, according to the wave-lengths of
the rays. Though we speak of the spectrum as consisting of a
few colors, such as red, orange, etc., there are an almost infinite
number of intermediate tints in the spectrum itself; and we
perceive in external nature a large number of colors, such as
purple, brown, gray, etc., which do not correspond to any of the
color sensations gained by regarding the successive parts of the
spectrum. We find, however, on examination that certain dis-
tinct color sensations, not corresponding to any of the colors of
the spectrum, may be obtained by the fusion of the sensations
caused by two or more of the prismatic colors. Thus purple,
which is not present in the spectrum, may be at once produced
by fusing the sensations of blue and red in proper proportions.
Moreover, many of the various tints and shades of nature may be
imitated by fusing a particular color sensation with the sensation
of white, or by allowing a certain quantity of light of a particular
color to fall sparsely over the area of the retina, which is at the
same time protected from the access of any other light—*i. e.*,
as we say, by mixing the color with black. Thus the browns of
nature result from various admixtures of yellow, red, white, and
black; and a small quantity of white light, scattered over a
large area of the retina—*i. e.*, white largely mixed with black,
forms a gray. In fact, the qualities of a color depend (1) on the
nature of the prismatic color or colors—*i. e.*, on the wave-lengths
of the constituent rays, falling on a given area of the retina;
(2) on the amount of this colored light which falls on the area
of the retina in a given time; and (3) on the amount of white
light falling on the same area at the same time. When rays
corresponding to a prismatic color fall upon the retina unac-
companied by any white light, the color is said to be "saturated";
and a color is spoken of as more or less saturated according as
it is mixed with less or more white light. When we are led to
describe a color as being of such a tint or hue, we are guided by
the first of the above conditions. But we have no common
phrases by which we distinguish the second of the above condi-
tions from the third. The word "pale," it is true, is most fre-
quently used to express a color very slightly saturated; but the
words "rich" or "deep" are used sometimes as meaning highly
saturated, sometimes as meaning simply that a large quantity of
light of the particular hue is passing into the eye. So also with
the phrase "bright;" this we often use when a large amount of
colored and white light falls at the same time on the same retinal

area, but we sometimes also use it to express the mere intensity of the sensation.

The best method of fusing color sensations is that adopted by Maxwell, of allowing two different parts of the spectrum to fall on the same part of the retina at the same time. The use of the pure prismatic colors eliminates errors which arise when pigments, the colors of which are not pure but mixed, are employed. And where pigments are used, it is the sensations to which the pigments give rise which must be mixed and not the pigments themselves. Thus while the sensations gained by looking at gamboge yellow and indigo respectively when fused give rise to a sensation of white, gamboge and indigo themselves when mixed appear green. The color of the mixed pigment is due to the fact that the rays which reach the eye from the mixture are those which are least absorbed by the two pigments. The gamboge absorbs the blue rays very largely, but the green to a much less extent, while the indigo absorbs the red and yellow rays very largely, but also absorbs very little of the green. Hence green is the predominant hue of the mixture. When pure pigments—*i. e.*, pigments corresponding as closely as possible to the prismatic colors, are used, satisfactory results may be gained, either by using the reflected image of one pigment, and arranging so that it falls on the retina at the same spot as the direct image of the other pigment, or by allowing the image of one pigment to fall on the retina before the sensation produced by the other has passed away. The first result is easily reached by Helmholtz's simple method of placing two pieces of colored paper a little distance apart on a table, one on each side of a glass plate inclined at an angle. By looking with one eye down on the glass plate the reflected image of the one paper may be made to coincide with the direct image of the other, the angle which the glass plate makes with the table being adjusted to the distance between the pieces of paper. In the second method the "color top" is used; sectors of the colors to be investigated are placed on a disk made to rotate very rapidly, and the image of one color is thus brought to bear on the retina so soon after the image of another that the two sensations are fused into one.

When the sensations corresponding to the several prismatic colors are fused together in various combinations, the following remarkable results are brought about.

1. When red and yellow in certain proportions are mixed together the result is a sensation of orange, quite indistinguishable from the orange of the spectrum itself. Now the latter is produced by rays of certain wave-lengths, whereas the rays of red and of yellow are respectively of quite different wave-lengths. The *orange of the spectrum* cannot be made up by any mixture of the *red and the yellow of the spectrum* in the sense that the red and yellow rays can unite together to form rays of the same wave-lengths as the orange rays; the three things are absolutely different. It is simply the mixed *sensation* of the red and yellow which is so like the *sensation* of orange; the mixture is entirely and absolutely a physiological one. In the same way we may by appropriate mixtures produce the sensations corresponding to

other parts of the spectrum. Now we must suppose that rays of different wave-lengths give rise to different sensory impulses— that, for instance, the sensory impulses generated by orange rays are different from those generated by red and by yellow rays. Hence, we are led by the fact of mixed sensations being identical with other apparently simple sensations to infer that the sensory impulses which any ray originates are either themselves of a complex character, or in becoming converted into sensations give rise to complex or mixed sensations; that, for instance, the impulse or sensation which a ray in the middle of the orange gives rise to, is not a simple impulse or sensation answering exclusively to the color of that ray, but that the ray gives rise either to a complex impulse which becomes converted into a complex sensation, or to a simple impulse which eventually develops into a mixed or complex sensation, into the composition of which in each case other orange tints and shades of red and yellow enter.

2. When certain colors are mixed together in pairs in certain definite proportions, the result is white. These colors are—

Red (near a),[1]	and Blue-Green (near F),
Orange (near C),	and Blue (between F and G),
Yellow (near D),	and Indigo-Blue (near G),
Green-Yellow (near E),	and Violet (between G and H),

and are said to be "complementary" to each other. To these might be added the peculiar non-prismatic color, purple, which, with green, also gives white.

3. If we select arbitrarily any three colors corresponding to any three parts of the spectrum sufficiently far apart—say, for instance, red, green, and blue—we can, by a proper adjustment of the proportions of each, produce white. Further, these three colors can be taken in such proportions as with a proper addition, if necessary, of white to produce the sensations of all other colors.[2] That is to say, given three standard sensations, all the other sensations may be gained by the proper mixture of these.

It is obvious from the foregoing, that our real color sensations are much fewer in number than those which we appear to have when we look on the colors of the spectrum or of nature; that rays of light awake in us certain simple sensations, which mixed in various proportions reproduce all our sensations. And the question arises, What is the nature or what are the characters of these simple sensations?

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[1] These letters refer to Frauenhofer's lines.

[2] A few highly saturated colors cannot be so reproduced, but a mixture of any one of them with white can. We may perhaps, therefore, speak of these saturated colors as being reproduced by a proper combination of the three arbitrarily selected colors, with the *subtraction* of white.

When we examine our own sensations of light we find that certain of these seem to be quite distinct in nature from each other, so that each is something *sui generis*, whereas we easily recognize all other sensations as various mixtures of these. Thus red and yellow are to us quite distinct; we do not recognize any thing common to the two, but orange is obviously a mixture of red and yellow. The sensations caused by different kinds of light which thus appear to us distinct, and which we may speak of as "fundamental sensations," are white, black, red, yellow, green, blue. Each of these seems to us to have nothing in common with any of the others, whereas in all other colors we can recognize a mixture of two or more of these.

This result of common experience suggests the idea that these fundamental sensations are the primary or simple sensations, spoken of above as those out of which all other sensations may be supposed to be compounded. And a theory has been proposed to reconcile the various facts of color vision, with the supposition that we possess these six fundamental sensations. This theory, known as that of Hering, is somewhat as follows: The six sensations readily fall into three pairs, the members of each pair having analogous relations to each other. White and black naturally go together, the one being the antagonistic or correlative of the other. There is a similar connection between red and green, the one being the complementary of the other, and between yellow and blue, which are similarly complementary. We saw reason a short time back (p. 611), for believing that vision originates in the changes taking place in certain visual substances (or a visual substance) in the retina. And the theory of which we are speaking supposes that there exist in the retina, or at least somewhere in the visual apparatus, three distinct visual substances which are continually undergoing a double metabolism, one constructive, of assimilation or building up, and the other destructive, of dissimilation or breaking down. One of these substances is further of such a nature that when dissimilation is in excess of assimilation we have a sensation of white, and when assimilation is in excess, a sensation of black, With a second substance excess of dissimilation provokes red, of assimilation green, and with the third substance, yellow and blue respectively. When in the latter two substances dissimilation and assimilation are exactly equal, no effect is produced, but with the first substance, this condition produces in us the effect of gray. Further, these substances are of such a kind that while the first or white-black substance is influenced by rays along the whole range of the spectrum, the two other substances are differently influenced by rays of different wave-length. Thus in the part of the spectrum which we call red, the rays promote a

rapid dissimilation of the red-green substance with compara-
tively slight effect in either direction on the yellow-blue sub-
stance, hence our sensation of red. In that part of the spectrum
which we call yellow the rays effect a marked dissimilation of
the yellow-blue substance but their action on the red-green sub-
stance is equal in the direction of both assimilation and dissimi-
lation, hence our sensation of yellow. The green rays, again,
promote assimilation of the red-green substance, leaving the
assimilation of the yellow-blue substance equal to the dissimila-
tion, and similarly blue rays cause assimilation of the yellow-
blue substance, and leave the red-green substance neutral,
Finally, at the extreme blue end of the spectrum, the rays once
more provoke dissimilation of the red-green substance. When
orange rays fall on the retina, there is an excess of dissimilation
of both the red-green and the yellow-blue substance; when
greenish-blue rays are perceived there is an excess of assimila-
tion of both these substances, and other intermediate tints cor-
respond to variable amounts of dissimilation or assimilation of
two or more of these substances.

When all the rays together fall on the retina, the red-green
and yellow-blue substance remain in equilibrium, but the white-
black substance is violently dissimilated, and we say the light is
white.

Another theory (known as the Young-Helmholtz theory, be-
cause it was introduced by Young, and more fully elaborated by
Helmholtz) strives to reduce the matter to still further simplicity.
Starting from the fact mentioned a short time since, that all
color sensations, including the sensation of white, may he ob-
tained by the appropriate mixture of three standard sensations,
this theory teaches that our visual apparatus is so constituted as,
when excited, to give rise to three primary sensations, and that
these primary sensations are called forth in different degrees by
different rays of light, so that each ray gives rise to a different
mixture of the three. Several sets of three such primary sensa-
tions might be chosen, which would satisfy the conditions of
giving rise, by appropriate mixture, to all sensation of color in-
cluding white; but for reasons into which we cannot enter fully
here, the sensations which may thus he taken as primary sensa-
tions appear to correspond to our sensations of red, green, and
blue, or violet. Such a view of three primary color sensations is
represented in the diagram (Fig. 196). Thus, the red primary
sensation, excited to a certain extent by the rays of the extreme
red end, is most powerfully affected by the rays at a little dis-
tance from the end, the rays from this point onwards towards the
blue end producing less and less effect. The curve of the green
primary sensation begins later and reaches its maximum in the

green of the spectrum, while the blue or violet primary sensation is still later and only reaches its maximum towards the blue end of the spectrum. Each ray calls forth each sensation, but to a different degree, and the total result of each ray, or of each group of rays, is determined by the proportionate amount of the three sensations. Thus, the sensation of orange (O in the figure) is brought about by a mixture of a great deal of the primary red

DIAGRAM OF THREE PRIMARY COLOR SENSATIONS.

1 is the so-called "red," 2 "green," and 3 "violet" primary color sensation R, O, Y, etc., represent the red, orange, yellow, etc., color of the spectrum, and the diagram shows, by the height of the curve in each case, to what extent the several primary color sensations are respectively excited by vibrations of different wave-lengths.
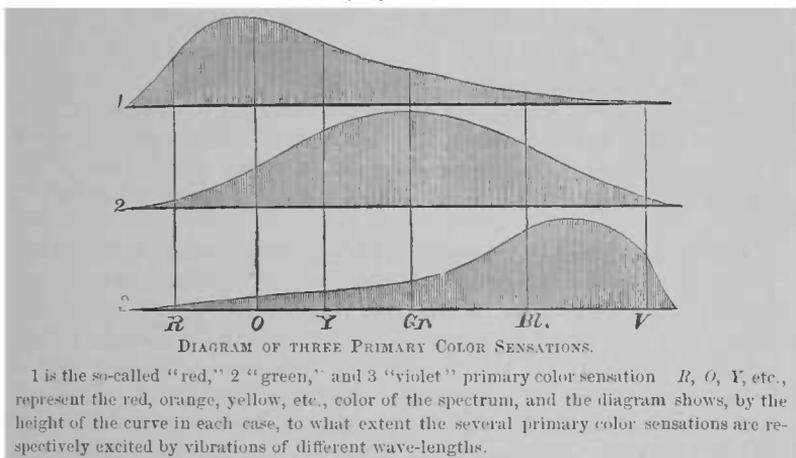
with much less of the primary green, and hardly any of the primary blue; the orange sensation is converted into a yellow sensation by diminishing the primary red and largely increasing the primary green, the primary blue undergoing also some slight increase. And similarly with all the other sensations. When each of the primary sensations is excited to a maximum, as when ordinary light falls on the retina, the result is a sensation of white. According to this theory, black is simply the absence of sensation from the visual apparatus.

In the view, as originally put forward by Young, the three primary sensations were supposed to be represented by three sets of fibres, each set of fibres being differently affected by different rays of light, and the impulses passing to the brain along each set awakening a distinct sensation. No such distinction of fibres can be found in the retina; but an anatomical basis of this kind is not necessary for the theory; we can easily conceive of the same fibre transmitting three distinct kinds of impulses; or we may suppose that the visual substances are three in number, instead of six, the changes in each substance provoking a primary sensation.

Such are the two main theories of color vision; and much may be said in favor of both of them; at the same time, both of them present many difficulties. To discuss them fully, is a task beyond the limits of this book, and to discuss them in any but a full manner would be unsatisfactory. We must be satisfied, therefore, with the foregoing simple statement of the two views. Independently of any theory, however, we may remember (1) that all the sensations which we experience under the action of light of whatever kind may be reduced to six—white, black, red, yellow, green, and blue; and (2) that these may be all reproduced by various mixtures of three standard sensations, if black be allowed to indicate the absence of all sensation. These are matters of fact: what is at present debated is whether the six fundamental sensations are the outcome of three primary sensations, or whether they represent six distinct conditions of the visual apparatus.

Color Blindness.—Persons vary much in their power of appreciating and discriminating color—*i. e.*, in the intensity and accuracy of their color sensations; and some people regard as similar, colors which to most people are glaringly distinct; these latter are said to be "color blind." The most common form of color blindness is that of persons unable to distinguish green and red from each other. As in the case of Dalton, they tell a red gown lying on a green grass plot, or a red cherry among the green leaves, by its form, and not by its color. They confound not only red, green, and certain forms of brown, but also rose, purple, and blue. Such persons are often spoken of as "red blind." On the Hering theory they lack the red-green visual substance; hence, all the color sensations they possess must be those of yellow and blue freed from all mixture of red or green; and such accounts as have been given of their sensations by those persons who are "red-blind" in one eye, but possess normal vision with the other, accord with this conclusion. On the Young-Helmholtz theory, such persons lack the primary red sensation; and hence the sensations which they have must be mixtures of green and blue alone, our yellow appearing to them a bright green, and our green-blue a kind of gray.

All such red-blind people ought, on either theory, to be less affected than are persons with normal eyes, by the red end of the spectrum: this ought, with them, to be shortened and obscure. In a certain number of persons who confound red and green, this is the case; but in some instances no such lack of appreciation of the red end of the spectrum can be ascertained. Such cases have been supposed to be green-blind—that is, lacking the primary sensation of green. According to the Hering theory, green

blindness, apart from red blindness is impossible, the only two possible color defects being red-green and blue-yellow blindness. And the existence of distinct green blindness has been held to contradict that theory. On the other hand, the Hering theory admits the possibility of total color blindness—*i. e.*, the inability to see anything but white and black; and this, on the Young-Helmholtz theory, is impossible, since for vision to exist at all, one of the three primary sensations must be present; a man to see at all must see things in various shades of either red, or of green, or of violet, though he may confound this single-colored vision with the normal vision of white of different intensities. But, indeed, a full examination of color blindness rather increases than diminishes the difficulties of deciding between the two rival theories.

Influence of the Pigment of the Yellow Spot.—In the macula lutea, which part of the retina we use chiefly for vision, images falling on other parts of the retina being said to give rise to "indirect vision," the yellow pigment absorbs some of the greenish-blue rays. Hence, the sensation which we receive from objects which we are in the habit of calling white, is that which, if this pigment were absent, we should receive from objects more or less yellow. We may use this feature of the yellow spot for the purpose of making the spot, so to speak, visible to ourselves, by an experiment suggested by Maxwell. A solution of chrome alum, which only transmits red and greenish-blue rays, is held up between the eye and a white cloud. The greenish-blue rays are absorbed by the yellow spot, and here the light gives rise to a sensation of red; whereas, in the rest of the field of vision the sensation is that ordinarily produced by the purplish solution. The yellow spot is consequently marked out as a rosy patch. This very soon, however, dies away.

In speaking of sensation as a function of the stimulus, p. 613, we referred to white light only; but the different colors are unequal in the relations borne by the intensity of the stimulus to the amount of sensation produced. Thus, the more refrangible blue rays produce a sensation more readily than the yellow or red rays. Hence in dim lights, as those of evening and moonlight, the blues preponderate, and the reds and yellow are less obvious. So also when a landscape is viewed through a yellow glass, the yellow hue suggests to the mind bright sunlight and summer weather, although the actual illumination which reaches the eye is diminished by the glass. Conversely, when the same landscape is viewed through a blue glass, the idea of moonlight or winter is suggested.

The theory of three primary color sensations may be used to

explain why any colored light, if made sufficiently intense, appears white. Thus, a violet light of moderate intensity appears violet because it excites the primary sensation of violet much more than those of green and red. If the stimulus be increased, the maximum of violet stimulation will be reached, while the stimulation of green will continue to be increased, and even that of red to a slight degree. The result will be that the light appears violet mixed with green—that is, blue. If the stimulus be still further increased, while the green and violet are both excited to the maximum, the red stimulation may be increased until the result is violet, green, and red in the proportions which make white light. And so with light of other colors.

After-images.—We have already seen that in vision the sensation lasts much longer than the stimulus. Under certain circumstances, such as particular conditions of the eye, an intense stimulus, etc., the sensation is so prolonged, that it is spoken of as an after-image. Thus, if the eye be directed to the sun, the image of that body is present for a long while after; and if, on early waking, the eye be directed to the window for an instant and then closed, an image of the window with its bright panes and darker sashes, the various parts being of the same color as the object, will remain for an appreciable time. These images, which are simply continuations of the sensation, are spoken of as *positive after-images*. They are best seen after a momentary exposure of the eye to the stimulus.

When, however, the eye has been for some time subject to a stimulus, the sensation which follows the withdrawal of the stimulus is of a different kind; what is called a *negative after-image*, or *negative image*, is produced. If, after looking steadfastly at a white patch on a black ground, the eye be turned to a white ground, a gray patch is seen for some little time. A black patch on a white ground similarly gives rise on a gray ground to a negative image in the form of a white patch. This may be explained as the result of exhaustion. When the white patch has been looked at steadily, for some time, that part of the retina on which the image of the patch fell becomes tired; hence the white light, coming from the white ground subsequently looked at, which falls on this part of the retina, does not produce so much sensation as in other parts of the retina; and the image, consequently, appears gray. And so, in the other instance, the whole of the retina is tired, except at the patch; here the retina is for a while most sensitive, and hence the white negative image.

When a red patch is looked at, the negative image is a green-blue—that is, the color of the negative image is complementary to that of the object. Thus also orange produces a blue, green a

pink, yellow an indigo-blue, negative image; and so on. This too can be explained as a result of exhaustion on either hypothesis of color vision. When the colored patch is looked at, one of the three primary color sensations is much exhausted, and the other two less so, in varying proportions, according to the exact nature of the color of the patch; and the less exhausted sensations become prominent in the after-image. Thus, the red patch exhausts the red sensation, and the negative image is made up chiefly of green and blue sensations—that is, appears to be greenish-blue, or bluish-green, according to the tint of the red. On the other hypothesis, we may suppose that, owing to the continued effect of looking at the red patch, dissimilation of the red-green substance becomes less and less, leading to a prominence and indeed to an actual increase of the process of assimilation of the same substance; hence the sensation of green dominating in the negative image.

Similarly, when the eye, after looking at a colored patch, is turned to a colored ground, the effects may easily be explained by reference to the comparative exhaustion of the color sensations excited by the patch and the ground respectively; if a yellow ground be chosen after looking at a green object, the negative image will appear of a reddish-yellow, and so on.

The theory of three primary sensations does not so readily explain why negative images should make their appearance without any subsequent stimulation of the retina. When the eyes are shut, and all access of light, even through the eyelids, carefully avoided, the field of vision is not absolutely dark; there is still a sensation of light, the so-called "proper light" of the retina. If a white patch on a black ground be looked at for some time, and the eyes then shut, a negative (black) image of the spot will be seen on the ground of the "proper light" of the retina, having in its immediate neighborhood a specially bright corona. So, also, if a window be looked at, and the eyes then closed, the positive after-image with bright panes and dark sashes gives rise to a negative after-image with bright sashes and dark panes; and similar effects appear with colors. These and similar facts have been largely used in support of the Hering theory. When the eye has been looking at red, and so has caused dissimilation of the red-green substance mere rest, as on shutting the eyes, favors assimilation of the same substance, and thus leads to a sensation of green. And the rhythmic oscillations from one color to its correlative and back again, frequently observed under these conditions and which point to assimilation and dissimilation alternately gaining the upper hand, are not without analogies in other common instances of protoplasmic metabolism.

SEC. 3.—VISUAL PERCEPTIONS.

Hitherto we have studied sensations only, and have considered an external object, such as a tree, as simply a source of so many distinct sensations, differing from each other in intensity and kind (color). In the mind these sensations are coördinated into a perception. We are not only conscious of a number of sensations of bright and dim lights, of green, brown, black, etc., but these sensations are so related to each other and by virtue of cerebral processes so fashioned into a whole, that we "see a tree." We sometimes, in illustration of such an effect, speak of an image or picture in the mind corresponding to the physical image on the retina.

When we look upon the external world, a variety of images are formed at the same time on the retina, and give rise to a number of contemporaneous visual sensations. The sum of these sensations constitutes "the field of vision," which varies, of course, with every movement of the eye. This field of vision, being in reality an aggregate of sensations, is, of course, a *subjective* matter; but we are in the habit of using the same phrase to denote the sum of external objects which give rise to the aggregate of visual sensations; in common language, the field of vision is "all that we can see" in any position of the eye, and we have a field of vision for each eye separately and for the two eyes combined.

Using for the present the words in their subjective sense, we may remark that we are able to assign to each constituent sensation its place among the aggregate of sensations constituting the field of vision; we can, as we say, *localize* the sensation. We can say whether it belongs to (what we regard as) the right-hand or left-hand, the upper or the lower part, of the field of vision. We are able to distinguish the relative positions of any two distinct sensations; and the relative positions, together with the relative intensities and qualities (color) of the sensations arising from any object determine our perception of the object. It need hardly be remarked that this localization is purely subjective. We simply determine the position of the *sensation* in the field of vision (which is itself a wholly subjective matter); we do not determine the position of the *object*. The connection between the position of the object in the external world and the position of the sensations in the field of vision, cannot be determined by visual observation alone. All the information which can be gained by the eye is limited to the field of vision, and provided that the relative position of the sensations in the field of vision remained the same, the actual position of external objects might,

as far as vision is concerned, be changed without our being aware of it.

As a matter of fact, the field of vision in one important particular does not correspond to the field of external objects. The image on the retina is inverted; the rays of light proceeding from an object which by touch we know to be on what we call our right hand, fall on the left-hand side of the retina. If therefore the field of vision corresponded to the retinal image, the object would be seen on the left hand. We however see it on the right hand, because we invariably associate right-hand tactile localization with left-hand visual localization; that is to say, our field of vision, when interpreted by touch, is a reinversion of the retinal image.

The dimensions of the field of vision of a single eye are about 145° for the horizontal and 100° for the vertical meridian, the former being distinctly greater than the latter. The horizontal dimension of the field of vision for the two eyes is about 180° By movements of the eyes, however, even apart from those of the head, the extent may be considerably increased.

The satisfactory perception of external objects requires distinct vision; and of this, as we have already said, the formation of a distinct image on the retina is an essential condition. We can receive visual sensations of all kinds with the most imperfect dioptric apparatus, but our perception of an object is precise in proportion to the clearness of the image on the retina.

Region of Distinct Vision.—If we take two points, such as two black dots, only just so far apart that they can be seen distinctly as two when placed near the axis of vision, and then, keeping the axis fixed, move the two points out into the circumferential parts of the field of vision, it will be found that the two soon appear as one. The two sensations become fused, as they would do if brought nearer to each other in the centre of the field. The further away from the centre of the field, the further apart must two points be in order that they may be seen as two. In other words, vision is much more distinct in the centre of the field than towards the circumference. Practically the region of distinct vision may be said to be limited to the macula lutea, or even to the fovea centralis; by continual movements of the eye we are constantly bringing any object which we wish to see in such a position that its image falls on this region of the retina.

The diminution of distinctness does not take place equally from the centre to the circumference along all meridians. The outline described by a line uniting the points where two spots cease to be seen as two when moved along different radii from the centre, is a very irregular figure.

The sensations of color are much more distinct in the centre of the retina, than towards the circumference. If the visual axis be fixed and a piece of colored paper be moved towards the outside of the field of vision, the color undergoes changes and is eventually lost, red disappearing first, and blue last, the object remaining visible, though with very indistinct outlines, when its color can be no longer recognized. A purple color becomes blue, and a rose color a bluish-white. In fact there seems to be a certain amount of red blindness in the peripheral parts of the retinas.

Modified Perceptions.

Since our perception of external objects is based on the distinctness of the sensations which go to form the perception, it might be expected that when an image of an object is formed on the retina the sensory impulses would correspond to the retinal image, the sensations correspond to the sensory impulses and the perceptions correspond to the sensations, and that therefore the mental condition resulting from our looking at any object or view would correspond exactly to the retinal image. We find, however, that this is not the case. The sensations and probably even the simple sensory impulses produced by an image react upon each other, and these reactions modify our perceptions, independently of the physical conditions of the retinal image. There arise certain discrepancies between the retinal image and the perception, some having their source in the retina, some in the brain, and others being of such a nature that it is difficult to say where the irrelevancy is introduced.

Irradiation.—A white patch on a dark ground appears larger, and a dark patch on a white ground smaller, than it really is. This is especially so when the object is somewhat out of focus, and may, in this case, be partly explained by the diffusion circles which, in each case, encroach from the white upon the dark. But over and beyond this, any sensation, coming from a given retinal area, occupies a larger share of the field of vision, when the rest of the retina and central visual apparatus are at rest, than when they are simultaneously excited. It is as if the neighboring, either retinal or cerebral, structures were sympathetically thrown into action at the same time.

Contrast.—If a white strip be placed between two black strips, the edges of the white strip, near to the black, will appear whiter than its median portion, and if a white cross be placed on a black background, the centre of the cross will appear sometimes so dim, compared with the parts close to the black, as to seem

shaded. This occurs even when the object is well in focus; the increased sensation of light which causes the apparent greater whiteness of the borders of the cross is the result of the "contrast" with the black placed immediately close to it. Still more curious results are seen with colored objects. If a small piece of gray paper be placed on a sheet of green paper, and both covered with a sheet of thin tissue paper, the gray paper will appear of a pink color, the complementary of the green. This effect of contrast is far less striking, or even wholly absent, when the small piece of paper is white instead of gray, and generally disappears when the thin covering of tissue paper is removed. It also vanishes if a bold broad black line be drawn round the small piece of paper, so as to isolate it from the ground color. If a book or pencil be placed vertically on a sheet of white paper, and illuminated on one side by the sun, and on the other by a candle, two shadows will be produced, one from the sun, which will be illuminated by the yellowish light of the candle, and the other from the candle, which will in turn be illuminated by the white light of the sun. The former naturally appears yellow, the latter, however, appears not white but blue; it assumes, by contrast, a color complementary to that of the candle-light which surrounds it. If the candle be removed, or its light shut off by a screen, the blue tint disappears, but returns when the candle is again allowed to produce its shadow. If, before the candle is brought back, a vision be directed through a narrow blackened tube at some part falling entirely within the area of what will be the candle's shadow, the area, which in the absence of the candle appears white, will continue to appear white when the candle is made to cast its shadow, and it is not until the direction of the tube is changed so as to cover part of the ground outside the shadow, as well as part of the shadow, that the latter assumes its blue tint.

Filling up the Blind Spot.—Though, as we have seen, that part of the retina which corresponds to the entrance of the optic nerve is quite insensible to light, we are conscious of no blank in the field of vision. When in looking at a page of print we fix the visual axis so that some of the print must fall on the blind spot, no gap is perceived. We could not expect to see a black patch, because what we call black is the absence of the sensation of light from structures which are sensitive to light; we must have visual organs to see black. But there are no visual organs in the blind spot, and consequently we are *in no way at all* affected by the rays of light which fall on it. There is in our subjective field of vision no gap corresponding to the gap in the retinal image. We refer the sensations coming from

two points of the retina lying on opposite margins of the blind spot to two points lying close together, since we have no indication of the space which separates them. Concerning the effects which are produced when an object in the field of view passes into the region of the blind spot there has been much discussion. In ordinary vision, of course, the existence of the blind spot is of little moment since it is outside the region used for distinct vision, and besides the image of an object does not fall on the blind spots of both eyes at the same time.

Ocular Spectra.—So far from our perceptions exactly corresponding to the arrangements of the luminous rays which fall on the retina, we may have visual sensations and perceptions in the entire absence of light. Any stimulation of the retina or of the optic nerve sufficiently intense will give rise to a visual sensation. Gradual pressure on the eyeball causes a sensation of rings of colored light, the so-called phosphenes; a sudden blow on the eye causes a sensation of flashes of light, and the seeming identity of the visual sensations so brought about with visual sensations produced by light is well illustrated by the statement once gravely made in a German court of law, by a witness who asserted that on a pitch dark night he recognized an assailant by help of the flash of light caused by the assailant's hand coming in violent contact with his eye. Electrical stimulation of the eye or optic nerve will also give rise to visual sensations.

The sensations which may arise without any light falling on the retina need not necessarily be undefined; on the contrary they may be most clearly defined. Complex and coherent visual images or perceptions may arise in the brain without any corresponding objective luminous cause. These so-called ocular spectra or phantoms, which are the result of an intrinsic stimulation of some (probably cerebral) part of the visual apparatus, have a distinctness which gives them an apparent objective reality quite as striking as that of ordinary visual perceptions. They may occasionally be seen with the eyes open (and therefore while ordinary visual perceptions are being generated) as well as when the eyes are closed. They sometimes become so frequent and obtrusive as to be distressing, and form an important element in some kinds of delirium, such as delirium tremens.

Appreciation of Apparent Size.—By the eye alone we can only estimate the *apparent* size of an object, we can only tell what space it takes in the field of vision, we can only perceive the dimensions of the retinal image, and therefore have a right only to speak of the angle which the diameter of the object subtends. The *real* size of an object must be determined by other means.

But our perception of even the apparent size of an object is so modified by concurrent circumstances that in many cases it cannot be relied on. The apparent size of the moon must be the same to every eye, and yet while some persons will be found ready to compare the moon in mid-heavens with a threepenny piece, others will liken it to a cart-wheel; that is to say, the angle subtended by the moon seems to the one to be about equal to that subtended by a threepenny piece held at the distance from the eye at which it is most commonly looked at, and to the other about equal to that subtended by a cart-wheel similarly viewed at the distance at which it is most commonly looked at. If a line, such as *A C*, Fig. 197, be divided into two equal parts,

FIG. 197.

A B, *B C*, and *A B* be divided by distinct marks into several parts, as is shown in the figure, while *B C* is left entire, the distance *A B* will always appear greater than *C B*. So, also, if two equal squares be marked, one with horizontal and the other with vertical alternate dark and light bands, the former will appear higher, and the latter broader, than it really is. Hence, short persons affect dresses horizontally striped in order to increase their apparent height, and very stout persons avoid longitudinal stripes. Two perfectly parallel lines or bands, each of which is crossed by slanting parallel short lines, will appear not parallel, but diverging or converging, according to the direction of the cross-lines.

Again, when a short person is placed side by side with a tall person, the former appears shorter and the latter taller than each really is. The moon on the horizon appears larger than when at the zenith, because in the first position it can be most easily compared with terrestrial objects. The absence of comparison may, however, contribute to an opposite effect, as when a person looks larger in a fog; being seen indistinctly, he is judged to be further off than he really is, and so appears larger than he naturally would do at the distance at which he is supposed to be. So, conversely, distant mountains when seen distinctly in a clear atmosphere appear small, because on account of their distinctness they are judged to be nearer than they really are. Indeed, our daily life is full of instances in which our direct perception is modified by circumstances. Among those circumstances previous experience is one of the most potent, and thus simple perceptions become mingled with what are in reality judgments, though frequently made unconsciously. But this intrusion of

past experience into present perceptions and sensations is most obvious in binocular vision, to which we now turn.

SEC. 4.—BINOCULAR VISION.

Corresponding or Identical Points.

Though we have two eyes, and must therefore receive from every object two sets of sensations, our perception of any object is, under ordinary circumstances, a single one; we see one object, not two. By putting either eye into an unusual position, as by squinting, we can render the perception double; we see two objects where only one exists. From which it is evident that singleness of perception depends on the image of the object falling on certain parts of each retina at the same time, these parts being so related to each other, that the sensations from each are blended into one perception; and it is also evident that the movements of the eyeballs are adapted to bring the image of the object to fall on these "corresponding" or "identical" parts, as they are called, of each retina.

When we look at an object with one eye, the visual axis of that eye is directed to the object; and when we use two eyes, the

FIG. 198.

DIAGRAM ILLUSTRATING CORRESPONDING POINTS
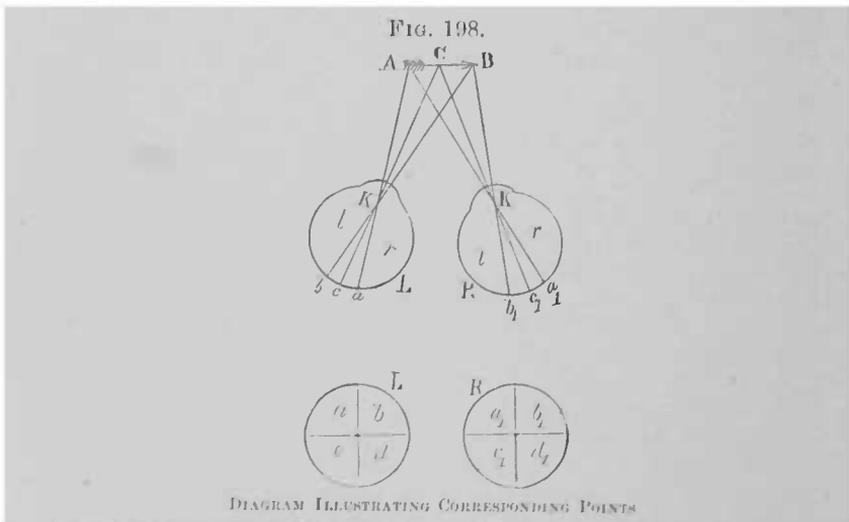
L the left *R* the right eye, *K* the optical centre, a_1, b_1, c_1, are points in the right eye corresponding to the points a, b, c, in the left eye. The two figures below are projections of *L* the left and *R* the right retina. It will be seen that a on the *malar* side of *L* corresponds to a_1, on the *nasal* side of *R*.

visual axes of the two eyes converge at the object, the eyeballs moving accordingly. The corresponding points of the two retinas

are those on which the two images of the object fall when the visual axes converge at the object. Thus in Fig. 198, if Cc, Cc_1 be the two visual axes, c, c_1 being the centres of the foveæ centrales of the two eyes, then, the object ACB being seen single, the point a on the one retina will "correspond" to or be "identical" with the point a_1 on the other, and the point b in the one to the point b_1 in the other. Hence a point lying anywhere on the right side of one retina has its corresponding point on the right side of the other retina, and the points on the left of one correspond with those on the left of the other. Thus, while the upper half of the retina of the left eye corresponds to the upper half of the retina of the right eye, and the lower to the lower, the *nasal* side of the left eye corresponds with the *malar* side of the right, and the *malar* of the left with the *nasal* side of the right.

The blending of the two sensations into one only occurs when the two images of an object fall on these corresponding points of the two retinas. Hence it is obvious that in single vision with two eyes the ordinary movements of the eyeballs must be such as to bring the visual axes to converge at the object so that the two images may fall on corresponding points. When the visual axes do not so converge, and when, therefore, the images do not fall on corresponding points, the two sensations are not blended into one perception and vision becomes double.

Movements of the Eyeballs.

The eye is virtually a ball placed in a socket, the bulb and the orbit forming a ball-and-socket joint. In its socket-joint the optic ball is capable of a variety of movements, but it cannot by any voluntary effort be moved out of its socket. It is stated that by a very forcible opening of the eyelids the eyeball may be slightly protruded; but this trifling locomotion may be neglected. By disease, however, the position of the eyeball in the socket may be materially changed.

Each eyeball is capable of rotating round an immobile centre of rotation, which has been found to be placed a little (1.77 mm.) behind the centre of the eye; but the movements of the eye round the centre are limited in a peculiar way. The shoulder-joint is also a ball-and-socket joint; and we know that we can not only move the arm up and down round a horizontal axis passing through the centre of rotation of the head of the humerus, and from side to side round a vertical axis, but we can also rotate it round its own longitudinal axis. When, however, we come to

examine closely the movements of the eyeball, we find that
though we can move it up and down round a horizontal axis, as
when with fixed head we direct our vision to the heavens or to
the ground, and from side to side, as when we look to left or
right, and though by combining these two movements we can
give the eyeball a variety of inclinations, we cannot, by a volun-
tary effort, rotate the eyeball round its longitudinal visual axis.
The arrangement of the muscles of the eyeball will permit of
such a movement, but we cannot by any direct effort of will
bring it about by itself. In certain movements of the eye, rota-
tion of the eyeball does take place; and by bringing about these
movements, we can indirectly cause rotation; but we cannot
rotate the eyeball, except thus indirectly as a part of these move-
ments.

If, when vision is directed to any object, the head be moved
from side to side, the eyes do not move with it; they appear to
remain stationary, very much as the needle of a ship's compass
remains stationary when the head of the ship is turned. The
change in the position of the visual axes to which the movement
of the head would naturally give rise is met by compensating
movements of the eyeballs; were it not so, steadiness of vision
would be impossible.

There is one position of the eyes which has been called the
primary position. It corresponds to that which may be attained
by looking at the distant horizon with the head vertical and the
body upright; but its exact determination requires special pre-
cautions. The visual axes are then parallel to each other and
to the median plane of the head. All other positions of the eyes
are called *secondary positions*.

Muscles of the Eyeball.—The eyeball is moved by six muscles,
the *recti inferior, superior, internus,* and *externus,* and the *obliqui
inferior* and *superior*. It is found by calculation from the attach-
ments and directions of the muscles, and confirmed by actual
observation, that the six muscles may be considered as three
pairs, each pair rotating the eye round a particular axis. The
relative attachments and the axes of rotation are diagrammatically
shown in Fig. 199. The rectus superior and the rectus inferior
rotate the eye round a horizontal axis, which is directed from
the upper end of the nose to the temple; the obliquus superior
and obliquus inferior round a horizontal axis directed from the
centre of the eyeball to the occiput; and the rectus internus and
rectus externus round a vertical axis (which, being at right
angles to the plane of the paper, cannot be shown in the dia-
gram), passing through the centre of rotation of the eyeball

parallel to the median plane of the head when the head is vertical. Thus, the latter pair acting alone would turn the eye from side to side, the other straight pair acting alone would move the eye up and down, while the oblique muscles acting alone would give the eye an oblique movement. The rectus externus acting alone would turn the eye to the malar side, the internus to the nasal side, the rectus superior upwards, the rectus inferior downwards, the oblique superior downwards and outwards, and the inferior upwards and outwards. The recti superior and inferior in moving the eye up and down also turn it some-

FIG. 199.
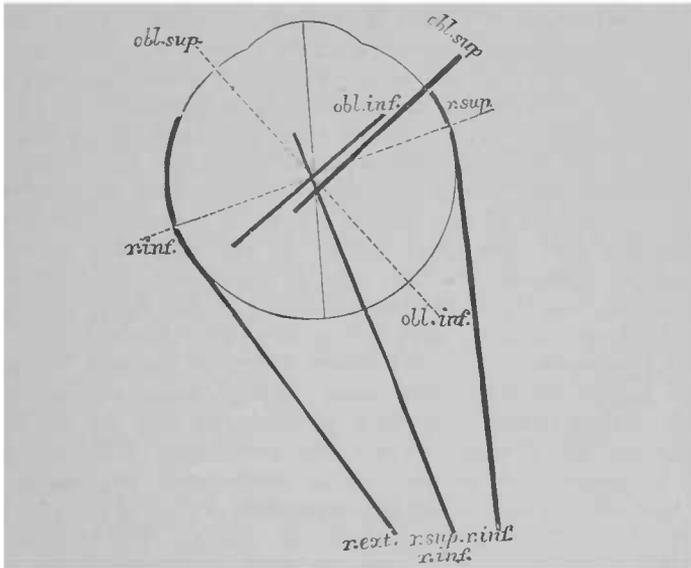
DIAGRAM OF THE ATTACHMENTS OF THE MUSCLES OF THE EYE, AND OF THEIR AXES OF ROTATION, the latter being represented by dotted lines. The axis of rotation of the rectus externus and internus, being perpendicular to the plane of the paper, cannot be shown. After FICK.

what inward and, at the same time, give it a slight amount of rotation; but this is corrected if the oblique muscles act at the same time; and it is found that the rectus superior acting with the obliquus inferior moves the eye upwards, and the rectus inferior with the obliquus superior downwards in a vertical direction. In oblique movements also, the obliqui are always associated with the recti. Hence the various movements of the eyeball may be arranged as follows:

Straight movements.	Elevation.	Rectus superior and obliquus inferior.
	Depression.	Rectus inferior and obliquus superior
	Adduction to nasal side.	Rectus internus.
	Adduction to malar side.	Rectus externus.
Oblique movements.	Elevation with adduction.	Rectus superior and internus with obliquus inferior.
	Depression with adduction.	Rectus inferior and internus with obliquus superior.
	Elevation with abduction.	Rectus superior and externus with obliquus inferior.
	Depression with abduction.	Rectus inferior and externus with obliquus superior.

Coordination of Visual Movements.—Thus, even in the movements of a single eye, a considerable amount of coördination takes place. When the eye is moved in any other than the vertical and horizontal meridians, impulses must descend to at least three muscles, and in such relative energy to each of the three as to produce the required inclination of the visual axis. But the coordination observed in binocular vision is more striking still. If the movements of any person's eyes be watched, it will be seen that the two eyes move alike. If the right eye moves to the right, so does also the left; and, if the object looked at be a distant one, exactly to the same extent; if the right eye looks up, the left eye looks up also, and so in every other direction. Very few persons are able by a direct effort of the will to move one eye independently of the other; though some, and among them one distinguished both as a physiologist and an oculist, have acquired this power. In fact, the movements of the two eyes are so arranged that in the various movements the images of any object should fall on the corresponding points of the two retinas, and that thus single vision should result. We cannot by any direct effort of our will place our eyes in such a position that the rays of light proceeding from any object shall be brought to a focus on parts of the two retinas which do not correspond, and thus give rise to two distinct visual images. We can bring the visual axes of the two eyes from a condition of parallelism to one of great convergence, but we cannot, without special assistance, bring them from a condition of parallelism to one of divergence. The stereoscope will enable us to create a divergence. If in a stereoscopic picture the distance between the pictures be increased very gradually so as carefully to maintain the impression of a single object, the visual axes may be brought to diverge. Similarly, if a distant object be looked at with a prism before one eye, and the image of the object be kept carefully single, while the prism is turned very slowly up or down, then on suddenly re-

moving the prism a double image is for a moment seen ; showing that the eye before which the prism was placed had moved in disaccordance with the other. The double image, however, in a few seconds after the removal of the prism becomes single, on account of the eyes coming into accordance.

It is only when loss of coördination occurs, as in various diseases and in alcoholic or other poisoning, that the movements of the two eyes cease to agree with each other. It is evident, then, that when we look at an object to the right, since we thereby abduct the right eye and adduct the left, we throw into action the rectus externus of the right eye and the rectus internus of the left; and, similarly, when we look to the left we use the rectus externus of the left and the rectus internus of the right eye. On the other hand, when we look at a near object, and, therefore, converge the visual axes, we use the recti interni of both eyes; and when we look at a distant object, and bring the axes from convergence towards parallelism, we use the recti externi of both eyes. In the various movements of the eye there is, therefore, so to speak, the most delicate picking and choosing of the muscular instruments. Bearing this in mind, it cannot be wondered at that the various movements of the eye are dependent for their causation on visual sensations. In order to move our eyes, we must either look at or for an object; when we wish to converge our axes, we look at some near object, real or imaginary, and the convergence of the axes is usually accompanied by all the conditions of near vision, such as increased accommodation and contraction of the pupil. And so with other movements. The close association of the movements of the eye may be illustrated by the following case. Suppose the eyes, to start with, directed for the far distance, and that it is desired to direct attention to a nearer point lying in the visual line of the right eye. In this case no movement of the right eye is required; all that is necessary is for the left eye to be turned to the right—that is, for the rectus internus of the left eye to be thrown into action. But in ordinary movements the contraction of this muscle is always associated with either the rectus externus of the right eye, as when both eyes are turned to the right, or the rectus internus of that eye, as in convergence; the muscle is quite unaccustomed to act alone. This would lead us to suppose that in the case in question the contraction of the rectus internus of the left eye is accompanied by a contraction of both recti externus and internus of the right eye, keeping that eye in lateral equilibrium. And the peculiar oscillating movements seen in the right eye, as well as the sense of efforts in the right eye which is felt by the person, show this to be the case.

Such a complex coördination requires for its carrying out a

distinct nervous machinery; and we have reasons for thinking that such a machinery exists in certain parts of the corpora quadrigemina or in the underlying structures. In the nates, there appears to be a common centre for both eyes, stimulation of the right side producing movements of both eyes to the left, of the left side movements to the right; while stimulation in the middle line behind causes a downward movement of both eyes with convergence of the axes, and in the front an upward movement with return to parallelism, both accompanied by the naturally associated movements of the pupil. Stimulation of various parts of the nates causes various movements, depending on the position of the spot stimulated. After an incision in the middle line, stimulation of the nervous centre on one side produces movements in the eye of the same side only.

The Horopter.

When we look at any object we direct to it the visual axes, so that when the object is small, the "corresponding" parts of the two retinas, on which the two images of the object fall, lie in their respective foveæ centrales. But while we are looking at

FIG. 200.

DIAGRAM ILLUSTRATING A SIMPLE HOROPTER.
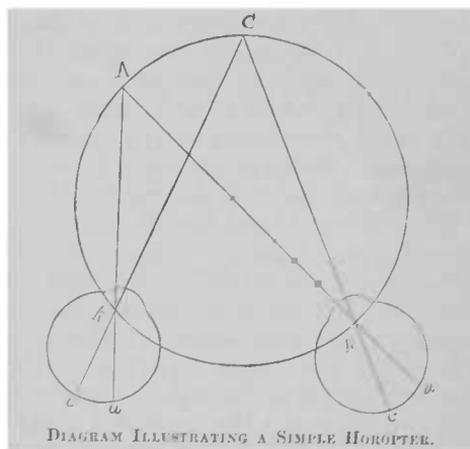
When the visual axes converge at C, the images a a of any point A on the circle drawn through C and the optical centres k, k, will fall on corresponding points.

the particular object, the images of other objects surrounding it fall on the retina surrounding the fovea, and thus go to form what is called indirect vision. And it is obviously of advantage that these images also should fall on "corresponding" parts in the two eyes. Now for any given position of the eyes there exists

in the field of vision a certain line or surface of such a kind that the images of the points in it all fall on corresponding points of the retina. A line or surface having this property is called a Horopter. The horopter is, in fact, the aggregate of all those points in space which are projected on to corresponding points of the retina; hence its determination in any particular case is simply a matter of geometrical calculation. In some instances it becomes a very complicated figure. The case whose features are most easily grasped is a circle drawn in the plane of the two visual axes through the point of the convergence of the axes and the optic centres of the two eyes. It is obvious from geometrical relations that in Fig. 200 the images of any point in the circle will fall on corresponding points of the two retinas. When we stand upright and look at the distant horizon, the horopter is (approximately, for normal emmetropic eyes) a plane drawn through our feet—that is to say, is the ground on which we stand; the advantage of this is obvious.

Sec. 5.—Visual Judgments.

Binocular vision is of use to us inasmuch as one eye is able to fill up the gaps and imperfections of the other. For example, over and above the monocular filling up of the blind spot, of which we spoke in page 631, since the two blind spots of the two eyes, being each on the nasal side, are not "corresponding" parts, the one eye supplies that part of the field of vision which is lacking in the other. And other imperfections are similarly made good. But the great use of binocular vision is to afford us means of forming visual judgments concerning the form, size, and distance of objects.

Judgment of Distance and Size.—The perceptions which we gain simply and solely by our field of vision, concern two dimensions only. We can become aware of the apparent size of any part of the field corresponding to any particular object, and of its topographical relations to the rest of the field, but no more. Had we nothing more to depend on, our sight would be almost valueless as far as any exact information of the external world was concerned. By association of the visual sensations with sensations of touch, and with sensations derived from the movements of the eyeballs required to make any such part of the field as corresponds to a particular object distinct, we are led to form judgments—i. e., to draw conclusions concerning the external world by means of an interpretation of our visual perceptions. Looking before us, we say we see a certain object of a certain

color nearly in front of us, or much on our right hand or much on our left; that is to say, we judge such an object to be in such a position because from the constitution of our brain, strengthened by all our experience, we associate such a part of our field of vision with such an object. The subjective visual complex sensation or perception is to us a symbol of the external object.

Even with one eye we can, to a certain extent, form a judgment, not only as to the position of the object in a plane at right angles to our visual axis, but also as to its distance from us along the visual axis. If the object is near to us, we have to accommodate for near vision; if far from us, to relax our accommodation mechanism so that the eye becomes adjusted for distance. The muscular sense (of which we shall speak presently) of this effort enables us to form a judgment whether the object is far or near. Seeing the narrow range of our accommodation, and the slight muscular effort which it entails, all monocular judgments of distance must be subject to much error. Everyone who has tried to thread a needle without using both eyes, knows how great these errors may be. When, on the other hand, we use two eyes, we have still the variations in accommodation, and in addition have all the assistance which arises from the muscular effort of so directing the two eyes on the object that single vision shall result. When the object is near, we converge our visual axes; when distant, we bring them back towards parallelism. This necessary contraction of the ocular muscles affords a muscular sense, by the help of which we form a judgment as to the distance of the object. Hence, when by any means the convergence which is necessary to bring the object into single vision is lessened, the object seems to become more distant, when increased, to move towards us : as may be seen in the stereoscope.

The judgment of size is closely connected with that of distance. Our perceptions, gained exclusively from the field of vision, go no further than the *apparent* size of the image—*i. e.*, of the angle subtended by the object. The real size of the object can only be gathered from the apparent size of the image when the distance of the object from the eye is known. Thus perceiving directly the apparent size of the image, we judge the distance of the object giving the image, and upon that come to a conclusion as to its size. And conversely, when we see an object, of whose real size we are otherwise aware, or are led to think we are aware, our judgment of its distance is influenced by its apparent size. Thus when in our field of vision there appears the image of a man, knowing otherwise the ordinary size of a man, we infer, if the image be very small, that the man is far off. The reason of the image being small may be because the man is far off, in which case our judgment is correct; it may be, however, because the

image has been lessened by artificial dioptric means, as when the man is looked at through an inverted telescope, in which case our judgment becomes a delusion. So also an image on a screen when gradually enlarged seems to come forward, when gradually diminished seems to recede. In these cases the influence on our judgment of the muscular sense of binocular adjustment, or monocular accommodation, is thwarted by the more direct influence of the association between size and distance.

Judgment of Solidity.—When we look at a small circle all parts of the circle are at the same distance from us, all parts are equally distinct at the same time, whether we look at it with one eye or with two eyes. When, on the other hand, we look at a sphere, the various parts of which are at different distances from us, a sense of the accommodation, but much more a sense of the binocular adjustment, of the convergence or the opposite of the two eyes, required to make the various parts successively distinct, makes us aware that the various parts of the sphere are unequally distant; and from that we form a judgment of its solidity. As with distance of objects, so with solidity, which is at bottom a matter of distance of the parts of an object, we can form a judgment with one eye alone; but our ideas become much more exact and trustworthy when two eyes are used. And we are much assisted by the effects produced by the reflection of light from the various surfaces of a solid object; so much so, that raised surfaces may be made to appear depressed, or *vice versa*, and flat surfaces either raised or depressed, by appropriate arrangements of shadings and shadow.

Binocular vision, moreover, affords us a means of judging of the solidity of objects, inasmuch as the image of any solid object which falls on to the right eye cannot be exactly like that

FIG. 201.
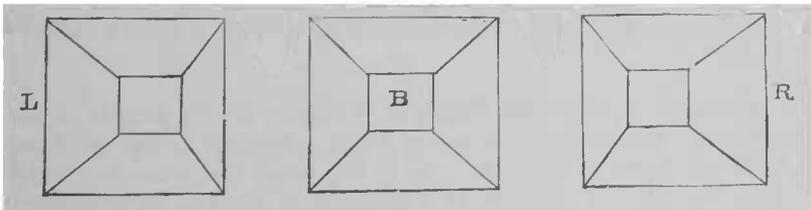
which falls on the left, though both are combined in the single perception of the two eyes. Thus, when we look at a truncated pyramid placed in the middle line before us, the image which falls on the right eye is of the kind represented in Fig. 201, R, while that which falls on the left eye has the form of Fig. 201, L; yet the perception gained from the two images together corre-

sponds to the form of which 201, B, is the projection. Whenever we thus combine iu one perception two dissimilar images, one of the one and the other of the other eye, we judge that the object giving rise to the images is solid.

This is the simple priuciple of the stereoscope, in which two slightly dissimilar pictures, such as would correspond to the vision of each eye separately, are, by means of reflecting mirrors, as in Wheatstone's original instrument, or by prisms, as in the form iutroduced by Brewster, made to cast images on corresponding parts of the two retinas so as to produce a single perception. Though each picture is a surface of two dimensions only, the resulting perception is the same as if a single object, or group of objects, of three dimensions had been looked at.

It might be supposed that the judgment of solidity which arises when two dissimilar images are thus combined in one perception, was due to the fact that all parts of the two images cannot fall on corresponding parts of the two retinas at the same time, and that therefore the combination of the two needs some movement of the eyes. Thus, if we superimpose R on L (Fig. 201), it is evident that when the bases coincide the truncated apices will not, and *vice versa;* hence when the bases fall on corresponding parts, the apices will not be combined into one image, and *vice versa;* in order that both may be combined, there must be a slight rapid movement of the eyes from the one to the other. That, however, no such movement is necessary *for each particular case* is shown by the fact that solid objects appear as such when illuminated by an electric spark, the duration of which is too short to permit of any movements of the eyes. If the flash occurred at the moment that the eyes were binocularly adjusted for the bases of the pyramids, the two apices not falling on exactly corresponding parts would give rise to two perceptions, and the whole object ought to appear confused. That it does not, but, on the contrary, appears a single solid, must be the result of cerebral operations, resulting in what we have called a judgment.

Struggle of the Two Fields of Vision.—If the images of two surfaces, one black and the other white, are made to fall on corresponding parts of the eye, so as to be united into a single perception, the result is not always a mixture of the two impressions—that is, a gray—but, in many cases, a sensation similar to that produced when a polished surface, such as plumbago, is looked at: the surface appears brilliant. The reason probably is because when we look at a polished surface the amount of reflected light which falls upon the retina is generally different in the two eyes; and hence we associate an unequal stimulation of

the two retinas with the idea of a polished surface. So also when the impressions of two colors are united in binocular vision, the result is in most cases not a mixture of the two colors, as when the same two impressions are brought to bear together at the same time on a single retina, but a struggle between the two colors, now one, and now the other, becoming prominent, intermediate tints however being frequently passed through. This may arise from the difficulty of accommodating at the same time for the two different colors (see p. 601); if two eyes, one of which is looking at red, and the other at blue, be both accommodated for red rays, the red sensation will overpower the blue, and *vice versa*. It may be, however, that the tendency to rhythmic action, so manifest in other simpler manifestations of protoplasmic activity, makes its appearance also in the higher cerebral labors of binocular vision.

Sec. 6.—The Protective Mechanisms of the Eye.

The eyeball is protected by the eyelids, which are capable of movements called respectively opening and shutting the eye. The eye is shut by the contraction of the orbicularis muscle, carried out either as a reflex or voluntary act, by means of the facial nerve. The eye is opened chiefly by the raising of the upper eyelid, through the contraction of the levator palpebræ carried out by means of the third nerve. The upper eyelid is also raised and the lower depressed, the eye being thus opened, by means of plain muscular fibres existing in the two eyelids and governed by the cervical sympathetic. The shutting of the eye as in winking is in general effected more rapidly than the opening.

The eye is kept continually moist partly by the secretion of the glands in the conjunctiva, and of the Meibomian glands, but chiefly by the secretion of the lachrymal gland. Under ordinary circumstances the fluid thus formed is carried away by the lachrymal canals into the nasal sac and thus into the cavity of the nose. When the secretion becomes too abundant to escape in this way it overflows on to the cheeks in the form of tears.

If a quantity of tears be collected, they are found to form a clear faintly alkaline fluid, in many respects like saliva, containing about one per cent. of solids, of which a small part is proteid in nature. Among the salts present sodium chloride is conspicuous.

The nervous mechanism of the secretion of tears, in many respects, resembles that of the secretion of saliva. A flow is usually brought about either in a reflex manner by stimuli ap-

plied to the conjunctiva, the nasal mucous membrane, tongue, optic nerve, etc., or more directly by emotions. Venous congestion of the head is also said to cause a flow. The efferent nerves belong either to the cerebro-spinal system (the lachrymal and orbital branches of the fifth nerve), or arise from the cervical sympathetic, the afferent nerves varying according to the exciting cause.

The act of blinking undoubtedly favors the passage of tears through the lachrymal canals into the nasal sac, and hence when the orbicularis is paralyzed tears do not pass so readily as usual into the nose; but the exact mechanism by which this is effected has been much disputed. According to some authors, the contraction of the orbicularis presses the fluid onwards out of the canals, which, upon the relaxation of the orbicularis, dilate and receive a fresh quantity. Others maintain that a special arrangement of muscular fibres keeps the canals open even during the closing of the lids, so that the pressure of the contraction of the orbicularis is able to have full effect in driving the tears through the canals.

CHAPTER III.

HEARING, SMELL, AND TASTE.

SEC. 1.—HEARING.

[Physiological Anatomy of the Ear.

THE ear, or organ of hearing, is composed of three parts, called the *external, middle,* and *internal* ear.

The *external ear* consists of an outer projecting portion, called the *pinna,* and the auditory canal, or *meatus auditorius externus.* (Fig. 202.) The pinna is a somewhat oblong funnel-shaped
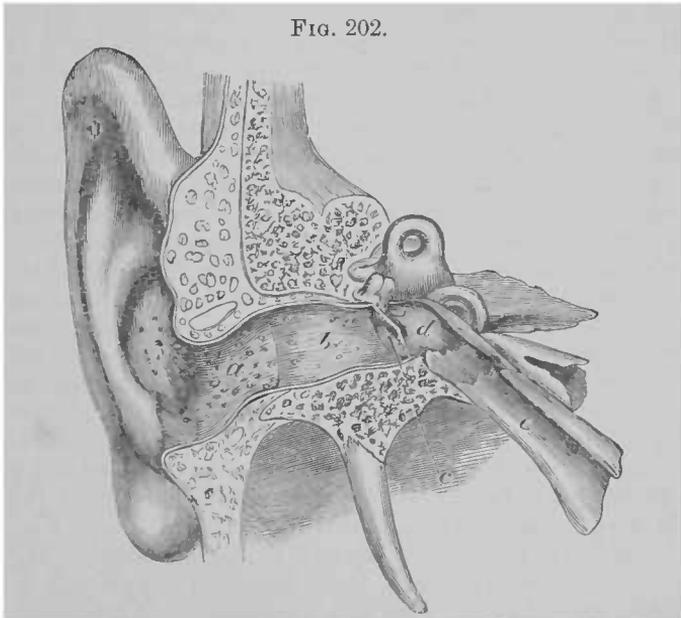
FIG. 202.

VERTICAL SECTION OF THE MEATUS AUDITORIUS AND TYMPANUM (SCARPA).
a, cartilaginous part of the meatus; *b,* osseous portion; *c,* membrana tympani; *d,* cavity of the tympanum; *e,* Eustachian tube.

organ, the smaller portion of the funnel being attached to the skull by ligamentous tissue; the larger portion serving to collect and convey the sonorous undulations to the meatus. It is com-

posed of cartilage covered by integument. Its surface is irregularly curved and depressed. The outer projecting rim is tho *helix;* anterior to the *helix* is a second elevation, called the *antihelix*, which describes a curve partially around a deep depression which leads to the meatus, called the *concha.* Between the helix and antihelix is the *fossa* of the helix. The antihelix bifurcates at its superior portion, and encloses the *fossa* of the antihelix. Projecting posteriorly from the anterior portion of the concha is a papillary prominence called the *tragus;* posterior to this, separated by a fissure, is the *antitragus,* which is a continuation of the helix. On the inferior portion of the pinna is a soft pendulous portion, termed the *lobule.* The meatus leads from the concha to the middle ear, from which it is separated by the tympanic membrane. Its direction is forwards, inwards, and slightly upwards; its lower surface being longer than the upper, on account of the obliquity of the position of the tympanic membrane. The canal consists of an external *membrano-cartilaginous* portion, which is continuous with the pinna, and an internal *osseous* portion formed by the mastoid bone. In the external portion of the canal are found numerous hairs and sebaceous glands; in the internal portion are found the *ceruminous glands,* which secrete a peculiar substance commonly known as the earwax.

The *middle ear* or *tympanum* is an irregular flattened cavity, situated in the petrous portion of the temporal bone, and lined with a mucous membrane. It is separated from the meatus by a membranous diaphragm, which is the *tympanic membrane;* and from the internal ear by an osseo-membranous partition, which forms a common wall for both. Through the Eustachian tube it communicates with the pharynx. On its posterior wall are seen orifices of the mastoid cells. The tympanic membrane is a semitransparent, oval membrane, concave on its external, and convex on its internal surface, where it has attached the long process of the malleus, one of the ossicles. It is placed in an oblique position, sloping downwards, forwards, and inwards at an angle of about $45°$. Its circumference is attached to a groove in the temporal bone. In the fœtus this portion of the bone exists as a separate piece, called the *tympanic bone* (Fig. 203), but it afterwards becomes ossified to the temporal. The tympanic membrane consists of three layers: the external, middle, and internal. The external is a continuation of the integument covering the meatus; the internal is a continuation of the mucous membrane lining the tympanum; the middle layer, which is the most important, is tense, strong, and fibrous, made up of circular and radiating fibres, with a small amount of elastic tissue intermixed.

In the internal wall of the tympanum are two small openings,

the *fenestra ovalis* and *fenestra rotunda,* which communicate with the labyrinth. The fenestra rotunda is closed by a membrane. Extending between the tympanic membrane and the fenestra ovalis are the *ossicles,* consisting of three small bones, which form a system of levers. These ossicles are termed, from their resemblance to particular objects, the *malleus, incus,* and *stapes.* (Fig. 204.) The malleus consists of a head, neck, long and short process, and handle. The head articulates with the roof of the tympanum, and in a depression of the incus; the handle
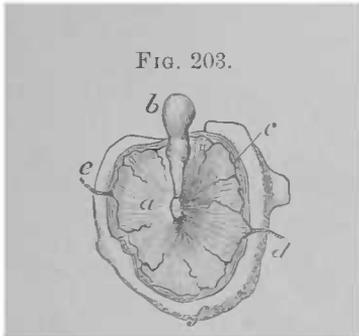
Fig. 203.—INNER VIEW OF THE MEMBRANA TYMPANI IN THE FŒTUS, WITH THE MALLEUS ATTACHED.

a, membrane or drum of the tympanum; *b,* malleus; *c,* band of circular fibres at the circumference; *d,* inferior, and *e,* superior tympanic artery; *f,* tympanic bone.

FIG 204.—PLAN OF THE OSSICLES IN POSITION IN THE TYMPANUM WITH THEIR MUSCLES.

a, cavity of the tympanum; *b,* membrana tympani; *c,* Eustachian tube; *d,* malleus; *e,* incus; *f,* stapes; *g,* laxator tympani muscle; *h,* tensor tympani; *i,* stapedius.

is directed downwards, and attached by its whole length to the tympanic membrane; the long process (*processus gracilis*) is directed forwards, and has attached the insertion of the *laxator tympani muscle;* the short process, which is at the base of the long process, has attached the insertion of the *tensor tympani muscle.* The *incus* consists of a body, a long and short process. The body of the incus has a depression, in which articulates the head of the malleus; the short process is attached to the posterior wall of the tympanum; the long process (lenticular process) is placed almost vertically, and at its end is a rounded process (the *os orbiculare*) which articulates with the head of the stapes. The *stapes* consists of a head, neck, two crura, and a base. The head

articulates with the long process of the incus; the neck serves
as a point of insertion of the stapedius muscle; the crura diverge
from the neck, and unite with the oval base at its greatest
diameter.   The base is fixed in the fenestra ovalis by attach-
ments formed by the lining membranes of both the tympanum
and internal ear.   These ossicles are connected with each other,
and to the walls of the tympanum by ligaments, and at their
articulations they are furnished with cartilages and synovial

FIG. 205.

INTERIOR OF THE OSSEOUS LABYRINTH.
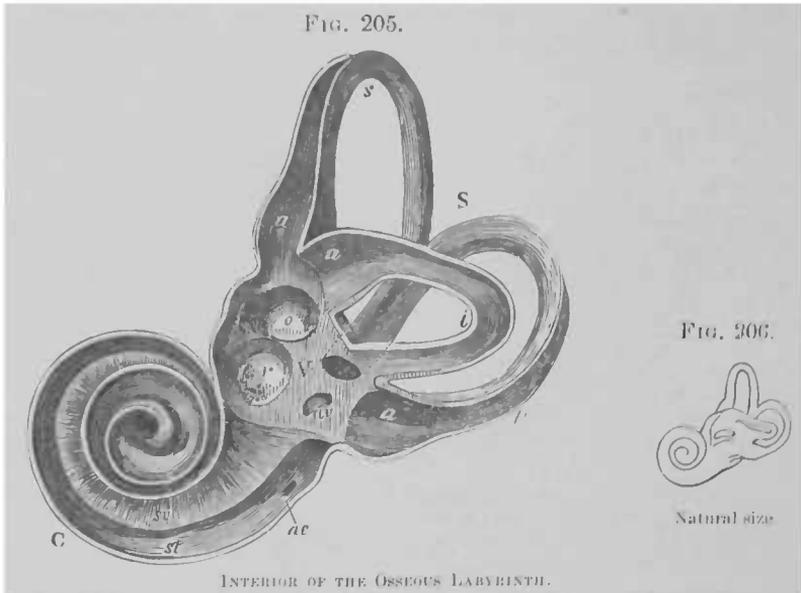
V, vestibule ; av, aqueduct of the vestibule ; o, fovea hemielliptica ; r, fovea hemispherica
S, semicircular canals ; s superior ; p, posterior ; i, horizontal ; a, a, a, the ampullar extremity
of each ; C, cochlea ; ac, aqueduct of the cochlea ; sv, osseous zone of the lamina spiralis,
above which is the scala vestibuli, communicating with the vestibule ; st, scala tympani below
the spiral lamina.   After SÖMMERING.

FIG. 206.

Natural size.

membranes.   They are enveloped by prolongations of the mu-
cous membrane lining the tympanum.
    The *internal ear* or *labyrinth* is the most essential portion of
the auditory apparatus.   It consists of three portions : the *vesti-
bule, semicircular canals,* and *cochlea ;* and is situated within the
petrous portion of the temporal bone.   Within the osseous laby-
rinth is a membranous labyrinth to which the auditory nerve is
distributed.   The vestibule is an irregular chamber, which serves
as a common means of communication between the tympanum
and the semicircular canals and cochlea.   On its external wall is
the fenestra ovalis, closed by the base of the stapes.   On its
internal wall is a depression called the *fovea hemispherica,* which

is perforated by minute openings for the passage of auditory nerve-filaments. Above and posterior to this depression is another, the *fovea hemielliptica*. Posterior to the fovea hemispherica is the orifice of the aqueductus vestibuli. In the posterior wall are five openings leading to the semicircular canals. Anteriorly, it communicates with the cochlea by the *aperturæ scalæ vestibuli cochleæ*. The *semicircular canals* are three in number: the *superior*, *posterior* or *inferior*, and *horizontal*. They form the greater portion of a circle, and communicate with the
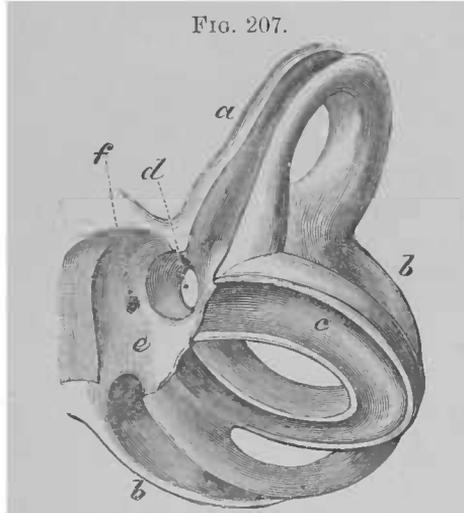
FIG. 207.

REPRESENTATION OF THE SEMICIRCULAR CANALS ENLARGED. (From a model in University College Museum.)

a, superior vertical; *b*, posterior or inferior vertical; and *c*, horizontal canal; *d*, common opening of the two vertical canals; *e*, part of the vestibular cavity; *f*, opening of the aqueduct of the vestibule.

vestibule by five openings, one of which is common to the superior and horizontal canals. The superior canal is situated vertically, and at right angles with the posterior surface of the petrous bone; the posterior canal is also vertical, and parallel with the posterior surface of the petrous bone; the inferior canal is placed horizontally and at right angles to the others. At the commencement of each of these canals is a dilated portion, called the *ampulla*.

The *cochlea* occupies the anterior portion of the labyrinth. Its base, which corresponds to the *internal auditory meatus*, is perforated by many minute orifices for the passage of filaments of the cochlear branch of the auditory nerve. The cochlea consists of a central axis, or *modiolus*, which has a spiral canal wound around it. This canal makes two and a half complete

turns, and terminates in the apex of the cochlea in an expansion termed the *infundibulum*. (Fig. 208.) The modiolus is somewhat cone-shaped, and forms the internal wall of the canal, being perforated in its centre and sides by apertures for the passage of the filaments of the auditory nerve. The canal is divided into two passages or *scalæ* by a septum called the *lamina spiralis*,

FIG. 208.

SECTION THROUGH THE COCHLEA (BRESCHET).
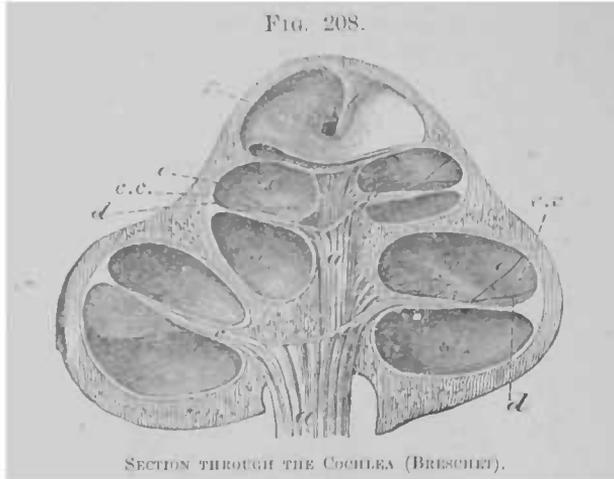
a, axis with its canals; *b*, infundibulum or enlarged upper end of the axis; *c*, septum of the cochlea; *d*, membrane of Corti; *e*, membrane of Reissner; *f*, hiatus or helicotrema; *st*, scala tympani; *sr*, scala vestibuli.

which is partly osseous and partly membranous. The osseous portion projects from the modiolus, midway across the canal; it consists of two laminæ between which the nerve-filaments run. The membranous portion extends from the external margin of the osseous lamina to the external wall of the canal. It consists of two layers; the superior is the membrane of Corti or *membrana tectoria*; the inferior, the *membrana basilaris*, which is attached externally to the *planum semilunare*. These membranes are placed parallel with each other, and contain between them the *organ of Corti*, which rests on the basilary membrane. (Fig. 209.)

The *scala vestibuli*[1] communicates below with the vestibule by the *aperturæ scalæ vestibuli cochleæ;* the lower passage, or *scala tympani*, communicates with the tympanum by the fenestra rotunda. These scalæ communicate at the apex of the cochlea by an opening termed the *hiatus* or *helicotrema*, which exists in consequence of a deficiency of the last half turn of the lamina spiralis.

[1] The upper scala is divided into two parts by a membranous partition, the upper of which is called the scala vestibuli; the other, ductus cochlearis. (Fig. 209.)

The osseous portion of the lamina spiralis has on its superior external portion a denticulated cartilaginous substance called the *lamina denticulata.* From the superior surface of the spiral lamina, and internal to the lamina denticulata, is a delicate membrane extending upwards and outwards at an angle of about 45° to the external wall of the scala. This is called the *membrane of Reissner.* It divides the scala into two passages, the lower of which is the *ductus cochlearis.* This duct ends in the apex of the cochlea in a cœca, and communicates at the base with the saccule by the *ductus reuniens;* it contains the essential portion of the auditory apparatus of the cochlea, and is a part of the membranous labyrinth.

The *organ of Corti* rests upon the basilary membrane. It consists of the inner and outer hair-cells, and two rows of elongated cells, placed parallel with each other, having an

Fig. 209.
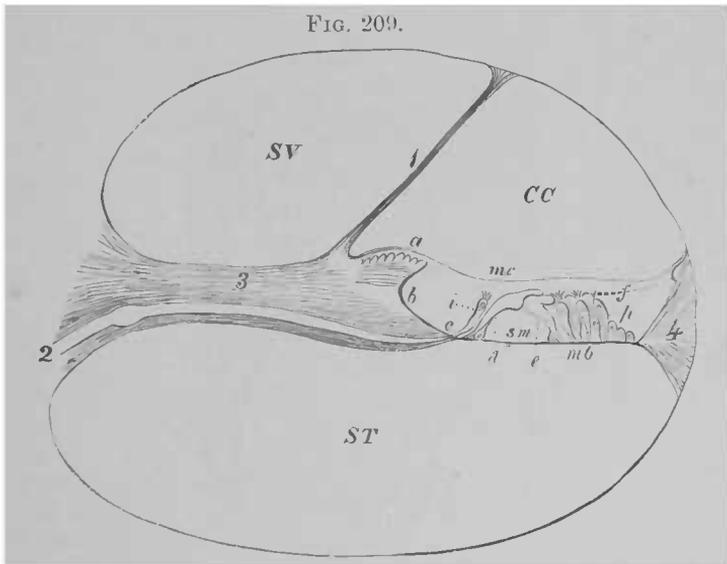
A DIAGRAM OF A SECTION OF THE TUBE OF THE COCHLEA ENLARGED. Modified from HENLE. *SV*, scala vestibuli; *ST*, scala tympani; *CC*, canal of the cochlea; 1, membrane of Reissner; 2, cochlear branch of the auditory nerve; 3, lamina spiralis ossea; 4, planum semilunare; *a*, lamina denticulata; *b*, sulcus spiralis; *c*, tympanic lip of the sulcus spiralis; *d*, inner rods of Corti; *e*, outer rods of Corti; *f*, lamina reticularis; *i*, inner hair-cells; *mb*, membrana basilaris; *mc*, membrane of Corti; *p*, outer hair-cells; *sm*, central space between the rods.

inclining position so that their free extremities rest against each other and thus form the *arch of Corti,* which covers the *central space.* (Fig. 209.) These rows are called the *inner* and *outer* rods, or pillars of Corti. From the superior extremity of both the inner and outer rods, finger-like processes project externally.

At their bases corresponding to the central space are single rows of nucleated cells. On the internal side of the inner rods is a single row, and on the external side of the outer rods are three rows of elongated ciliated cells. Extending across the top of the organ of Corti, from the inner hair-cells to the external wall of the canal, is a very delicate structure called the *reticular membrane*. The auditory nerve-filaments probably terminate in the ciliated cells, being intimately connected with the cilia.

The osseous labyrinth is lined by a fibro-serous membrane which secretes a watery fluid called the *perilymph*. The perilymph fills the scalæ of the cochlea, and surrounds the *ductus cochlearis* and the membranous portions of the labyrinth, which are situated in the vestibule and semicircular canals.

The *membranous labyrinth* is a closed sac consisting of the semicircular canals, a vestibular portion, and the ductus coch-
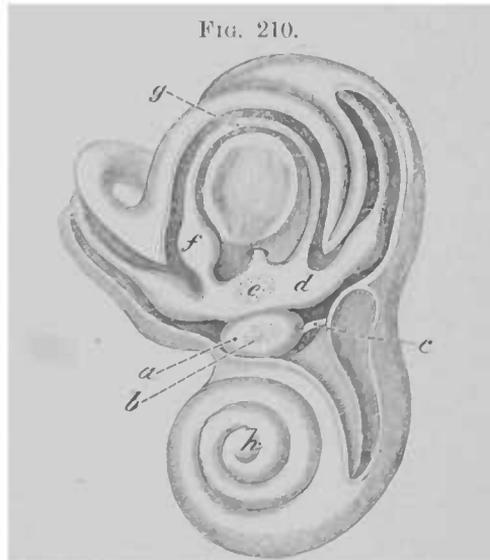
FIG. 210.

PETROUS BONE PARTLY REMOVED TO SHOW THE MEMBRANOUS LABYRINTH IN PLACE
(BRESCHET)

a, small sac ; *b*, its otolith ; *c*, ductus reuniens ; *d*, large sac or utricle ; *e*, its otolith ; *f*, ampullary enlargements on a semicircular tube ; *g*, semicircular tube.

learis of the cochlea. The semicircular canals are of the same form as the osseous canals, and are contained within them. The vestibular portion consists of an expanded body, the *utricle*, and a smaller body, the *saccule*. The utricle is situated at the fovea hemielliptica ; the semicircular canals open on its internal surface. The saccule lies at the fovea hemispherica ; it is con-

nected with the ductus cochlearis by the *ductus reuniens*. In the walls of the saccule and utricle are two calcareous bodies called the *otoliths*. The walls of the ampulla, according to Bowman, also contain some grains of a similar substance. The walls of the membranous labyrinth consist of a fibrous tissue, lined by pavement nucleated epithelium cells, having a structure-less basement-membrane. These epithelial cells are much modified at the place of entrance of the fibres of the auditory nerve. The vestibular branches of the auditory nerve are distributed to the ampullæ, utricle, and saccule. (Fig. 211.) In the utricle

FIG 211.
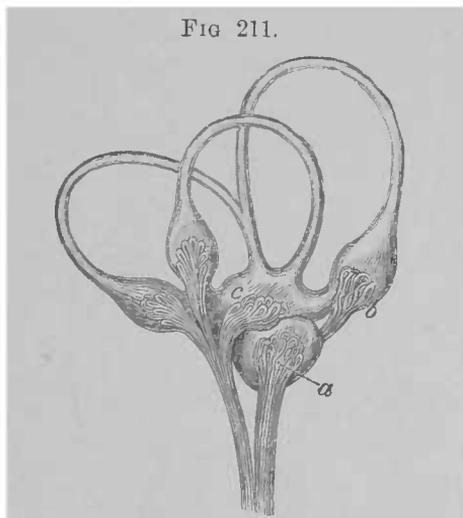
DISTRIBUTION OF NERVES TO THE MEMBRANOUS LABYRINTH. (BRESCHET.)
a, nerve to the saccule; *b*, nerve entering the ampullary enlargement on a semicircular tube; *c*, branch of nerve entering the large sac or utricle.

and the saccule the fibres terminate in oval plates, called the *maculæ acusticæ*, which are more or less colored by the deposition of yellow pigment. In the ampullæ the fibres terminate in elevations called the *cristæ acusticæ*. After the nerve-filament pierces the membranous wall at these points, the axis-cylinder alone penetrates the basement-membrane; it then forms a plexus of delicate nerve-fibres with nuclei, and finally terminates in fusiform epithelial cells which have terminal cilia called the auditory hairs. (Fig. 212.) These ciliated cells are supported by columnar epithelium.

The membranous labyrinth is lined by polygonal nucleated epithelium, which secretes the *endolymph* which fills the sac.]

As in the eye, so in the ear, we have to deal, first, with a nerve of special sense, the stimulation of which gives rise to a special

sensation; secondly, with terminal organs through which the physical changes proper to the special sense are enabled to act on the nerve; and, thirdly, with subsidiary apparatus, by which the usefulness of the sense is increased.   The central connections of the auditory nerve are such that whenever the auditory fibres are stimulated, whether by means of the terminal organs in the usual way or by the direct application of stimuli—electrical, mechanical, etc.—the result is always a sensation of sound.   Just

[Fig 212.
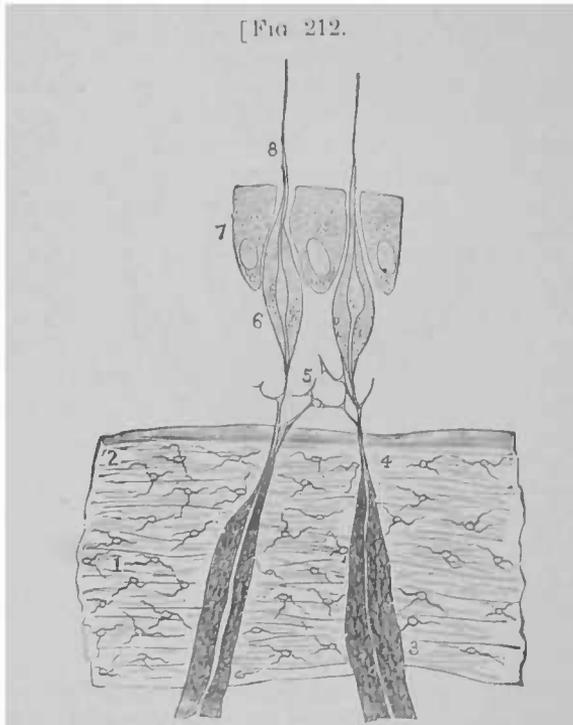
DIAGRAM OF THE MODE OF TERMINATION OF THE AUDITORY NERVE IN THE AMPULLÆ AND SACCULI.

1, the wall of the ampulla; 2, structureless basement-membrane; 3, doubly contoured nerve-fibres; 4, axis-cylinder traversing the basement-membrane; 5, plexiform union of fine nerve-fibres with interspersed nuclei; 6, fusiform cells, with nucleus and dark fibre in their interior; 7, supporting cells; 8, auditory hairs.]

as stimulation of the optic fibres produces no other sensation than that of light, so stimulation of the auditory fibres produces no other sensation than that of sound.[1]   The terminal organs of the

[1] It will be seen later on that there are reasons for thinking that impulses passing along the auditory *nerve* may give rise to other effects than auditory sensations.

auditory nerve are of two kinds : the complicated organ of Corti in the cochlea, and the epithelial arrangements of the maculæ and cristæ acusticæ in other parts of the labyrinth. Waves of sound falling on the auditory nerve itself produce no effect whatever ; it is only when, by the medium of the endolymph, they are brought to bear on the delicate and peculiar epithelium cells which constitute the peripheral terminations of the nerve, that sensations of sound arise. Such delicate structures are, for the sake of protection, naturally withdrawn from the surface of the body, where they would be subject to injury. Hence, the necessity of an acoustic apparatus, forming the middle and external ear, by which the waves of sound are most advantageously conveyed to the terminal organs.

The Acoustic Apparatus.

Waves of sound can and do reach the endolymph of the labyrinth by direct conduction through the skull. Since, however, sonorous vibrations are transmitted with great difficulty from the air to solids and liquids, and most sounds come to us through the air, some special apparatus is required to transfer the aerial vibrations to the liquids of the internal ear. This apparatus is supplied by the tympanum and its appendages.

The Concha.—The use of this, as far as hearing is concerned, is to collect the waves of sound coming in various directions, and to direct them on to the membrana tympani. In ourselves of moderate service only, in many animals it is of great importance.

The Membrana Tympani.—It is a characteristic property of stretched membranes that they are readily thrown into vibration by aerial waves of sound. The membrana tympani from its peculiar conformation, being funnel-shaped with a depressed centre surrounded by sides gently convex outwards, is peculiarly susceptible to sonorous vibrations, and is most readily thrown into corresponding movements when waves of sound reach it by the meatus. It has moreover this useful feature, that unlike other stretched membranes, it has no marked note of its own. It is not thrown into vibrations by waves of a particular length more readily than by others. It answers equally well within a considerable range, to vibrations of very different wave-lengths. Had it a fundamental tone of its own, we should be distracted by the prominence of this note in most of the sounds we hear. When sounds impinge on the solids of the head, as when a watch is held between the teeth, the membrana tympani is still functional. Vibrations are conveyed from the temporal bone to it

and hence pass in the usual way, in addition to those transmitted directly from the bone to the perilymph.

The Auditory Ossicles.—The malleus, the handle of which descending forwards and inwards, is attached to the membrana tympani, and the incus, whose long process is connected by means of its os orbiculare or lenticular process and the stapes to the fenestra ovalis, form together a body which rotates round an axis, passing through the short process of the incus, the bodies of the incus and malleus, and the processus gracilis of the malleus. When the malleus is carried inwards, the incus moves inwards too, and when the malleus returns to its position, the incus returns with it, the peculiar saddle-shaped joint with its catch teeth permitting this movement readily, but preventing the stapes being pulled back when the membrana tympani with the malleus is, for any reason, pushed outwards more than usual; the joint then gapes, so as to permit the malleus to be moved alone. Various ligaments, the superior or suspensory, anterior, and external, also serve to keep the malleus in place. The whole series of ossicles may be regarded as a single-armed lever, moving on the ligamental attachment of the short process of the incus to the posterior wall of the tympanum, the weight being brought to bear at the end of the long process of the incus, and the power at the end of the handle of the malleus. The long, malleal arm of this lever is about $9\frac{1}{2}$ mm., the short, stapedial, $6\frac{1}{4}$ mm. in length; hence the movements of the stapes are less than those of the tympanum; but the loss in amplitude is made up by a gain of force, which is in itself an obvious advantage.

Thus every movement of the tympanic membrane is transmitted through this chain of ossicles to the membrane of the fenestra ovalis, and so to the perilymph of the labyrinth; the vibrations of the tympanic membrane are conveyed with increased intensity, though with diminished amplitude, to the latter. That the bones thus move *en masse* has been proved by recording their movements in the usual graphic method. A very light style attached to the incus or stapes is made to write on a travelling surface; when the membrana tympani is thrown into vibrations by a sound, the curves described by the style indicate that the chain of bones moves with every vibration of the tympanum. On the other hand, the comparatively loose attachments of the several bones is an obstacle to the molecular transmission of sonorous vibrations through them. Moreover, sonorous vibrations can only be transmitted to or pass along such bodies as either are very long compared to the length of the sound-waves, or, as in the case of membranes and strings, have one dimension very much smaller than the others. Now the bones

in question are not especially thin in any one dimension, but are in all their dimensions exceedingly small compared with the length of the vibrations of even the shrillest sounds we are capable of hearing; hence they must be useless for the molecular propagation of vibrations.

The Tensor Tympani Muscle even in a quiescent state is of use in preventing the membrana tympani being pushed out far. When it contracts it renders the membrana tympani more tense, and hence has been supposed to act as a damper lessening the amount of vibration of the membrane in the case of too powerful sounds; it is said to be readily thrown into contraction at the commencement of a sound or noise, but to return to rest during the continuance of a musical note. Efferent impulses reach it through fibres of the fifth nerve, and its activity is regulated by a reflex action. In some persons the muscle seems to be partly under the dominion of the will, since a peculiar crackling noise which these persons can produce at pleasure appears to be caused by a contraction of the tensor tympani.

The so-called laxator tympani is considered to be not a muscle at all, but a part of the ligamentous supports of the malleus.

The Stapedius Muscle is supposed to regulate the movements of the stapes, and especially to prevent its base being driven too far into the fenestra ovalis during large or sudden movements of the membrana tympani. It is governed by fibres from the facial nerve.

The Eustachian Tube.—This serves to maintain an equilibrium of pressure between the external air and that within the tympanum, and to serve as an exit for the secretions of that cavity. Were the tympanum permanently closed the vibrations of the membrana tympani would be injuriously affected by variations of pressure occurring either inside or outside. The Eustachian tube is undoubtedly open during swallowing, but it is still disputed whether it remains permanently open, or is opened only at intervals; probably it is, at most times, neither widely open nor closely shut.

Auditory Sensations.

Each vibration communicated by the stapes to the perilymph travels as a wave over the vestibule, the semicircular canals, and other parts of the labyrinth; and from the perilymph is transmitted through the membranous walls to the endolymph. From the vestibule it passes on into the scala vestibuli of the cochlea,

and descending the scala tympani, ends as an impulse against
the membrane of the fenestra rotunda. In the regions of the
maculæ and cristæ the vibrations of the endolymph are supposed
to throw into corresponding vibrations the so called auditory
hairs. In the cochlea the vibrations of the perilymph are sup-
posed to throw into vibration the basilar membrane with the
superimposed organ of Corti, consisting of the rods of Corti with
the inner and outer hair-cells. The vibrations thus transmitted
to these structures give rise to nervous impulses in the termina-
tions of the auditory nerves, and these impulses reaching certain
parts of the brain produce what we call auditory sensations.
We are accustomed to divide our auditory sensations into those
caused by noises and those caused by musical sounds. It is the
characteristic of the latter that the vibrations which constitute
them are periodical; they occur and recur at regular intervals.
When no marked periodicity is present in the vibrations, when
the repetition of the several vibrations is irregular, or the period
so complex as not to be readily appreciated, the sensation pro-
duced is that of a noise. There is however no abrupt line between
the two. Between a pure and simple musical sound produced
by a series of vibrations each of which has exactly the same
wave-length, and a harsh noise in which no consecutive vibra-
tions may be alike, there are numerous intermediate stages.

In both noises and musical sounds we recognize a character
which we call loudness. This is determined by the amplitude of
the vibration; the greater the disturbance of the air (or other
medium) the louder the sound. In a musical sound we recognize
also a character which we call pitch. This is determined by the
wave-length of the vibrations; the shorter the wave-lengths, the
larger the number of consecutive vibrations which fall upon the
ear in a second, the higher the pitch. We are able to speak of a
whole series of tones or musical sounds of different pitch, from
the lowest to the highest audible tone. And even in many
noises we can, to a certain extent, recognize a pitch, indicating
that among the multifarious vibrations there is a periodicity of
certain groups of vibrations.

Lastly, we distinguish musical sounds by their quality; the
same note sounded on a piano and on a violin produce very
different sensations, even when a series of vibrations having in
each case the same period of repetition is set going. This arises
from the fact that the musical sounds generated by most musical
instruments are not simple but compound vibrations. When the
note C in the treble for instance is struck on the piano, and we
analyze the total sound, we find that it can be resolved partly
into a series of vibrations with a period characteristic of the pure
tone of the treble C, and partly into other series of vibrations

with periods characteristic of the C in the octave above, of the G above that, of the C in the next octave, and of the E above that. And the sensation which we associate with the sound of the treble C on the piano is determined by the characters of the complex vibration arising out of these several constituent simple vibrations. Almost all musical sounds are thus composed of what is called a "fundamental tone" accompanied by a number of "overtones." And the overtones varying in number and relative prominence in different instruments, give rise to a difference in the sensation caused by the whole tone. So that while the fundamental tone determines the pitch of the sound, the quality of the sound is determined by the number and relative prominence of the overtones. In a somewhat similar way we distinguish the quality of noises, such as a banging, crackling, or rustling noise, by an appreciation of sudden or irregular changes in the amplitude and period of the constituent vibrations.

Since we have a very considerable appreciation, capable by exercise of astonishing enlargement, of the loudness, pitch, and quality of a wide range of noises and musical sounds, it is clear that, within the limits of hearing, each vibration or series of vibrations must produce its effect on the auditory nerves, according to the measure of its intensity and period. Out of those effects, out of the sensory impulses to which the several vibrations thus give rise, are generated our sensations of the noise or of the sound.

The vibrations of a musical sound (and since noises are so imperfectly understood, we may, with benefit, chiefly confine ourselves to musical sounds), as they pass through the air (or other medium) are not discrete; the vibrations corresponding to the fundamental tone and overtones do not travel as so many separate waves; they altogether form one complex disturbance of the medium; and it is as one *composite* wave that the sound falls on the membrana tympani, and passing through the auditory apparatus, breaks on the terminations of the auditory nerve. And when two or more musical sounds are heard at the same time, the same fusion of the waves occurs. Since we can distinguish several tones reaching our ear at the same time, it is clear that we must possess in our minds or in our ears some means of analyzing these composite waves of sound which fall on our acoustic organs, and of sorting out their constituent vibrations.

There is at hand a simple and easy physical method of analyzing composite sounds. If a person standing before an open piano sings out any note, it will be observed that a number of the strings of the piano will be thrown into vibrations, and on examination it will be found that those strings which are thus set going correspond in pitch to the fundamental tone and to the

several overtones of the note sung. The note sung reaches the strings as a complex wave, but these strings are able to analyze the wave into its constituent vibrations, each string taking up those vibrations and those vibrations only which belong to the tone given forth by itself when struck. If we suppose that each terminal fibril of the auditory nerve is connected with an organ so far like a piano-string that it will readily vibrate in response to a series of vibrating impulses of a given period and to none other, and that we possess a number of such terminal organs sufficient for the analysis of all the sounds which we can analyze, and that each terminal organ so affected by particular vibrations gives rise to a sensory impulse and thus to a sensation of a distinct character—if we suppose these organs to exist, our appreciation of sounds is in a large measure explained. In the organ of Corti we find structures the arrangement of which irresistibly suggests to us that these are the organs we are seeking. We have only to suppose that of the long series of rods of Corti, varying regularly as these do from the bottom to the top of the spiral, in length and in the span of their arch, each pair will vibrate in response to a particular tone, and the whole matter seems explained. But the more the subject is inquired into, the more complex and difficult it appears; and we are obliged to conclude that the part played by the rods of Corti is only a subordinate part of the function of the whole organ of Corti.

In the first place, it is difficult to see how the rods of Corti, even if they are thrown into vibration, can originate sensory impulses, for the fibrils of the auditory nerve terminate in the inner and outer hair-cells, and it is in these cells, and not along the course of the fibrils as they pass under and between the rods of Corti, that the sensory impulses must begin. In the second place, the variation in length of the fibres along the series is insufficient for the work assigned to them. Morever, they appear not to be elastic. Lastly, they are wholly absent in birds, who very clearly can appreciate musical sounds. This last fact proves indubitably that the rods in question are not absolutely essential for the recognition of tones. In the face of these difficulties it has been suggested that the basilar membrane, which is present in birds as well as in mammals, and which, being tense radially but loose longitudinally—*i. e.*, along the spiral of the cochlea, may be considered as consisting of a number of parallel radial strings, each capable of independent vibrations, is the sought-for organ of analysis; for it may be shown mathematically that a membrane so stretched in one direction only is capable of vibrating in such a manner. And the radial dimensions of the basilar membrane give a much greater range of difference than do the rods of Corti, diminishing in man down-

wards from 0.495 mm. at the top to 0.04125 mm. near the bottom
of the spiral, whereas the difference in length of the latter is
simply that between 0.048 and 0.085 mm. for the inner, and
between 0.019 and 0.085 for the outer fibres. According to this
view, a particular simple vibration reaching the scala tympani
of the cochlea throws into sympathetic vibrations a small portion
of the basilar membrane, the vibrations of which in turn so affect
the structures overlying it, that sensory impulses are generated.
These sensory impulses reaching the brain give rise to a corre-
sponding sensation of a particular tone.

The remarkable reticular membrane which has such peculiar
relations with the hair-cells, and through them with the basilar
membrane, must, one might imagine, have some special function;
but it is impossible at present to assign to it any satisfactory duty.
The structural arrangements seem, if anything, to indicate that
when a segment of the basilar membrane is thrown into vibra-
tions, the overlying hair-cells, reticular membrane, and rods of
Corti vibrate *en masse* together with it. But this renders the
whole matter still more difficult. Indeed the whole subject is in
the highest degree obscure, and the most we can say is that the
organ of Corti as a whole seems to be in some way connected
with the appreciation of tones, but that at present it is very
hazardous to attempt to explain how it acts, or to assign par-
ticular functions to particular parts. The distinction between
the inner and outer hair-cells seems to be very parallel to that
between the rods and the cones of the retina; but even this
analogy may be a fallacious one.

It has been observed that among the auditory hairs of the
crustacea, some will vibrate to particular notes; but the audi-
tory hairs of the mammal are far too much of the same length
to permit the supposition that they can act as organs of analysis.

If the organ of Corti is the means by which we appreciate
tones, it is evident that by it also we must be able to estimate
loudness, for the quality of a musical sound is dependent on the
relative intensity, as well as on the nature of the overtones. And
since noise is at best but confused music, the cochlea must be a
means of appreciating noises as well as sounds. But this would
leave nothing whatever for the rest of the labyrinh to do in
respect to the appreciation of sound save so far as the difference
in structure between the hair-cells of Corti, with their short thick
rods, and the hair-bearing structures in the maculæ and cristæ
with their thin delicate hairs, may possibly indicate a difference
of function, the latter being more susceptible to the irregular
vibrations of noises. That the vestibule and semicircular canals
are however concerned in hearing is shown by its being the only
auditory organ in the ichthyopsida, unless we suppose that in

the higher vertebrates its function has been wholly transferred
to the cochlea.   That the semicircular canals may have duties
apart from hearing we shall show later on.

Concerning the function of the other parts of the internal ear
we know very little.   The otoliths have been supposed to in-
tensify the vibrations of the endolymph; but since apparently
they are lodged in a quantity of mucus it is probable that they
really act as dampers.   A similar damping action has been
suggested for the membrane of Corti (*membrana tectoria*) over-
hanging the fibres and hair-cells; and some writers have sup-
posed that muscular fibres present in the planum semilunare may
by tightening the basilar membrane serve us a sort of accommo-
dation mechanism.

It must, however, be borne in mind that even making the
fullest allowance for the assistance afforded us by the organ of
Corti, the appreciation of any sound is ultimately a mental act.
The analysis of the vibrations by the fibres of Corti or the basilar
membrane is simply preliminary to a synthesis of the sensory
impulses so generated into a complex sensation.   We do not re-
ceive a distinct series of specific auditory impulses resulting in a
specific sensation for every possible variation in the wave-length
of sonorous vibrations any more than we receive a distinct series
of specific visual impulses for every possible wave-length of
luminous vibrations.   In each case we have probably a number
of primary sensations, from the various mingling of which, in
different proportions, our varied complex sensations arise; the
difference between the eye and the ear being that whereas in the
former the number of primary sensations appears to be limited
to three or at least to six, in the latter, thanks to the organ of
Corti, the number is very large; what the exact number is we
cannot at present tell.   Our appreciation of a sound is at
bottom an appreciation of the combined effect produced by the
relative intensities to which the primary auditory sensations are,
with the help of the organ of Corti, excited by the sound.

Whatever be the explanation of the manner in which our
distinct auditory sensations arise, the range and precision of our
appreciation of musical sounds is very great.   Vibrations with a
recurrence below 30 a second[1] are unable to produce a sensation
of sound; if the waves are powerful enough we may feel them,
but we do not hear them if the vibrations are simple, and such
as would give rise to a pure tone; if the fundamental tone is
accompanied by overtones we may hear these, and are thus apt
to say we hear the former when in reality we only hear the
latter.   The note of the 16-feet organ pipe, 33 vibrations a

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[1] By some authors the limit is placed as low as 24 or even 15 a second.

second, gives us the sensation of a droning sound. A sound of 40 vibrations is however quite distinct. In the other direction it is possible to hear a note caused by 38,000 vibrations a second, though the limit for most persons is far lower, about 16,000. Some persons hear grave sounds more easily than high ones, and *vice versa*. This may be so pronounced as to justify the subjects being spoken of as deaf to grave or high tones respectively. The range in different animals is very different.

The power of distinguishing one note from another varies, as is well known, in different individuals, according as they have or have not a "musical ear." A well-trained ear can distinguish the difference of a single or even of a half vibration a second, and that through a long range of notes. The range of an ordinary appreciation of tones lies between 40 and 4000 vibrations a second—*i. e.*, between the lowest bass C (C_1 33 vibrations) and the highest treble C (C^5 4224 vibrations) of the piano; tones above and below these, even while audible, being distinguished from each other with great difficulty.

When two consecutive sounds follow each other at a sufficiently short interval the sensations are fused into one. In this respect auditory sensations are of shorter duration than ocular sensations. When ocular sensations are repeated ten times in a second they become fused (p. 613), whereas the ticks of a pendulum beating 100 in a second are readily audible as distinct sounds. When two tuning-forks not quite in tune are struck together the interference of the vibrations gives rise to an alternating rise and fall of the sound, known as "beats." When the beats follow each other as rapidly as 132 in a second they cease to be recognized—that is to say, the sensations which they cause become fused. Before they disappear they give a peculiar disagreeable roughness to the sound. The pleasure given by musical sounds depends largely on the absence of this incomplete fusion of sensations.

Corresponding to entoptic phenomena there are various *entotic* phenomena, sensations or modifications of sensations originating in the tympanum or in the labyrinth; moreover sensations of sound may rise in the auditory nerve or in the brain itself, without any vibration whatever falling on the labyrinth.

Auditory Judgments.

In seeking for the cause of our visual sensations we invariably refer to the external world. The sensation caused by a direct stimulation of the optic nerve or retina by a blow or a galvanic current, we identify with that caused by a flash of light. A sensation arising from any stimulation of the left side of our retina

we regard as caused by some object on the right-hand side of our external visible world. In a similar way, but to a less extent, we project our auditory sensations into the world outside us, and when the auditory nerve is affected we seek the cause in vibrations starting at a greater or less distance from us. We do not think of the sound as originating in the ear itself.

This mental projection of the sound is much more complete when the ear is stimulated by vibrations reaching it through the membrana tympani than when the vibrations are conducted by the solids of the head directly to the perilymph of the labyrinth. When the meatus externus is filled with fluid and the vibrations of the membrana tympani are in consequence interfered with, the apparent outwardness of sounds is to a very large extent lost; sounds, however caused, seem under these circumstances to arise in the ear. Hence it would seem that the vibrations of the membrana tympani, or possibly the action of the muscles attached to the ossicula, give rise to obscure sensations of which, by themselves, we are not distinctly conscious, but which nevertheless lead us to judge that the sounds heard by means of the tympanum come from outside the ear.

Our judgment of the *distance* of sounds is very limited. A sound whose characters we know appears to us near when it is loud, and far off when it is faint. A blindfold person will be unable to distinguish between the difference of intensity produced on the one hand by a tuning-fork being held before him, first with the broad edge of the fork toward him and then with the narrow edge, and the difference on the other hand caused by the removal of the tuning-fork to a distance. We can on the whole better appreciate the distance of noises than of musical sounds.

Our judgment of the *direction* of sounds is also very limited. Our chief aid in this is the position in which we have to place the head in order that we may hear the sound to the best advantage. If a tuning-fork be held in the median vertical plane over the head, though it is easy to recognize it as being in the median plane, it becomes very difficult when the eyes are shut to say what is its position in that plane—*i. e.*, whether it is more towards the front or back of the head. In this respect, too, our appreciation is more accurate in the case of noises than of musical sounds, with the exception of those given out by the human voice, the direction of which can be judged better than even that of a noise.

SEC. 2.—SMELL.

[*Physiological Anatomy of the Nasal Fossæ.*

The nasal fossæ are two irregular cavities which communicate anteriorly with the air, through the anterior nares and posteriorly with the pharynx through the posterior nares. The fossæ are partially divided into upper, middle, and lower air-passages or chambers by the superior, middle, and inferior turbinated bones. They are lined by the Schneiderian or pituitary mucous membrane, which is continuous anteriorly with the integument and posteriorly with the mucous membrane of the pharynx; and with the membrane lining the ducts and sinuses connected with
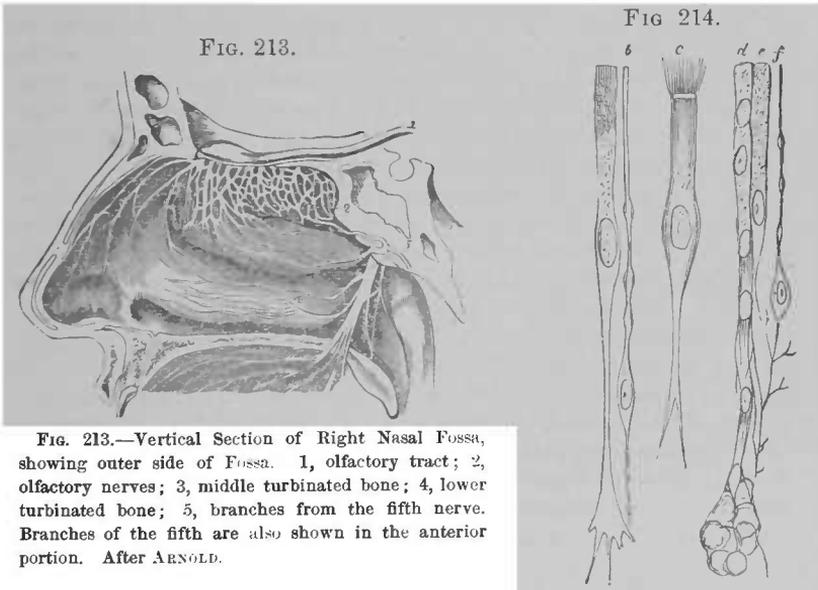
FIG. 213.—Vertical Section of Right Nasal Fossa, showing outer side of Fossa. 1, olfactory tract; 2, olfactory nerves; 3, middle turbinated bone; 4, lower turbinated bone; 5, branches from the fifth nerve. Branches of the fifth are also shown in the anterior portion. After ARNOLD.

FIG. 214.—Cells of the Olfactory Mucous Membrane. *a, b, c,* after Schultze; *d, e, f,* after Lockhart Clarke.

the fossæ. At the position of the distribution of the olfactory nerve-filaments it is much thicker, more vascular, pigmented, and lined by columnar nucleated epithelium cells; the remaining portion of the membrane covering the fossæ, excepting near the anterior nares, is lined by columnar ciliated epithelium. This membrane contains racemose mucous glands, which secrete mucus for the purpose of keeping the membrane constantly moist, which is a condition essential to perfect olfaction.

The olfactory tract is a prolongation of the cerebrum, which terminates anteriorly in a bulbous expansion, the olfactory ganglion. It consists principally of gray matter. This ganglion rests upon the cribriform plate of the ethmoid bone, and in this position sends about twenty filaments, which consist of gray matter alone, through the cribriform plate to be distributed to the pituitary membrane of the upper third of the septum nasi, the upper portion of the roof of the nose, the superior, and a portion of the middle turbinated bones. (Fig. 213.) The whole surface corresponding to the distribution of the olfactory nerve is colored brownish by the pigment in the epithelial cells of the mucous glands and membrane. This pigmented region is called the *regio olfactoria*, and is the essential portion of the nasal fossæ concerned in olfaction.

According to Schultze, the epithelium of the *regio olfactoria* is of two kinds: the first (Fig. 214, *a*) consists of yellow nucleated protoplasmic cells, which have a cylindrical body terminating at its free extremity as a squared truncated surface; the other extremity of the body is stretched out as a filamentous prolongation, which expands into a triangular plate as it approaches the submucous tissue. From the base of this plate a number of filaments are given off, which are prolonged into the submucous tissue. The second variety of epithelium cells (*c*) is found at the borders of the *regio olfactoria*. They are similar to those just described, excepting that their free surface is covered with *cilia*. Between the epithelium cells the olfactory nerves terminate. These terminal filaments (*b f*) are long delicate structures, which have a number of fusiform expansions along their course; in the largest expansion is found an oval nucleus. The terminal filaments are called the *olfactory cells*. As yet no connection between the subepithelial and interepithelial nerve-filaments has been demonstrated. The epithelial cells (*d* and *e*) in the above figure are shown connected with the subepithelial tissue. The fifth nerve supplies the fossæ with sensory filaments.]

Odorous particles present in the inspired air passing through the lower nasal chambers diffuse into the upper nasal chambers, and falling on the olfactory epithelium produce sensory impulses which, ascending to the brain, give rise to sensations of smell. We may presume that the sensory impulses are originated by the contact of the odorous particles with the peculiar rod-shaped olfactory cells described by Max Schultze; but we are as much in the dark about this matter as about the development of visual sensory impulses in the rods and cones or of auditory sensory impulses in the organ of Corti.

The subsidiary apparatus of smell is exceedingly meagre. By the forced nasal inspiration called sniffing, we draw air so forci-

bly through the nostrils that currents pass up into the upper as well as the lower nasal chambers; and thus a more complete contact of the odorous particles with the olfactory membrane than that supplied by mere diffusion is provided for.

We have every reason to think that any stimulus applied to the olfactory nerve will produce the sensation of smell; but the proof of this is not so clear as in the case of the optic and auditory nerves. We are, however, subject to sensations of smell not caused by objective odors. The olfactory membrane is the only part of the body in which odors as such can give rise to any sensations; and the sensations to which they give rise are always those of smell. The mucous membrane of the nose is, however, also an instrument for the development of afferent impulses other than the specific olfactory ones. Chemical stimulation of the olfactory membrane by pungent substances, such as ammonia, gives rise to a sensation distinct from that of smell, a sensation which affords us no information concerning the chemical nature of the stimulus, and which is indistinguishable from the sensations produced by chemical stimulation of other parts of the nasal membrane as well as of other surfaces equally sensitive to chemical action. It is probable that these two kinds of sensations thus arising in the olfactory membrane are conveyed by different nerves, the former by the olfactory, the latter by the fifth nerve.

For the development of smell it appears necessary that the odorous particles should be conveyed to the nasal membrane in a gaseous medium, or, at least, that the surface of the membrane should not be exposed at the same time to the action of fluids. Thus, when the nostril is filled with rose-water, the odor of roses is not perceived; and simply filling the nostrils with distilled water suspends for a time all smell, the sense returning gradually after the water has been removed; the water apparently acts injuriously on the delicate olfactory cells.

Each substance that we smell causes a specific sensation, and we are not only able to recognize a multitude of distinct odors, but also to distinguish individual odors in a mixed smell.

As in the previous senses, we project our sensation into the external world; the smell appears to be not in our nose, but somewhere outside us. We can judge of the position of the odor, however, even less definitely than we can of that of a sound.

The sensation takes some time to develop after the contact of the stimulus with the olfactory membrane, and may last very long. When the stimulus is repeated the sensation very soon dies out—the sensory terminal organs speedily become exhausted. Mental associations cluster more strongly round sensations of smell than round any other impressions we receive from without.

And reflex effects are very frequent, many people fainting in consequence of the contact of a few odorous particles with their olfactory cells.

Apparently the larger the surface the more intense the sensation; animals with acute scent having a proportionately large area of olfactory membrane. The quantity of material required to produce an olfactory sensation may be, as in the case of musk, almost immeasurably small.

When two different odors are presented to the two nostrils, an oscillation of sensation similar to that spoken of in binocular vision (p. 644) takes place.

The assertion that the olfactory nerve is the nerve of smell has been disputed. Cases have been recorded of persons who appeared to have possessed the sense of smell, and yet in whom the olfactory lobes were found after death to be absent. Direct experiments on animals, however, show that loss of the olfactory lobes entails loss of smell. On the other hand, it is stated that section or injury of the fifth nerve causes a loss of smell though the olfactory nerve remains intact, but in these cases it has not been shown that the olfactory membrane remains intact, and it is quite possible that, as in the case of the eye, changes may take place in the nasal membrane as the result of the injury to the fifth nerve, sufficient to prevent its performing its usual functions.

Sec. 3.—Taste.

[Physiological Anatomy of the Gustatory Mucous Membrane.

The peripheral organs concerned in the sense of taste are localized in the mucous membrane covering the dorsum of the tongue, the fauces, soft palate, and uvula, and possibly a portion of the upper part of the pharynx. This membrane is analogous in structure to other membranes of its type, except on the dorsum of the tongue, where its structure is similar to that of the integument. At this position it consists of a *corium*, with a *papillary* and a superficial *epithelial layer*.

The structure of the *corium* is similar to that of the skin, but is thinner and less compact. It serves as a point of insertion of the muscular fibres of the tongue.

The *papillæ* are thickly distributed over the whole dorsal surface, but more particularly marked in the anterior two-thirds. They project as minute prominences, which give the tongue a roughened, characteristic appearance. The papillæ are of two kinds, the *simple* and *compound*. The *simple* papillæ are similar to those found in the skin; they are found scattered over the whole dorsal surface, between the compound papillæ. They are most

numerous in the posterior portion of the organ. The *compound* papillæ are of three varieties; the papillæ maximæ or circumvallatæ, the papillæ mediæ or fungiformes, and the papillæ minimæ or filiformes.

The *papillæ circumvallatæ* (Fig. 215), which are the largest, are about eight or ten in number and form a V-shaped row at

FIG. 215.
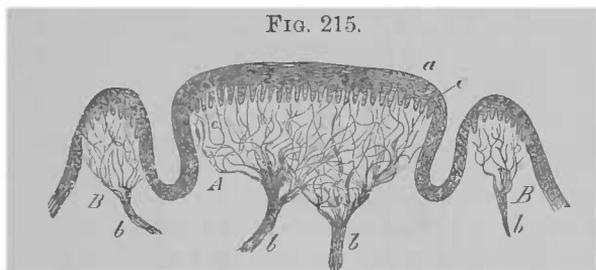
VERTICAL SECTION OF THE CIRCUMVALLATE PAPILLÆ. From KOLLIKER.

A, the papillæ ; *B*, the surrounding wall ; *a*, the epithelial covering ; *b*, the nerves of the papilla and wall spreading towards the surface ; *c*, the secondary papillæ. $\frac{10}{1}$.

the junction of the middle and posterior two-thirds of the tongue. They consist of a central broad papilla, surrounded by an annular ring or wall of about the same elevation, and separated from the centre papilla by a circular fissure. The central papilla, as well as the surrounding wall, is covered by simple papillæ. Each of them receives one or more capillary loops and nerve-filaments.

FIG. 216.
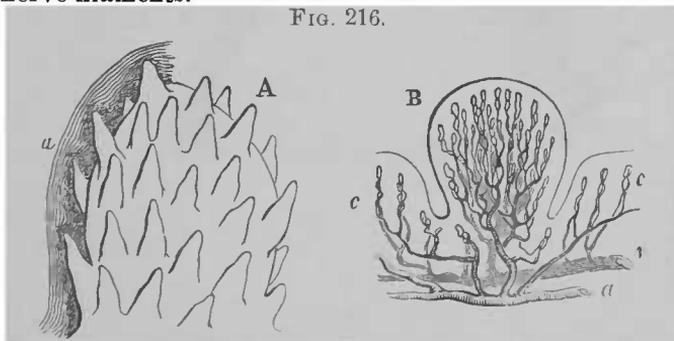
SURFACE AND SECTION OF THE FUNGIFORM PAPILLÆ. From KOLLIKER, and after TODD and BOWMAN.

A, the surface of a fungiform papilla, partially denuded of its epithelium, $\frac{3.5}{1}$; *a*, epithelium ; *B*, section of a fungiform papilla with the bloodvessels injected ; *a*, artery ; *v*, vein ; *c*, capillary loops of simple papillæ in the neighboring structure of the tongue.

The *papillæ fungiformes* (Fig. 216) are found principally on the tip and sides of the tongue, although scattered sparsely over

the whole of the anterior two-thirds. These are so named from their fungiform shape, being expanded at their free extremity and projecting on a short thick pedicle. They are covered by simple papillæ, and contain plexuses of vessels and nerves.

FIG. 217.
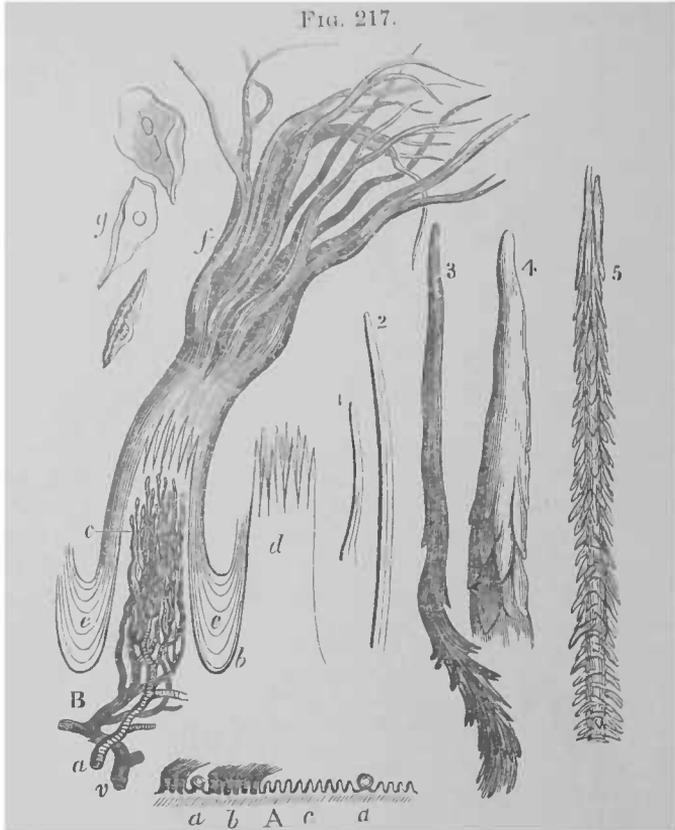
A, Vertical section near the middle of the dorsal surface of the tongue ; a, a, fungiform papillæ ; b, filiform papillæ, with their hairlike processes ; c, similar ones deprived of their epithelium ; magnified 2 diameters.

B, Filiform compound papillæ ; a, artery ; v, vein ; c, capillary loops of the secondary papillæ ; b, line of basement-membrane ; d, secondary papillæ, deprived of e, e, the epithelium ; f, hairlike processes of epithelium capping the simple papillæ, magnified 25 diameters ; g, separated nucleated particles of epithelium, magnified 300 diameters.

1, 2, hairs found on the surface of the tongue ; 3, 4, 5, ends of hairlike epithelial processes, showing varieties in the imbricated arrangement of the particles, but in all a coalescence of the particles towards the point 5, encloses a soft hair, magnified 160 diameters. After TODD and BOWMAN.

The *papillæ filiformes* (Fig. 217) are by far the most numerous, and are found thickly distributed over the entire surface of the

anterior two-thirds of the tongue. They are minute, conical in shape, and generally arranged in bipenniform rows, which are more or less parallel with the two rows of papillæ circumvallatæ. Their free surface is covered with simple papillæ. The epithelium covering them is greatly modified, and appears in the form of hairlike processes. (Fig. 217.) These processes are bathed in mucus, are movable, and have a general inclination pointing backwards. The existence of these hairlike processes on the filiform papillæ suggests that this variety of papillæ is intimately connected with the tactile sensibility of the tongue, and not with gustation. In carnivora and herbivora these processes are of a horny structure, and perform an active function in the attrition and prehension of food. In man their special function appears through their intimate connection with the tactile sense, to guide the tongue in its variable and complicated movements.

The ultimate terminations of the gustatory nerves are yet enveloped in obscurity. According to Engelmann, the glosso-pharyngeal nerves terminate in flask-shaped organs, which are termed the *gustatory bulbs* or *taste buds*. (Fig. 218.) These
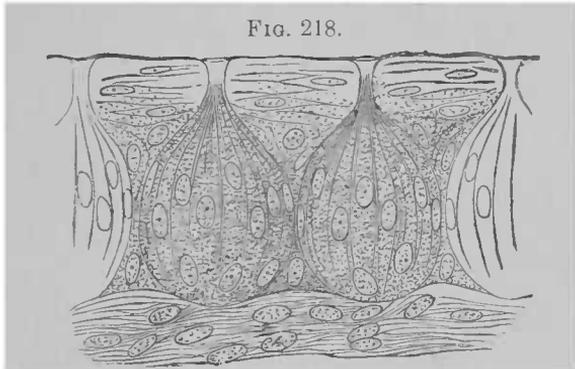
FIG. 218.

GUSTATORY BULBS FROM THE LATERAL GUSTATORY ORGAN OF THE RABBIT. Mag. 450 diam.

bulbs are found principally in the papillary surface of the wall of the circumvallate papillæ. They are also found in the fungiform papillæ, but are less numerous. They consist of a flask-shaped fundus, which rests upon the subepithelial tissue, and a mouth which opens upon the surface of the mucous membrane. The mouth is known as the *gustatory pore*. The fundus of the flask is composed of two varieties of cells; the outer or *investing cells* are fusiform, nucleated, and granular, placed parallel and arranged concentrically in a direction from the base to the neck, they thus form a wall which encloses elongated nucleated cells with filamentous processes, which extend through the gustatory pore and project as very finely pointed or truncated extremities.

These inner cells are called the *gustatory cells*, and are supposed to be the essential terminal elements concerned in gustation. Their relation to the gustatory nerves has not as yet been clearly demonstrated, but they are evidently connected with the ganglionic plexuses of nerve-fibres at the papillary bases. The gustatory nerves are also supposed to terminate in the epithelium of the papillæ.]

The word taste is frequently used when the word smell ought to be employed. We speak of " tasting " odoriferous substances, such as an onion, wines, etc., when in reality we only smell them as we hold them in our mouth; this is proved by the fact that the so-called taste of these things is lost when the nose is held, or the nasal membrane rendered inert by a catarrh.

The terminal organs of the sense of taste thus more strictly defined, are the endings of the glossopharyngeal and lingual nerves in the mucous membrane of the tongue and palate, those nerves serving as the special nerves of taste. Whether the so-called gustatory buds can be regarded as specific organs of taste, appears doubtful. The subsidiary apparatus is confined to the tongue and lips, which by their movements assist in bringing the sapid substances into contact with the mucous membrane of the mouth.

Though we can hardly be said to project our sensation of taste into the external world, we assign to it no subjective localization. When we place quinine in our mouth, the resulting sensation of taste gives us no information as to where the quinine is, though we may learn that by concomitant general sensations arising in the buccal mucous membrane.

We recognize a multitude of distinct tastes, which may be broadly classified into acid, saline, bitter, and sweet tastes. Sapid substances have the power of producing these sensations by virtue of their chemical nature. But other stimuli will also give rise to sensations of taste. When the tongue is tapped, a taste is felt, and when a constant current is passed through the mouth, an alkaline or, in some persons, a bitter metallic taste is developed when the anode, and an acid taste when the kathode, is placed on the tongue. It is probable that in these cases the terminal organs are indirectly affected by the current. When hot or pungent substances are introduced into the mouth, sensations of general feeling are excited, which obscure any strictly gustatory sensations which may be present at the same time.

Though analogy would lead us to suppose that a stimulus applied to any part of the course of the real gustatory fibres of either the glossopharyngeal or lingual nerves, would give rise to a sensation of taste and nothing else, the proof is not forthcom-

ing; since both these nerves are mixed nerves containing other afferent fibres as well as those of taste.

When the constant current is used as a means of exciting taste, gustatory sensations are found to be developed in the back, edges, and tip of the tongue, the soft palate, the anterior pillar of the fauces, and a small tract of the posterior part of the hard palate. They are absent from the anterior and middle dorsal, and under surface of the tongue, the front portion of the hard palate, the posterior pillars of the fauces, the gums, and the lips. Sapid substances are unsuitable as a test for this purpose, on account of their rapid diffusion. Bitter substances produce most effect when placed on the back of, and sweet substances when placed on the tip of the tongue; but the tasting power of the tip of the tongue varies very much in different individuals and in many seems almost entirely absent. It is said that acids are best appreciated by the edge of the tongue.

It is essential for the development of taste, that the substance to be tasted should be dissolved; and the effect is increased by friction. The larger the surface the more intense the sensation. The sensation takes some time to develop, and endures for a long time, though this may be in part due to the stimulus remaining in contact with the terminal organs. A temperature of about 40° is the one most favorable for the production of the sensation. At temperatures much above or below this, taste is much impaired. The nerves of taste are, as we have said, the glossopharyngeal and the lingual or gustatory. The former supplies the back of the tongue, and section of it destroys taste in that region. The latter is distributed to the front of the tongue, and section of it similarly deprives the tip of the tongue of taste. There is no reason for doubting that the gustatory fibres in the glossopharyngeal are proper fibres of that nerve; but it has been urged by many, that the gustatory fibres of the lingual are derived from the chorda tympani, and that those fibres of the lingual which come from the fifth are employed exclusively in the sensations of touch and feeling; the evidence in favor of this view is, however, inconclusive.

CHAPTER IV

FEELING AND TOUCH.

WE have taken the foregoing senses first in the order of discussion on account of their being eminently specific. The eye gives us only visual sensations, the ear only auditory sensations. The sensations are produced in each case by specific stimuli—the eye is only affected by light and the ear only by sound. Moreover, the information they afford us is confined to the external world; they tell us nothing about ourselves. The various visual sensations which arise in our retina are referred by us not to the retina itself, but to some real or imaginary object in the world without (including as part of the external world such portions of our own bodies as are visible to ourselves). Such also with diminishing precision is the information gained by hearing, taste, and smell.

All the other afferent nerves of the body, centripetal impulses along which are able to affect our consciousness, are the means of conveying to us information concerning ourselves. The sensations, arising in them from the action of various stimuli, are referred by us to appropriate parts of our own body. When any body comes in contact with our finger, we know that it is our finger which has been touched; from the resultant sensation we not only learn the existence of certain qualities in the object touched, but we also are led to connect the cognizance of these qualities with a particular part of our own body.

Like the more specific senses previously studied, the sensations of which we are now speaking, and which may be referred to under the name of touch, using that word, for the present, in a wide meaning, require for their production terminal organs; and the chief but not exclusive organ of touch is to be found in the epidermis of the skin and certain underlying nervous structures. For the development of specific tactile sensations these terminal organs are as essential as are the terminal organs of the eye for sight or of the ear for hearing. Contact of the skin with a hard or with a hot body gives rise to a distinct sensation, whereby we recognize that we have touched a hard or a hot body. But the application of either body or of any other stimulus to a nerve-

trunk give rise to a sensation of *general feeling* only, corresponding to the simple sensation of light which is produced by direct stimulation of the optic nerve. We have no more *tactile perception* of a body which is in contact with a nerve-trunk than we could have *visual perception* of any luminous object, the rays proceeding from which were strong enough to excite sensory impulses when directed on to the optic nerve instead of on to the retina, supposing such a thing to be possible. It is further characteristic of these ordinary nerves of general feeling, that the sensations caused by any stimulation of them beyond a certain degree develop that state of consciousness which we are in the habit of speaking of as "pain." Putting aside the general feeling which many parts of the eye possess, a very strong luminous stimulation of the retina is required to produce a sensation of pain, if indeed it can be at all brought about; whereas a very moderate stimulation of the skin, and almost every stimulation of an ordinary nerve-trunk, is said by us to be painful.

Though the skin is the chief organ of touch, the mucous membrane lining the various passages of the body also serves as an instrument for the same sense, but only for a short distance from the respective orifices. We can recognize hard or hot bodies with our lips or mouth, but a hot liquid, when it has reached the œsophagus or stomach, simply gives rise to a sensation of pain: we cannot distinguish the sensation caused by it from the sensation caused by a draught of a too acid fluid.

From parts and tissues of the body other than the skin and the portions of mucous membrane just mentioned we have obscure sensations of general feeling, by which we are made vaguely aware of the general condition of our body, though our judgments in this matter are chiefly influenced by what we shall have to speak of directly as a muscular sense. In all parts of the body, however, on occasions all too frequent, this general feeling may become prominent as pain.

The stimuli which, when applied to the skin give rise to tactile perceptions are of two kinds only: (1) mechanical—that is, the contact of bodies exerting varying degrees of pressure; and (2) thermal—*i. e.*, the raising or lowering of the temperature of the skin by the approach or contact of hot or cold bodies. We can judge of the weight and of the temperature of a body, because we can, through touch, perceive how much it presses when allowed to rest on our skin or how hot it is. But we can through touch derive no other perceptions and form no other judgments. An electric shock sent through the skin will give rise to a sensation, but the sensation is an indefinite one, because the electric current acts not on the terminal organs of touch, but on the fine nerve-branches of the skin. We cannot distinguish the sensation

so caused from a mechanical prick of similar intensity, we cannot
perceive that the sensation is caused by an electric current.
Similarly certain chemical substances, such as a strong acid, will
give rise to a sensation, but we cannot perceive the acid, we can
form no judgment of its nature such as we could if we tasted it;
and if the acid does not permeate the skin so as to act directly
and chemically on the fine nerve-fibres, we cannot distinguish
the acid from any other liquid giving rise to the same simple
contact impressions. The terminal organs of the skin are such
as are only affected by pressure or by temperature. Conversely
pressure or a variation in temperature brought to bear on a nerve-
trunk, instead of on the terminal organs, produces no specific
tactile sensations of pressure or temperature, but merely general
sensations of feeling rapidly rising into pain.

SEC. 2.—TACTILE SENSATIONS.

Sensations of Pressure.

As with visual, so with tactile, and, indeed, with all other
sensations, the intensity of the sensation maintains that general
relation to the intensity of the stimulus which we spoke of at
p. 614 as being formulated under Weber's law. We can distin-
guish the difference of pressure between one and two grammes
as readily as we can that between ten and twenty or one hundred
and two hundred.

When two sensations follow each other in the same spot at a
sufficiently short interval, they are fused into one; thus, if the
finger be brought to bear lightly on a rotating card having a
series of holes in it, the holes cease to be felt as such when they
follow each other at a rapidity of about 1500 in a second. The
vibrations of a cord cease to be appreciable by touch when they
reach the same rapidity. When sensations are generated at
points of the skin too close together, they become fused into one;
but to this point we shall return presently.

The sensation caused by pressure is at its maximum soon
after its beginning, and thenceforward diminishes. The more
suddenly the pressure is increased, the greater the sensation;
and, if the increase being sufficiently gradual, even very great
pressure may be applied without giving rise to any sensation.
A sensation in any spot is increased by contrast when the sur-
rounding areas are not subject to pressure. Thus, if the finger
be dipped into mercury, the pressure will be felt most at the
surface of the fluid; and, if the finger be drawn up and down,

the sensation caused will be that of a ring moving along the finger.

All parts of the skin are not equally sensitive to pressure; small differences of simple pressure are more readily appreciated when brought to bear on the palmar surface of the finger, or on the forehead, than on the arm or on the sole of the foot. In making these determinations, all muscular movements should be avoided in order to eliminate the muscular sense of which we shall speak presently; and the area stimulated should be as small and the surfaces in contact as uniform as possible. In a similar manner small consecutive variations of pressure, as in counting a pulse, are more readily appreciated by certain parts of the skin than by others; and the minimum of pressure which can be felt differs in different parts. In all such cases variations of pressure are more easily distinguished when they are successive than when they are simultaneous.

Sensations of Temperature.

When the temperature of the skin is raised or lowered in any spot, we receive sensations of heat and cold respectively; and by these sensations of the temperature of our own skin we form judgments of the temperature of bodies in contact with it. Bodies of exactly the same temperature as the region of the skin to which they are applied produce no such thermal sensations, though we can, from the very absence of sensations, form a judgment as to their temperature; and good conductors of heat appear respectively hotter and colder than bad conductors raised to the same temperature.

We may consider the skin as having at any given time and in any given spot a normal temperature at which the sensation of temperature is at zero; for, under ordinary circumstances, we are not directly conscious of the temperature of our skin; it is only when the normal temperature at the spot is raised or lowered that we have a sensation of heat or cold respectively. This normal temperature may be at the same time different in different parts of the body; thus, at a time when neither the forehead nor the hand is giving rise to any sensation of temperature, we may, by putting the hand to the forehead, frequently feel the former hot or cold, because the normal temperatures of the two parts differ. The normal temperature in any spot may also vary from time to time. Thus, when the hand is placed in a warm medium for some time, the sensation of warmth ceases; a new normal temperature is established with the zero of sensation at a higher level, a depression or elevation of this new temperature giving rise, however, as before, to sensations of heat and cold

respectively. That it is the changed condition, and not the change itself, of which we are conscious, is shown by the fact that when a portion of skin is cooled, by brief contact with a cold metal for instance, we are still conscious of the spot being cold after the cooling agent has been removed—that is, at a time when the cooled spot is in reality being heated by the surrounding warmer tissues.

The change in temperature of the skin necessary to produce a sensation must have a certain rapidity; and the more gradual the change the less intense the sensation. The repeated dipping of the hand into hot water produces a greater sensation than when the hand is allowed to remain all the time in the water, though in the latter case the temperature of the skin is most affected. The effects of contrast are also seen in these sensations as in those of pressure.

We can with some accuracy distinguish variations of temperature, especially those lying near the normal temperature of the skin. These sensations, in fact, follow Weber's law, though apparently sensations of slight cold are more vivid than those of slight heat, the range of most accurate sensation seeming to lie between 27° and 33°

The regions of the skin most sensitive to variations in temperature are not identical with those most sensitive to variations in pressure. Thus the cheeks, eyelids, temples, and lips, are more sensitive than the hands. The least sensitive parts are the legs, and front and back of the trunk.

The simplest view which can be taken with regard to the distinction between pressure sensations and temperature sensations, and which is suggested by the facts just mentioned, is to suppose that two distinct kinds of terminal organs exist in the skin, one of which is affected only by pressure, and the other only by variations in temperature; and that the two kinds of peripheral organs are connected with different parts of the central sensory organs by separate nerve-fibres. Certain pathological cases have been quoted as showing not only that this is the case, but that the two sets of fibres pursue different courses in the spinal cord. Thus, in certain diseases or injuries to the brain or spinal cord, hyperæsthesia as regards temperature has been observed unaccompanied by an augmentation of sensitiveness to pressure; and, conversely, instances have been seen where the patient could tell when he was touched, but could not distinguish between hot and cold. On the other hand, there are facts which show a close dependence between the sensations of pressure and temperature. When each stimulus is brought to bear on a very limited area, the two sensations are frequently confounded, especially in those regions of the body where sensations are not acute. So, also, a

penny cooled down nearly to zero and placed on the forehead, will be judged by most people to be as heavy or even heavier than two pennies of the temperature of the forehead itself; and, conversely, a body warmer than the skin will often appear heavier than a body of the same weight but of the same temperature as the skin. Moreover, cases have been recorded where a hot body, such as a heated spoon, was felt, though the application of the same spoon at the temperature of the body produced no sensations, and yet the heated spoon was not recognized as a hot body, but appeared to be simply something touching the skin. It may be argued that these instances show nothing more than that the changes in the skin, whatever they be, which give rise to sensations of pressure, are modified by the temperature of the skin for the time being, whereby the judgment as to the pressure which is being exerted is rendered faulty; but they may also be taken to indicate that variations in pressure and temperature affect the same terminal organs, and the same nerve-fibres, though affecting them in a different way and generating nervous impulses so far different that they give rise to different sensations. And we may here note that we certainly cannot speak of nerves of warmth in the same sense in which we speak of nerves of sight or of hearing. A stimulus (of whatever kind) applied to an optic or auditory nerve, if adequate, gives rise, as we have seen, to a sensation of light or of sound; a stimulus, on the other hand, applied to the trunk of a cutaneous nerve gives rise only to general feeling or pain; though the nerve certainly contains fibres by which sensations of pressure and of temperature reach the brain, the general feeling which stimulation of the trunk causes is akin neither to sensations of pressure nor to those of warmth.

The rapidity with which hot or cold bodies brought into contact with the skin give rise to sensations of temperature, suggests that the terminal apparatus for generating these sensations, whatever be its nature, is placed in the epidermis, and indeed, as near as possible, to the surface. Pressure, on the other hand, can be readily transmitted through even a thick layer of skin. And those who maintain the existence of different terminal organs for pressure and temperature, regard the nerve-endings in the epidermis as the latter and the corpuscula tactus, end-bulbs and allied organs as the former. But the evidence we possess concerning this matter is at present inconclusive.

SEC. 3.—TACTILE PERCEPTIONS AND JUDGMENTS.

When a body presses on any spot of our skin, or when the temperature of the skin at that spot is raised, we are not only conscious of pressure or of heat, but perceive that a particular part of our body has been touched or heated. We refer the sensations to their place of origin, and we thus by touch perceive the relations to ourselves of the body which gives rise to the tactile sensations, in the same way as in our visual perception of external objects we refer to external nature the sensations originating in certain parts of the retina. When we are touched on the finger and on the back we refer the sensations to the finger and to the back respectively, and when we are touched at two places on the same finger at the same time we refer the sensations to two points of the finger. In this way we can localize our sensations, and are thus assisted in perceiving the space relations of objects with which we come in contact.

This power of localizing pressure-sensations varies in different parts of the body. The following table from Weber gives the distance at which two points of a pair of compasses must be held apart, so that when the two points are in contact with the skin, the two consequent sensations can be localized with sufficient accuracy to be referred to two points of the body, and not confounded together as one :

	Millimetres.
Tip of tongue	1.1
Palm of last phalanx of finger	2.2
Palm of second phalanx of finger	4.4
Tip of nose .	6.6
White part of lips	8.8
Back of second phalanx of finger	11.1
Skin over malar bone	15.4
Back of hand	29.8
Forearm	39.6
Sternum	44.0
Back	66.0

And an analogous distribution has been observed in reference to the localization of sensations of temperature. As a general rule, it may be said that the more mobile parts are those by which we can thus discriminate sensations most readily. The lighter the pressure used to give rise to the sensations, the more easily are two sensations distinguished ; thus two points, which, when touching the skin lightly, appear as two, may, when firmly pressed, give rise to one sensation only. The distinction between the sensations is obscured by neighboring sensations arising at the same time. Thus two points brought to bear within a ring of

heavy metal pressing on the skin, are readily confused into one. And it need hardly be said that these tactile perceptions, like all other perceptions, are immensely increased by exercise.

Our "field of touch," if we may be allowed the expression, is composed of tactile areas or units, in the same way that our field of vision is composed of visual areas or units. The tactile sensation is, like the visual sensation, a symbol to us of some external event, and we refer the sensation to its appropriate place in the field of touch. All that has been said (p. 616) concerning the subjective nature of the limits of visual areas, applies equally well, *mutatis mutandis*, to tactile areas. When two points of the compasses are felt as two distinct sensations, it is not necessary that two and only two nerve-fibres should be stimulated; all that is necessary is that the two cerebral sensation-areas should not be too completely fused together. The improvement by exercise of the sense of touch must be explained not by an increased development of the terminal organs, not by a growth of new nerve-fibres in the skin, but by a more exact limitation of the sensational areas in the brain, by the development of a resistance which limits the radiation taking place from the centres of the several areas.

By a multitude of simultaneous and consecutive tactile sensations thus converted into perceptions we are able to make ourselves acquainted with the form of external objects. We can tell by variations of pressure whether a surface is rough or smooth, plane or curved, what variations of surface a body presents, and how far it is heavy or light; and from the information thus gained we build up judgments as to the form and nature of objects, judgments however which are most intimately bound up with visual judgments, the knowledge derived by one sense correcting and completing that obtained by the other. As in other senses so in this, our sensations may mislead us and cause us to form erroneous judgments. This is well illustrated by the so-called experiment of Aristotle. It is impossible in an ordinary position of the fingers to bring the radial side of the middle finger and the ulnar side of the ring finger to bear at the same time on a small object such as a marble. Hence when with the eyes shut we cross one finger over the other, and place a marble between them so that it touches the radial side of the one and the ulnar side of the other, we recognize that the object is such as could not, under ordinary conditions, be touched at the same time by these two portions of our skin, and, therefore, judge that we are touching not one, but two, marbles. Upon repetition, however, we are able to correct our judgment, and the illusion disappears.

Distinct tactile sensations are, as we have seen, produced only when a stimulus is applied to a terminal organ. When sensa-

tions or affections of general sensibility other than the distinct tactile sensations are developed in the termination of a nerve, we are still able, though with less exactitude, to refer the sensation to a particular part of the body. Thus, when we are pricked or burnt, we can feel where the prick or burn is. When a sensory nerve-trunk is stimulated, the sensation is always referred to the peripheral terminations of the nerve. Thus, a blow on the ulnar nerve at the elbow is felt as a tingling in the little and ring fingers corresponding to the distribution of the nerve, and sensations started in the stump of an amputated limb are referred to the absent member. When cold is applied to the elbow, it is felt as cold in the skin of the elbow; but a cooling of the ulnar nerve at this spot, since stimulation of a nerve-trunk gives rise to general sensations only, simply gives rise to pain which is referred to the ulnar side of the hand and arm.

Sec. 4.—The Muscular Sense.

When we come into contact with external bodies, we are conscious not only of the pressure exerted by the object on our skin, but also of the pressure which we exert on the object. If we place the hand and arm flat on a table, we can estimate the pressure exerted by bodies resting on the palm of the hand, and so come to a conclusion as to their weights; in this case we are conscious only of the pressure exerted by the body on our skin. If, however, we hold the body in the hand, we not only feel the pressure of the body, but we are also aware of the muscular exertion required to support and lift it. We possess a muscular sense; and we find by experience that when we trust to this muscular sense as well as to sensations of pressure, we can form much more accurate judgments concerning the weight of bodies than when we rely on sensations of pressure alone. When we want to tell how heavy a body is, we are not in the habit of allowing it simply to press on the hand laid flat on a table; we hold it in our hand and lift it up and down. We appeal to our muscular sense to inform us of the amount of exertion necessary to move it, and by help of that, judge of its weight. And in all the movements of our body we are guided, even to an astonishing degree of accuracy, as is well seen in the discussions concerning vision, by an appreciation, more or less distinctly conscious, of the amount of the contraction to which we are putting our muscles. In some way or other, we are made aware of what particular muscles or groups of muscles are being thrown into action, and to what extent that action is being carried. We are also conscious of the varying condition of our muscles, even when

they are at rest; the tired and especially the paralyzed limb is said to "feel" heavy. In this way the state of our muscles largely determines our general feeling of health and vigor, of weariness, ill-health, and feebleness.

It has been suggested that since muscle possesses little or no general sensibility, comparatively little pain being felt for instance when muscles are cut, our muscular sense is chiefly derived from the traction of the contracting muscle on its attachments; and undoubtedly in many instances of cramp, the pain is chiefly felt at the joints; and, as we know, Pacinian bodies are abundant around the joints. Afferent nerves, however, having a different disposition from the ordinary motor nerves which terminate in end-plates, have been described as present in muscle; and analogy would lead us to suppose that these afferent fibres, though possessing a low general sensibility, might be easily excited in a specific manner by a muscular contraction; but further investigations are necessary before these can be accepted as the true nerves of the muscular sense.

In favor of the view that the muscular sense is peripheral and not central in origin, may be urged the fact that the sense is felt when the muscles are thrown into contraction by direct galvanic stimulation instead of by the agency of the will. Many authors, even while admitting the existence of a muscular sense of peripheral orgin, contend that we also possess and are very largely guided in our movements by what might be called a "neutral" sense of central origin. That is to say, the changes in the central nervous system involved in initiating and carrying out a movement of the body, so affect our consciousness, that we have a sense of the effort itself.

It has been observed that when the posterior roots are divided, movements become less orderly, as if they lacked the guidance of a muscular sense; and although the impairment of the movements may be due in part to the coincident loss of tactile sensations, it is probable that it is increased by the loss of the muscular sense. There is a malady or rather a condition attending various diseased states of the central nervous system called locomotor ataxy, the characteristic feature of which is that, though there is no loss of direct power over the muscles, the various bodily movements are effected imperfectly and with difficulty, from want of proper coördination. In such diseases the pathological mischief is frequently found in the posterior columns of the spinal cord and the posterior roots of the spinal nerves—that is, in distinctly afferent structures; and the phenomena seem in certain cases at least to be due to inefficient coördination caused by the loss both of the muscular sense and of ordinary tactile sensations.

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The patients walk with difficulty, because they have imperfect sensations both of the condition of their muscles and of the contact of their feet with the ground. In many of their movements they have to depend largely on visual sensations ; hence, when their eyes are shut, they become singularly helpless. In other cases again ataxy may be present without any impairment of touch ; but a discussion of the varied phenomena of this class of maladies cannot be entered into here.

CHAPTER V

THE SPINAL CORD.

[The Physiological Anatomy of the Spinal Cord.

THE spinal cord extends from the foramen magnum to the second lumbar vertebra. Above, it is continuous with the medulla oblongata; below, it terminates in an extremity of gray matter, tbe *filum terminale,* which lies in the midst of a number of nervous cords that form the *cauda equina.*

The spinal cord is a long, somewhat flattened, cylindriform body. It consists of a central portion of gray matter, which is covered by longitudinal strands of wbite fibrous matter. It is a bilateral, symmetrical organ, the halves of whicb are separated anteriorly and posteriorly by the *anterior* and *posterior median* fissures, and joined in the middle longitudinal line by a band of nervous matter which is termed the *commissure* (Fig. 219). The anterior median fissure is wider and shallower than the posterior median fissure. Each half of the cord is marked by two longitudinal furrows, from which emerge the anterior and posterior roots of the spinal nerves. These furrows are termed the antero-lateral and postero-lateral grooves. They divide each half into three portions: the *anterior, lateral,* and *posterior* columns. The anterior column is situated between the anterior median fissure and the antero-lateral groove; the middle column, between the antero- and postero-lateral grooves; the posterior column, between the postero-lateral groove and the posterior median fissure. The anterior and lateral columns are sometimes spoken of as the antero-lateral column. The fibres of the columns are continuations of the fibres of the spinal nerves, or of fibres which arise in the ganglionic cells of the cord, and have for the most part a longitudinal direction; otber fibres have a transverse or oblique direction in their course to other columns or to nerve cells.

The gray substance of the cord (Fig. 219) is in the form of two crescentic portions, which are connected together by the gray commissure, and presents an appearance similar to that of the letter H. Each crescentic portion consists of two extremities, which are termed the cornua. The anterior cornu is thicker, larger, and contains a much greater proportion of nerve-cells. It consists principally of very fine nerve-fibres, and three distinct

columns of larger multipolar cells. These columns are best seen in the cervical and lumbar regions, and are frequently spoken of as the motor cells; and some of them as trophic cells.

The posterior cornu is smaller and narrower than the anterior; the cells, also, are of much smaller size. Near the posterior extremity of the cornu is an expanded gelatinous portion, which is termed the *substantia gelatinosa* of Rolando (Fig. 219). At the

FIG. 219.
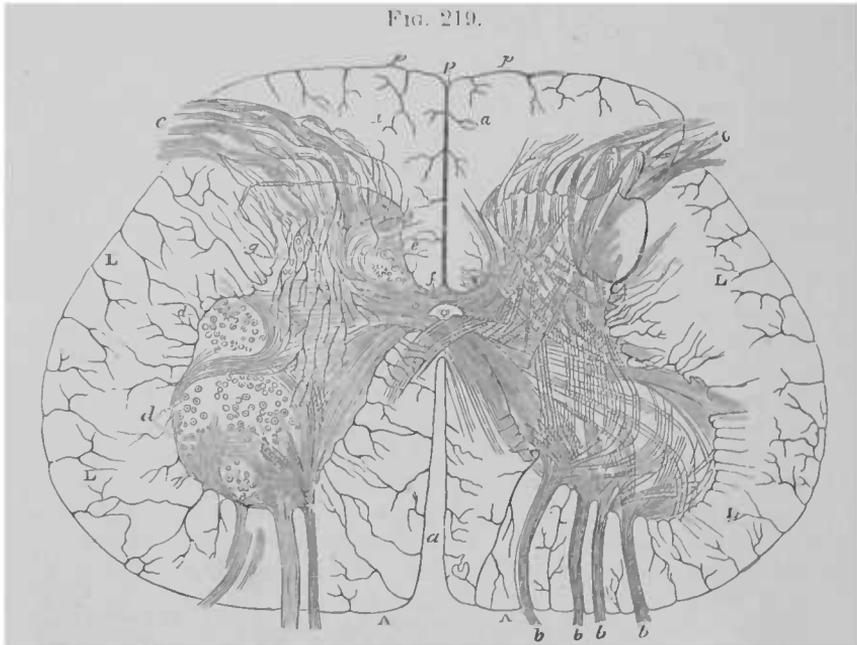
Transverse Section of Spinal Cord, through the middle of the Lumbar Enlargement, showing on the right side the course of the Nerve-roots, and on the left the position of the principal tracts of Vesicular Matter. A, A, anterior columns; c, c, posterior columns; L, L, lateral columns; a, anterior median fissure; p, posterior median fissure; b, b, b, b, anterior roots of spinal nerves; c, c, posterior roots; d, d, tracts of vesicular matter in anterior column; e, tracts of vesicular matter in posterior column; f, central canal, surrounded by the gray commissure; g, substantia gelatinosa of Rolando.

anterior internal portion, near the central canal, is a column of small nerve-cells, which is called the posterior vesicular or Clarke's column. This column is most distinct in the dorsal region. The cells of the posterior cornua are sometimes spoken of as the sensory cells.

The *commissure* (Fig. 220) consists of a band of gray and white fibrous matter, which serves to connect the two sides of the cord. The anterior portion or *white commissure* is composed of a band of decussating white fibres, which for the most part extends be-

tween the anterior cornua and columns of the two sides.   The *gray* commissure consists of an anterior and posterior transverse band of fibres, between which is a very fine nerve-fibre plexus, which are for the most part derived from the cell processes.   In

FIG. 220.
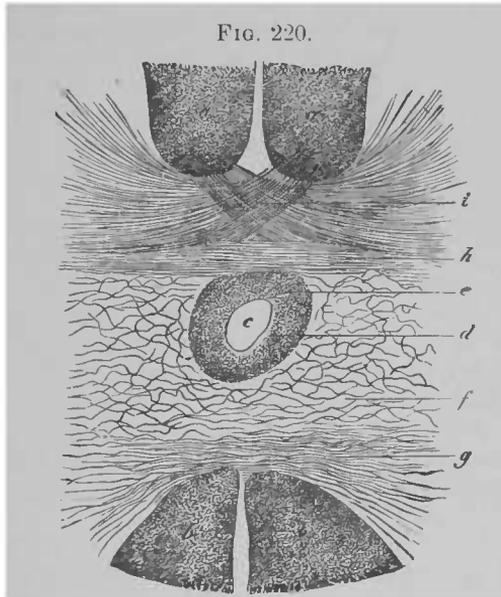
Median portion of a Transverse Section of the Spinal Cord of a Child six months old, from the lower part of the Cervical Region, treated with the double Chloride of Potassium and Gold.   Magnified 50 diameters.   *a, a,* anterior columns; *b, b,* posterior columns; *c,* central canal; *d,* line indicating the epithelium of the central canal; *e,* connective tissue surrounding the central canal; *f,* nerve-fibre plexus around the central canal; *g,* posterior transverse fibres of the gray commissure; *h,* anterior transverse fibres of the gray commissure; *i,* decussation of fibres in the anterior white commissure.

the centre of the commissure is the *central canal.*   The wall of the canal is formed by a connective tissue, and is lined by columnar epithelium.   It extends from the fourth ventricle of the brain to the filum terminale.

The cord is thicker in the cervical and the lumbar and lower dorsal regions, at points corresponding to the origin of the brachial, and the lumbar and sacral plexuses.   This enlargement is due, for the most part, to the increased proportion of gray matter.   The quantity of white matter progressively increases from below upwards.

The arrangement of the fibres of the spinal nerves after they have entered the substance of the cord is of great physiological interest.   Upon examining sections of the cord, these fibres appear to have a general horizontal, oblique, or longitudinal direc-

tion. The fibres of the *posterior* roots have at first either an oblique or horizontal direction. They then assume different courses: some of them are lost sight of in the gray matter of the posterior cornua; others pass obliquely downwards or upwards, through the posterior gray substance, and are finally traced to the anterior cornua or columns, where they assume a longitudinal direction, either running up or down; others, upon entering the posterior gray matter, have a longitudinal direction, running into the segments above or below the point; others, seen upon transverse sections (Fig. 219) run towards the anterior cornu, or across the commissure to the lateral or posterior columns of the opposite side. The fibres of the *anterior* roots (Fig. 219) run posteriorly, nearly horizontally, until they reach the anterior cornu. Some of the fibres then appear to be continuous with the processes of the multipolar cells; others run to the lateral or to the anterior columns; others run to the posterior gray matter; and others through the anterior white commissure, and are traced to the cells of the anterior cornu, or to the anterior or lateral columns.

The nervous elements of the spinal cord are bound together by a modified connective tissue, called the *neuroglia*, which serves also as a nidus for the ramification of the bloodvessels.]

Sec. 1.—As a Centre or Group of Centres of Reflex Action.

Of the several functions of the spinal cord perhaps the most striking and important is that of carrying out reflex actions. As we have already said, the spinal cord is par excellence the organ of reflex action; in by far the greater number of the reflex movements of the body, the centre is supplied by some part of the spinal cord. We have already (Book I. Chap. III.) touched on the general features of reflex actions, and elsewhere have incidentally dwelt on particular instances; we may therefore confine ourselves now to certain points of special interest.

Reflex movements are perhaps best studied in the frog and other cold-blooded animals, where the phenomena are less obscured by the working of the other so-called higher parts of the central nervous system. They obtain, however, in the warm-blooded mammal also, but in these special precautions are necessary to secure their full development.

In the frog the shock which follows upon division of the spinal cord, and which, as we shall presently see, for a while inhibits reflex activity, soon passes away; within a very short time after the medulla oblongata for instance has been divided the most

complicated reflex movements can be carried on by the frog's spinal cord when the appropriate stimuli are applied. With the mammal the case is very different. For days even after division of the spinal cord the parts of the body supplied by nerves springing from the cord below the section exhibit very feeble reactions only. In the dog for instance, after division of the spinal cord in the lower dorsal region, the hind-limbs hang flaccid and motionless, and pinching the hind-foot evokes as a response either slight irregular movements or none at all. Indeed were our observations limited to this period, we might infer that the reflex actions of the spinal cord in the mammal were but feeble and insignificant. If, however, the animal be kept alive for a longer period, for weeks or better still for months, though no union or regeneration of the spinal cord takes place, reflex movements of a powerful, varied, and complex character manifest themselves in the hind-limbs and hinder parts of the body; a very feeble stimulus applied to the skin of these regions promptly gives rise to extensive and yet coördinate movements. Compared with the reflex actions of the frog, the movements carried out by the lower portion of the spinal cord of the mammal while they are more energetic have hitherto been regarded as being less definite and complete and less purposeful; but it would be dangerous to insist on this, for recent experience tends to show that in the case of most mammals, the powers of the spinal cord have been unduly underrated. It is worthy of attention that the reflex phenomena in mammals vary very much not only in different species but also in different individuals and in the same individual under different circumstances. Race, age, and previous training, seem to have a marked effect in determining the extent and character of the reflex actions which the spinal cord is capable of carrying out, and these seem also to be largely influenced by passing circumstances, such as whether food has been recently taken or no. And it is asserted that the spinal cord of the rabbit, which has been the subject of so many experiments, is as compared with that of the dog and many other mammals, singularly deficient in the power of carrying out complex reflex movements.

Both in the cold-blooded and warm-blooded animals the salient feature of ordinary reflex actions is their purposeful character, though every variety of movement may be witnessed, from a simple spasm to a most complex manœuvre, and in all reflex movements, both simple and complex, we can recognize certain determining causes, the influences of which more or less directly contribute to the shaping of this purposeful character.

Thus the features of any movement taking place as part of a reflex action are in part determined by the nature of the afferent

impulses. Simple nervous impulses generated by the direct stimulation of afferent nerve-fibres generally evoke as reflex movements merely irregular spasms in a few muscles; whereas the more complicated differentiated sensory impulses generated by the application of the stimulus to the skin, readily give rise to large and purposeful movements. It is easier to produce a complex reflex action by a slight pressure on the skin than by even a strong single induction-shock applied directly to a nerve-trunk. If, in a brainless frog, the area of skin supplied by one of the dorsal cutaneous nerves be separated by section from the rest of the skin of the back, the nerve being left attached to the piece of skin and carefully protected from injury, it will be found that slight stimuli applied to the surface of the piece of skin easily evoke reflex actions, whereas the trunk of the nerve may be stimulated with even strong currents without producing anything more than irregular movements. In ordinary mechanical and chemical stimulation of the skin it is a series of impulses and not a single impulse which passes upwards along the sensory nerve, the changes in which may be compared to the changes in a motor nerve during tetanus. In every reflex action, in fact, the central mechanism may be looked upon as being thrown into activity through a summation of the afferent impulses reaching it. Hence, while a reflex action is readily called forth by even feeble single induction-shocks applied to the skin, if they be repeated sufficiently rapidly, a solitary induction-shock is ineffectual unless it be strong enough to cause profound changes in the skin or nerves.

When a muscle is thrown into contraction in a reflex action, the note which it gives forth does not vary with the stimulus, but is constant, being the same as that given forth by a muscle thrown into contraction by the will. From which we infer that in a reflex action the afferent impulses do not simply pass through the centre in the same way that they pass along afferent nerves, but are profoundly modified. And this explains why a reflex action takes always a considerable time, and frequently a very long time, for its development. When the toes of a brainless frog are dipped in dilute sulphuric acid, several seconds may elapse before the feet are withdrawn. Making every allowance for the time needed for the acid to develop sensory impulses in the peripheral endings of the afferent nerve, a very large fraction of the period must be taken up by the molecular actions going on in the nerve-cells. In other words, the interval between the advent at the central organ of afferent, and the exit from it of efferent impulses, is a busy time for the nerve-cells of that organ; during it many processes, of which we have at present very little exact knowledge, are being carried on.

The character of the movement forming part of a reflex action is also influenced by the intensity of the stimulus. A slight stimulus, such as gentle contact of the skin with some body, will produce one kind of movement; and a strong stimulus, such as a sharp prick applied to the same spot of skin, will call forth quite a different movement. When a decapitated snake or newt is suspended, and the skin of the tail lightly touched with the finger the tail bends towards the finger; when the skin is pricked or burnt, the tail is turned away from the offending object. And so in many other instances. Further, we have already pointed out (p. 143) that while the effects of a weak stimulus applied to an afferent nerve are limited to a few, those of a strong stimulus may spread to many efferent nerves. Granting that any particular afferent nerve is more especially associated with certain efferent nerves than with any others, so that the reflex impulses generated by afferent impulses entering the cord by the former, pass with the least resistance down the latter, we must evidently admit further that other efferent nerves are also, though less directly, connected with the same afferent nerve, the passage into the second efferent nerve meeting with an increased but not insuperable resistance. When a frog is poisoned with strychnia, a slight touch on any part of the skin may cause convulsions of the whole body; that is to say, the afferent impulses passing along any single afferent nerve may give rise to the discharge of efferent impulses along any or all of the efferent nerves. This proves that a physiological, if not an anatomical, continuity obtains between all the nerve-cells of the spinal cord which are concerned in reflex action, that the nerve-cells with their processes form a functionally continuous protoplasmic network. This network, however, we must suppose to be marked out into tracts presenting greater or less resistance to the progress of the impulses into which afferent impulses, coming from this or that afferent nerve, are transformed on their advent at the network; and accordingly the path of any series of impulses in the network will be determined largely by the energy of the afferent impulses. And the action of strychnia may be, in part, explained by supposing that it reduces and equalizes the normal resistance of this network, so that even weak impulses travel over all its tracts with great ease.

Further, the movement forming part of a reflex action varies in character, according to the particular area of the skin or the locality of the body to which the stimulus is applied. Pinching the folds of skin surrounding the anus of the frog produces different effects from those witnessed when the flank or toe is pinched; and, speaking generally, the stimulation of a particular spot calls forth particular movements. In the case of the

simpler reflex movements, it appears to be a general rule that a movement started by the stimulation of a sensory surface or region on one side of the body, is developed on the same side of the body, and if it spreads to the other side, still remains most intense on the same side; the movement on the other side, moreover, is symmetrical with that on the same side. It has been maintained that "crossed" or diagonal reflex movements, as where stimulation of one fore-foot leads to movements of the opposite hind-limb, do not occur unless some portion of the medulla oblongata be left attached to the spinal cord. Seeing that locomotion in four-footed animals is largely effected by diagonal movements of the limbs, one would rather have expected to find the spinal cord itself provided with mechanisms to assist in carrying them out; and, indeed, it is affirmed that in the case of cold-blooded animals and of many young mammals, after division of the spinal cord below the medulla, a gentle stimulation will provoke a diagonal movement—slight pressure on one fore-foot, for example, giving rise to movements in the opposite hind-leg; a strong stimulus, however, will produce an ordinary one-sided movement.

From these and similar phenomena, we may infer that the protoplasmic network spoken of above is, so to speak, mapped out into nervous mechanisms by the establishment of lines of greater or less resistance, so that the disturbances in it generated by certain afferent impulses are directed into certain efferent channels. But the arrangement of these mechanisms is not a fixed and rigid one. We cannot always predict exactly the nature of the movement which will result from the stimulation of any particular spot, because the result will vary according to the condition of the spinal cord, especially in relation to the strength of the stimulus. Moreover, under a change of circumstances a movement quite different from the normal one may make its appearance. Thus, when a drop of acid is placed on the right flank of a frog, the right foot is almost invariably used to rub off the acid; in this there appears nothing more than a mere "mechanical" reflex action. If, however, the right leg be cut off, or the right foot be otherwise hindered from rubbing off the acid, the left foot is, under the exceptional circumstances, used for the purpose. This, at first sight, looks like an intelligent choice. A choice it evidently is; and were there many instances of choice, and were there any evidence of a variable automatism, like that of a conscious volition, being manifested by the spinal cord of the frog, we should be justified in supposing that the choice was determined by an intelligence. It is, however, on the other hand, quite possible to suppose that the lines of resistance in the spinal protoplasm are so arranged as to admit

of an alternative, though still mechanical, action; and seeing how few and simple are the apparent instances of choice witnessed in a brainless frog, and how absolutely devoid of spontaneity or irregular automatism is the spinal cord of the frog, this seems the more probable view.   Moreover, this conclusion is supported by the behavior of other animals.   Thus, similar vicarious reflex movements may be witnessed in mammals, though not, perhaps, to such a striking extent as in frogs.   In dogs, in which partial removal of the cerebral hemispheres has apparently heightened the reflex excitability of the spinal cord, the remarkable scratching movements of the hind-leg which are called forth by stimulating a particular spot on the loins or side of the body, are executed by the leg of the opposite side, if the leg of the same side be gently held.   In this case the vicarious movements are ineffectual, and can hardly be considered as betokening intelligence.   Again, the "mechanical" nature of reflex actions is well illustrated by the behavior of a decapitated snake.   When the body of the animal in this condition is brought into contact at several places with any object, such as an arm or a stick, complex reflex movements are excited, the obvious purpose as well as effect of which is to twine the body round the object.   A decapitated snake will, however, with equal and fatal readiness twine itself round a red-hot bar of iron.

It may be added, that the movements evoked by even a segment of the cord may be purposeful in character; hence, we must conclude that every segment of the protoplasmic network is mapped out into mechanisms.

Lastly, the characters of a reflex movement are, as we need hardly say, dependent on the condition of the cord.   The action of strychnia just alluded to is an instance of an apparent augmentation of reflex action best explained by supposing that the resistances in the cord are lessened.   There are probably, however, cases in which the explosive energy of the nerve-cells is positively increased above the normal.   Conversely, by various influences of a depressing character, as by various anæsthetics or other poisons, reflex action may be lessened or prevented; and this, again, may arise either from an increase of resistance, or from a diminished action of the nerve-cells themselves.

In actual life, reflex movements, in by far the greater number of instances, are occasioned by stimulation of the skin or of the mucous membrane.   They may, however, occur as the result of stimulation of the organs of special sense.   A sound or a flash of light readily produces a start, a bright light causes many persons to sneeze, and reflex movements may even result from a taste or smell.

Inhibition of Reflex Action.—The reflex actions of the spinal cord, like other nervous actions, may be totally or partially inhibited—that is, may be arrested or hindered in their development by impulses reaching the centre while it is already in action. Thus, if a decapitated snake be suspended, slow, rhythmic, pendulous movements, which appear to be reflex in nature, soon make their appearance, and these may be for a while arrested by slight stimulation, as by gently stroking the tail. We have already seen that the action of such nervous centres as the respiratory and vaso-motor centres, which frequently at all events is of a reflex nature, may be either inhibited or augmented by afferent impulses. The micturition centre in the mammal, which is also largely a reflex centre, may be easily inhibited by impulses passing downward to the lumbar cord from the brain, or upward along the sciatic nerves. In the case of dogs, whose spinal cord has been divided in the dorsal region, micturition set up as a reflex act by simple pressure on the abdomen, or by sponging the anus, is at once stopped by sharply pinching the skin of the leg. And it is a matter of common experience that micturition may be suddenly checked by an emotion or other cerebral event. The erection centre in the lumbar cord also, in large measure a reflex centre, is similarly susceptible of being inhibited by impulses reaching it from various sources. And, indeed, many similar instances of the inhibition of reflex movements might readily be quoted.

Several apparent instances of the inhibition of reflex acts are not really such: in these cases all the nervous precesses of the act may take place in their entirety and yet fail to produce their effect on account of a failure in the muscular part of the act. Thus when we ourselves stop or inhibit the reflex movements which otherwise would be produced by tickling the soles of the feet, we achieve this to a large extent by throwing voluntarily into action certain muscles, the contractions of which antagonize the action of the muscles engaged in carrying out the reflex movements. But it may be doubted even in these cases, whether inhibition is always or wholly to be explained in this way; and certainly in very many instances of reflex inhibition, no such muscular antagonism is present, and the reflex act is checked at its nervous centre.

It is a remarkable fact that when the brain of a frog is removed, reflex actions are developed to a much greater degree than in the entire animal. This suggests the idea that there must be in the brain some mechanism or other for preventing the normal development of the spinal reflex actions. And we learn by experiment that stimulation of certain parts of the brain has a remarkable effect on reflex action. If a frog, from which the

cerebral hemispheres only have been removed (the optic thalami, optic lobes, medulla oblongata, and spinal cord being left intact), be suspended by the chin, and the toes of the pendent legs be from time to time dipped into very dilute sulphuric acid, a certain average time will be found to elapse between the dipping of the toe and the resulting withdrawal of the foot. If, however, the optic lobes or optic thalami is stimulated, as by putting a crystal of sodium chloride on them, it will be found on repeating the experiment while these structures are still under the influence of the stimulation, that the time intervening between the action of the acid on the toe and the withdrawal of the foot is very much prolonged. That is to say, the stimulation of the optic lobes has caused impulses to descend to the cord, which have there so interfered with the action of the nerve cells engaged in reflex action as greatly to retard the generation of reflex impulses; in other words, the stimulation of the optic lobes has inhibited the reflex action of the cord. And similiar results may be obtained in mammals by stimulating certain parts of the corpora quadrigemina, which bodies are analogous to the optic lobes of frogs. From this it has been inferred that there is present in this part of the brain a special mechanism for inhibiting the reflex actions of the spinal cord, the impulses descending from this mechanism to the various centres of reflex action being of a specific inhibitory nature. But, as we have already seen, impulses of an ordinary kind, passing along ordinary sensory nerves, may inhibit reflex action. We have quoted instances where a slight stimulus, as in the pendulous movements of the snake, and where a stronger stimulus as in the case of the micturition of the dog, may produce an inhibitory result; we may add that adequately strong stimuli applied to any afferent nerve will in the frog inhibit—*i. e.*, will retard or even wholly prevent reflex action. If the toes of one leg are dipped into dilute sulphuric acid at a time when the sciatic of the other leg is being powerfully stimulated with an interrupted current, the period of incubation will be found to be much prolonged, and in some cases the reflex withdrawal of the foot will not take place at all. And this holds good, not only in the complete absence of the optic lobes and medulla oblongata, but also when only a portion of the spinal cord, sufficient to carry out the reflex action in the usual way, is left. There can be no question here of any specific inhibitory centres, such as have been supposed to exist in the optic lobes.

Hence it is clear that inhibition may be brought about by impulses which are not in themselves of a specific inhibitory nature, and accordingly we may hesitate to accept the view that a special inhibitory mechanism in the sense of one giving rise to

nothing but inhibitory impulses is present in the optic lobes of frogs. Nor is there adequate proof that the exaltation of reflex actions which is manifest in decapitated animals is due to the withdrawal of such a specific inhibitory mechanism. We shall have occasion again to return to these inhibitory phenomena of the central nervous system. We have seen enough to show that the spinal cord, and the same holds good, as we shall see, for the whole central nervous system, may be regarded as an intricate mechanism in which the direct efforts of stimulation or automatic activity are modified and governed by the checks of inhibitory influences. Seeing that in the ordinary actions of life the spinal cord is to a large extent a mere instrument of the cerebral hemispheres, we may readily expect that among the many impulses passing from the latter to the former, some under certain circumstances should result in an inhibition of spinal activity, while others, or the same under different circumstances, should lead to an exaltation of the same spinal activity. The experiments quoted above show that the optic lobes when stimulated are especially prone to give rise to inhibitory results; but we have as yet much to learn before we can speak with certainty as to the exact manner in which such an inhibition is brought about.

The Time required for Reflex Actions.

When one eyelid is stimulated with a sharp electrical shock, both eyelids blink. Hence, if the length of time intervening between the stimulation of the right eyelid and the movement of the left eyelid be measured, this will give the total time required for the various processes which make up a reflex action. It has been found to be from 0.0662 to 0.0578 second. Deducting from these figures the time required for the passage of afferent and efferent impulses along the fifth and facial nerves to and from the medulla, and for the latent period of the contraction of the orbicularis muscle, there would remain 0.0555 to 0.0471 second for the time consumed in the central operations of the reflex act. The calculations, however, necessary for this reduction, it need not be said, are open to sources of error. Blinking thus produced is a reflex act of the very simplest kind; but, as we have seen in the preceding pages, reflex acts differ very widely in nature and character; and we accordingly find, as indeed we have incidentally mentioned, that the time taken up by a reflex movement varies very largely. This, indeed, is seen in the blinking itself. When the blinking is caused, not by an electric shock applied to the eyelid, but by a flash of light falling on the retina, in which case complex visual processes are involved, the time is exceedingly prolonged; moreover, the results in different

experiments of such a kind are not nearly so uniform as when the blinking is caused by stimulation of the eyelid.

In general, it may be said that the time required for any reflex act varies very considerably with the strength of the stimulus employed, being less for the stronger stimuli; this we should expect, seeing that the efferent impulses of the reflex act are not simply afferent impulses transmitted through the central organ, but result from internal changes in the central organ started by the afferent impulse or impulses; and these internal changes will naturally be more intense and more rapidly effective when the afferent impulses are strong. It is stated that when the movement induced is on the same side of the body as the surface stimulation of which starts the act, the time taken up is less than when the movement is on the other side of the body, allowance being made for the length of central nervous matter involved in the two cases—that is to say, the central operations of a reflex act are propagated more rapidly along the cord than across the cord. The rapidity of the act varies, of course, with the condition of the spinal cord, being greatly prolonged when the cord becomes exhausted. The time thus occupied by purely reflex actions must not be confounded with the interval required for mental operations; of the latter we shall speak presently.

Sec. 2.—As a Centre or Group of Centres of Automatic Action.

Irregular automatism—*i. e.*, a spontaneity comparable to our own volition, is wholly absent from the spinal cord. A brainless frog placed in a condition of complete equilibrium in which no stimulus is brought to bear on it—protected from sudden passing changes in temperature, from a too rapid evaporation and the like—remains perfectly motionless till it dies. Such apparently spontaneous movements as are occasionally witnessed are so few and seldom, that we can hardly do otherwise than attribute them to some stimulus, internal or external, which has escaped observation. In the mammal (dog) after division of the spinal cord in the dorsal region regular and apparently spontaneous movements may be observed in the parts governed by the lumbar cord. When the animal has thoroughly recovered from the operation the hind-limbs rarely remain at rest for any long period; they move restlessly in various ways; and when the animal is suspended by the upper part of the body, the pendent hind-limbs are continually being drawn up and let down again with a monotonous rhythmic regularity, highly but, perhaps, falsely suggestive of automatic rhythmic discharges from the

central mechanisms of the cord. In the newly born mammal too, after removal of the brain, apparently spontaneous movements are frequently observed. This greater proneness to activity is, however, just what might be expected, when we take into consideration the more rapid metabolic changes, and the consequent greater molecular mobility of the whole nervous system of the mammal. The movements, even when most highly developed, are wholly different from the movements irregular in their occurrence, but orderly and purposeful in their character, which result from the working of volition.

Of the various regular automatic centres, both the numerous ones in the medulla oblongata, such as the vaso-motor, respiratory, etc., and the more sparse ones in other regions of the cord, such as those connected with micturition, defecation, erection, parturition, and so on, we have treated, or shall have to treat so fully in reference to their respective mechanisms, and discussed how far they are purely automatic, or in reality merely reflex in nature, that nothing more need be said here.

It has been much disputed whether the spinal cord exercises over the skeletal muscles a tonic action comparable to that of the vaso-motor centres over the smooth muscles of the arteries. The arguments which were once brought forward as proving the existence of such a tone are invalid. It is true that when a muscle is cut across in the living body, the section gapes; but this is because all the muscles of the body are slightly stretched beyond their normal length. Again, when one side of the face is paralyzed, the mouth is drawn to the opposite side, not because the paralyzed muscles have lost tone, but because there are on the paralyzed side no contractions to antagonize the effect of the continually repeated contractions of the sound side. And, indeed, the existence of such a tone seems distinctly disproved by the fact that, according to most observers, when in the living body the nerve going to a muscle is cut, no permanent lengthening of the muscle is caused. On the other hand, when the sciatic plexus of one leg of a brainless frog is cut, and the animal is suspended, that leg hangs down more helplessly than the other; that is to say, the sound leg is rather more flexed than the other. The difference which is sometimes marked, but sometimes hardly visible, disappears entirely when the whole cord is destroyed. But the same flaccidity is observed in a leg in which the posterior roots only of the sciatic plexus have been divided. Hence it is to be regarded as an instance not so much of automatic tone, as of feeble reflex action occasioned by afferent impulses.

Though, however, the view of a real tone lacks adequate support, several considerations favor the idea that the condition of

a muscle, apart from its being in a state of contraction or at rest, is closely dependent on influences proceeding from the spinal cord. We saw, in treating of muscle and nerve (p. 123), that the irritability of a muscle is markedly affected by the section of its nerve—*i. e.*, by severance from the central nervous system; and more recently (p. 549) in speaking of the so-called trophic action of the nervous system, we referred to changes in the nutrition of muscles occasioned by diseases of the nervous system. An instance of a similar action is afforded by the so-called "tendon-phenomena." It is well known that when the leg is placed in an easy position, as when resting on the other leg, a sharp blow on the patellar tendon will cause a sudden jerk forward of the leg, brought about by a contraction of the quadriceps femoris. Similarly the muscles of the calf may be thrown into action by tapping the tendo Achillis; and in some cases the same muscles may be made to execute a series of rhythmic contractions, by suddenly pressing back the sole of the foot so as to put them on the stretch. These, and other instances of a like kind, at first sight appear to be, and indeed it has been maintained that they are cases of reflex action, due to afferent impulses started in the tendon; hence they have been frequently spoken of as "tendon-reflex." But the evidence on the whole shows that they are not reflex, but due to direct stimulation of the muscles. Nevertheless, and this is the interesting point, they are closely dependent on the integrity of the spinal cord, and of the connections between the cord and the muscles. In the case of animals they disappear when the spinal cord is destroyed, or the nerves going to the muscles are severed or even when the posterior roots only are divided. And in the case of man they are diminished or wanting in certain diseases of the spinal cord (locomotor ataxy), and exaggerated in others; so much so indeed that they have become of practical clinical importance as a means of diagnosis. Without discussing the matter any further, we may say that such phenomena indicate that the nutrition and the irritability of a muscle are in some way governed by influences of one kind or another which proceed from the spinal cord, and which, in certain cases at all events, are the result of, or are determined by, influences of a similarly obscure nature reaching the cord from the muscles by the posterior roots of the spinal nerves.

When we feel something touching our foot, or when we move our foot, afferent or efferent impulses must evidently pass along the whole length of the spinal cord on their way to and from the brain. We may say at once that it is impossible that sensory impulses should be conveyed straight along a fibre from the periphery to the sensorium, and volitional impulses straight along another fibre from the "organ of the will" to the muscular fibre; the number of fibres in the cord is wholly insufficient for such a purpose. Moreover, not only anatomical but physiological considerations show that conduction along the cord is not simple, but carried out by a more or less intricate system of relays.

The phenomena of reflex action have shown us that the cord contains a number of more or less complicated mechanisms capable of producing, as reflex results, coördinated movements altogether similar to those which are called forth by the will. Now it must be an economy to the body that the will should make use of those mechanisms already present, rather than that it should have recourse to a special apparatus of its own of a similar kind. It is therefore *à priori* probable that when the foot is pricked the sensory impulses so generated, on reaching the cord pass into the gray matter, there to undergo a certain amount of transformation and thence to be transmitted, either by direct and simple, or by indirect and complicated paths to the brain. Similarly, we may suppose that when the leg is moved by an effort of the will, volitional impulses starting from the brain, pass by a more or less direct path to certain portions of gray matter in the lumbar cord, with which the motor fibres of the nerves of the leg are specially connected, and induce such changes in this gray matter as to lead to the discharge of the appropriate impulses along those motor fibres. And such a view is strongly supported by the anatomical fact, as illustrated by Figs. 221, 222, 223, that along the length of the spinal cord the amount of gray matter varies according to the number of fibres passing into the cord, indicating that the fibres as they pass into the cord have a certain amount of gray matter allotted to them. Moreover, though the course which the fibres of the posterior roots take immediately upon entering the cord has perhaps not yet been satisfactorily determined, the fibres of the anterior root have been definitely traced to the nerve-cells of the anterior cornu; and, according to recent observations, in the frog at all events, the cells of the anterior cornu are equal in number to the fibres of the anterior root.

But, admitting this, there still remains the question, How do volitional and sensory impulses travel along the cord, between the brain on the one hand and the gray matter belonging to this or that nerve-root on the other?

FIG. 221.

DIAGRAM SHOWING THE RELATIVE SECTIONAL AREAS OF THE SPINAL NERVES, AS THEY JOIN THE SPINAL CORD.

FIG. 222.

DIAGRAM SHOWING THE UNITED SECTIONAL AREAS OF THE SPINAL NERVES, PROCEEDING FROM BELOW UPWARDS.

FIG. 223.

DIAGRAM SHOWING THE VARIATIONS IN THE SECTIONAL AREA OF THE GRAY MATTER OF THE SPINAL CORD ALONG ITS LENGTH.
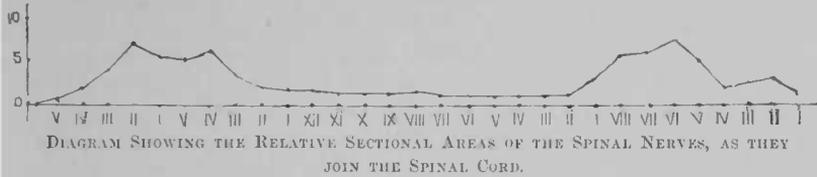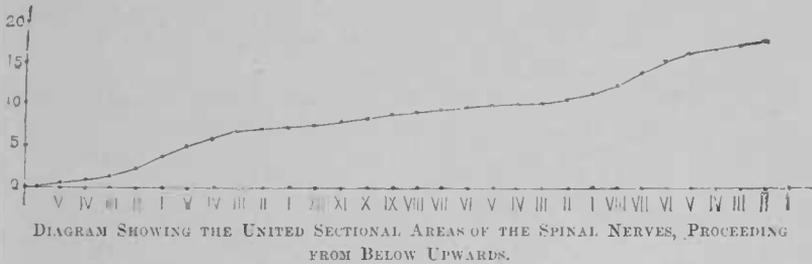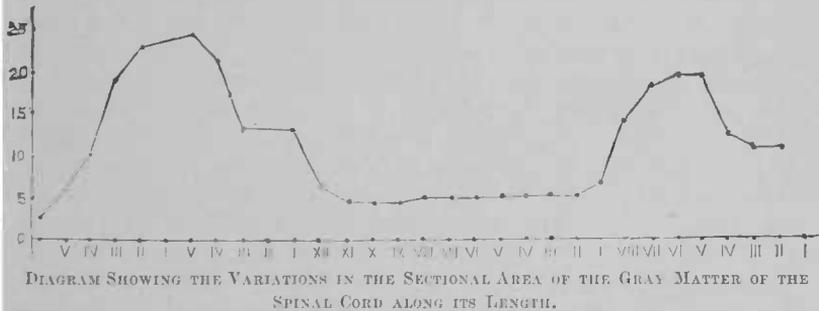
All three figures are to read from left (the bottom of the cord) to right (top of the cord), the numerals indicating successively the sacral, lumbar, dorsal, and cervical nerves. The figures are not drawn to the same scale.

Our information concerning the conduction of impulses along the spinal cord is derived partly by anatomical deduction, partly from experiment, and partly from pathological observation. These several methods have their advantages and disadvantages. We have just now brought forward a very general anatomical deduction. More detailed inferences are afforded by the Wallerian method (see p. 566). When the spinal cord is diseased or

injured at any point, tracts of degenerated fibres may at times be traced on the one hand upwards toward the brain, or on the other downwards in a peripheral direction. The former may be taken as being sensory or afferent, and the latter, together with tracts of degeneration in the cord which are found associated with disease of the brain, as motor or efferent. Again, when the development of the spinal cord is studied, it is found that the fibres of different tracts assume their medullary sheaths at different times; and by this means the longitudinal fibres of the cord may be differentiated into tracts having different terminal connections, some tracts being thus traced into the crura cerebri, others into the cerebellum, while others appear to terminate in the medulla oblongata, or both to begin and end in the cord itself. These different distributions obviously suggest different functions. But all such anatomical deductions must here, as elsewhere, be received with caution.

When experiments are used as a means of inquiry, we are met with the danger of confounding the immediate and temporary effects of the operation, such as those produced by shock, with the more real and lasting effects. It is difficult, too, in such cases to determine the existence of sensations, and to distinguish between reflex and purely voluntary movements. The difficulty of recognizing, and especially of quantitatively estimating the value of signs of sensation has, however, been met by an ingenious use of variations in blood-pressure. We have seen that, at all events in an animal under urari, afferent impulses occasion a rise of blood-pressure. If, having determined the amount of rise due to a definite stimulation of a sensory nerve, such as the sciatic, we make an incision into the spinal cord of the dorsal region—dividing, for instance, part of the lateral column on one side—and afterwards find that the same stimulus applied in the same way to the sciatic nerve leads to a greatly diminished rise of blood-pressure, we are justified in inferring that the afferent impulses affecting blood-pressure are largely conducted through the part of the lateral column which has been divided. We may thus obtain a definite measure, in millimetres of mercury, of the effect produced by the injury. On the other hand, the value of this precise measurement is diminished by the doubt whether we have a right to conclude that the afferent impulses which affect blood-pressure take the same course as those which give rise to sensations, and affect consciousness. And, further, in all experimental results on animals, we must bear in mind the probability that the functions of the spinal cord may vary in different animals, possibly to a very considerable extent.

In pathological cases we have the advantage of being able clearly to define sensation and volition, but this is frequently

more than counterbalanced by the diffuse nature of the injury or disease, and the want of exact anatomical verification. When these facts are borne in mind, it will easily be understood that in no part of physiology are the statements of investigators more conflicting and unsatisfactory.

One salient fact comes out in all observations, whether experimental or pathological, viz., that between the brain, where volitional impulses are started, or where conscious sensations are perfected, and the muscle which carries out the movement or the sentient surface where the sensory impulses begin, there is a complete crossing or decussation of all impulses, whether sensory or motor. When the right side of the brain is injured or diseased—when, for instance, damage is done to the right corpus striatum and optic thalamus, it is on the left side of the body, in the left limbs, and in the left face, that the paralysis and loss of sensation appear; it is on the left side that sensory impulses fail to affect consciousness, it is on the left side that the muscles can no longer be reached by volitional impulses. Results other than these indicate complications involving the other side of the brain.

Further, all observers are agreed that, as far as the spinal nerves are concerned (and since we are now treating of the spinal cord, we may for the present leave out of consideration the cranial nerves), the decussation is complete at about the level of the upper part of the medulla oblongata and pons Varolii when the paths are traced upwards; that is to say, all the sensory impulses coming from, and all the volitional impulses passing to, the left side of the body, make their way along the right crus cerebri. Nearly all observers, again, are agreed that the sensory impulses cross over lower down in the spinal cord than do the volitional impulses; but opinions differ as to the exact difference in the paths of the two kinds of impulse. Experiments conducted by some observers have seemed to show that transverse division of the lateral half of the cord in any part of its course below the medulla oblongata is followed on the same side, below the injury, by loss of voluntary movement, accompanied by no loss of sensation, but even by increased sensitiveness or hyperæsthesia, and on the opposite side by loss of sensation without any affection of voluntary movement. From these and other experiments, these authors conclude that sensory impulses entering into the cord at a posterior root immediately cross to the other side of the cord, and so ascend to the brain, whereas efferent impulses of volition cross wholly in the region of the medulla oblongata, and afterwards keep to the same side of the cord along its whole length. Other observers, and these, perhaps, are deserving of the greater confidence, find that a section of a lateral half of the cord affects both volitional and sensory impulses of both sides, though to different degrees, the loss both of sensation and motion being

greater on the side operated on than on the other. Hence, they maintain that the decussation of both kinds of impulses is gradual, extending some distance along the cord. Thus, they hold that the volitional impulses for the hind-limb, while crossing over largely in the upper part of the cord, continue to cross over right down to the lumbar region, and similarly that the sensory impulses from the hind-limb, while crossing largely in the lumbar region of the cord, continue to cross in the dorsal or even in the cervical region.

Admitting this latter view as the one most in accordance with facts, we have still to ask what are the exact paths taken by the volitional and sensory impulses in their respective courses—that is to say, What are the particular parts of the spinal cord which serve to conduct volitional impulses on the one hand and sensory impulses on the other? Upon the discovery of the distinctive functions of the anterior and posterior roots, it seemed natural to conclude that the anterior columns with which the anterior roots are more directly connected, should·serve as the path for volitional impulses, and similarly that the posterior columns should afford a path for sensory impulses. But this view was soon found to be untenable ; and it became modified into the conception that sensory impulses pass along the posterior columns and the gray matter, while volitional impulses descend in the antero-lateral columns. Further, this somewhat general statement has been reduced to greater definiteness by some authors in the following way. They hold that the impulses which when they reach the brain give rise to feelings of general sensibility only or of pain, and the impulses which form part of the chain of a reflex act, as when the foreleg or hindleg moves in response to a stimulus applied to the hindleg or foreleg, respectively, are transmitted by the gray matter, and by all parts of the gray matter, and that in any direction. Distinct tactile sensations, on the other hand, they contend, travel exclusively by the posterior columns, and distinct volitional impulses by the antero-lateral columns. That these several kinds of impulses should travel by separate paths, does not in itself seem improbable, and is, to a certain extent, suggested by pathological experience. For carefully observed cases have been recorded of disease of the cord, and apparently of the cord alone, in which the patient could appreciate even a slight touch but felt no pain when a needle was thrust into the skin, or when the skin was otherwise treated in a way which, under normal circumstances, would give rise to pain. Conversely, the sense of touch has been found to be absent, while pain was still felt. Similarly, as was stated on p. 680, cases have been recorded where the sensation of pressure was retained but that of temperature impaired or lost, and vice versa. Such cases however have not as yet afforded any clear insight as to what are

the actual paths of the respective sensory impulses. While they do not oppose they do not distinctly confirm the view we are speaking of as to the particular paths of these several kinds of impulse. Nor indeed can this view, either in its more general or in its more elaborate form, be considered as adequately supported by experimental evidence.

For the investigations of other observers, especially the more recent ones, including those conducted by the blood-pressure method, largely concur in showing that along the cord, at all events in the dorsal region, both volitional and sensory impulses, indeed we might say impulses of all kinds passing between the brain and various parts of the spinal cord, or between distinct parts of the cord itself, run in the lateral columns. This view is further supported by the anatomical facts that the lateral columns (Fig. 224) increase in bulk from below upwards to a much greater degree than do either the anterior or posterior columns (Figs. 225, 226), and that after certain diseases or injuries of the brain

FIG. 224.
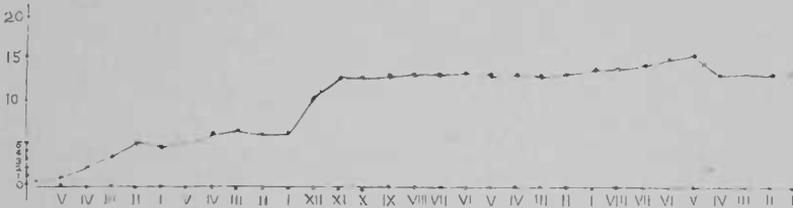
DIAGRAM SHOWING THE VARIATIONS IN THE SECTIONAL AREA OF THE LATERAL COLUMNS OF THE SPINAL CORD, ALONG ITS LENGTH

FIG. 225.
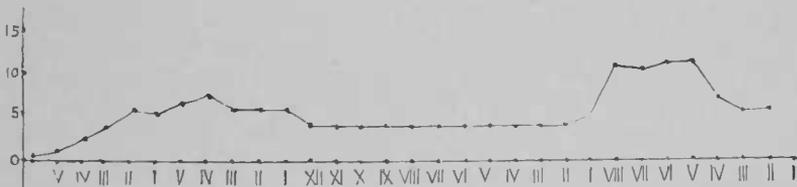
DIAGRAM SHOWING THE VARIATIONS IN THE SECTIONAL AREA OF THE ANTERIOR COLUMNS OF THE SPINAL CORD, ALONG ITS LENGTH.

FIG. 226.
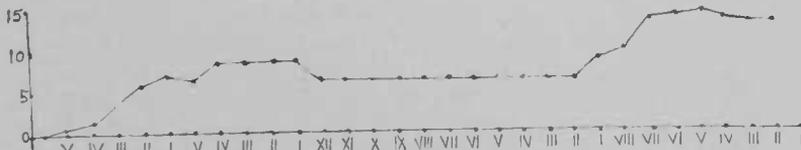
DIAGRAM SHOWING THE VARIATIONS IN THE SECTIONAL AREA OF THE POSTERIOR COLUMNS OF THE SPINAL CORD, ALONG ITS LENGTH.

or cord tracts of degeneration travel downwards and upwards respectively in the lateral columns (though accompanied by degeneration in other parts) ; moreover, the method of development spoken of at p. 703 teaches that a large part of each lateral column is associated with the pyramids (and hence sometimes called pyramidal tracts) and so with the crura cerebri and the brain. It may be added that the decussation of the pyramids in the medulla oblongata is chiefly a decussation of the lateral columns, though obviously, from what has been said before, decussation of impulses does not take place exclusively here. And such pathological evidence as is forthcoming also to a certain extent supports the same view. For while disease of the posterior cornua and posterior columns seems to affect the sensory impulses passing along the nerves which pass into the cord at the diseased part, and disease of the anterior cornua and (though this is less clear) of the anterior columns is similarly confined in its action to motor impulses passing out by the nerves belonging to the diseased part, disease of the lateral columns seems to affect chiefly the transmission of impulses along the length of the cord and especially the transmission of volitional impulses, for the evidence as to the interference in the conduction of sensations by disease other than of the posterior columns and cornua is by no means large or conclusive.

Accepting this view provisionally, we may form some such conception as follows of the conduction of volitional and sensory impulses. Volitional impulses cross, to a considerable extent in the medulla oblongata, but continue to cross probably to a less and less extent all the way down. In either case they appear to travel along the cord in the lateral columns. Eventually they become connected (possibly through part at least of the anterior columns) with the gray matter of the anterior cornua, where they join the local nervous mechanisms of which we have spoken above. From the gray matter the impulses proceed by the anterior roots to the appropriate muscles. Similarly sensory impulses make their way, with the intervention possibly of the posterior columns, first into the gray matter of the posterior cornua, and thence into the lateral columns, and so up to the brain, decussation being effected at first largely, and afterwards to a less extent, though continued upwards for some distance.

It must be remembered however that such a conception can only be regarded as provisional. And indeed continued experimental investigations teach us that this view also is in turn beset with many difficulties. We have already called and shall have occasion again to call attention to the importance of distinguishing between the immediate and the more permanent effects of any operation on the central nervous system. Now cases have been

recorded where section of the lateral columns on both sides in the dorsal region, has had for its immediate effect loss of sensibility and voluntary power in the hind-legs, but where without any regeneration in the divided tracts recovery has ultimately taken place, the return of voluntary power being nearly if not absolutely complete. So also cases have been recorded in which the section of a lateral (say right) half of the lower dorsal cord has led to an impairment of sensibility and voluntary power in the hind-legs, most marked on the same side, but in which the impairment has, in the course of time, completely or nearly completely disappeared without any regeneration of the cord taking place, and, further, in which a second lateral section higher up in the cord, and this time of the other (left) half, has again led to impairment, again to be followed by complete or nearly complete recovery. Cases of this kind, carefully conducted and observed by competent persons, place us in considerable difficulties. If we admit that the immediate effects of the operation are largely due to "shock" and inhibitory processes, and that after the lateral section of the right half of the cord, sensory volitional impulses passed to and from the hind-legs by the left half, then the recovery from the second operation shows that these impulses must have crossed between the two sections from the left to the right side. From which we might infer that impulses travelling along the cord were continually passing in a zigzag fashion from one lateral half to the other; and an analogous series of experiments in which the anterior and posterior halves were divided at different heights would lead us to infer in addition that the impulses also crossed in a similar zigzag fashion from front to back and back to front. But then the serious question is started, Is this serpentine path the normal one, or an artificial one forced upon the impulses by the abnormal condition of the cord? Finding their usual path blocked, did they make for themselves new tracts? But if such alternative passages be possible, how can we trust to either experiment or disease to show us the normal paths, or what right have we to speak of normal paths at all?

It will be seen from the foregoing that the time is not yet ripe for making any dogmatic statement concerning the conduction of impulses along the cord; and, indeed, the controversies concerning it have perhaps acquired a factitious importance. If we might venture to deduce any distinct lesson from all the various conflicting statements and results, it would be that the complexity and perfection of the nervous mechanisms of the spinal cord itself has been underrated rather than overrated. We spoke at the beginning of this section of a system of relays; we insisted on the existence of mechanisms with which the anterior

and posterior roots were respectively in immediate connection; and the results of experiment as well as of pathological experience seem to show that impulses, whether of volition or of sensation, work their way along the cord through a whole series of such and similar mechanisms, rather than through simple direct straightforward tracts of continuous fibres whether in the lateral columns or elsewhere.

In connection with this, a curious apparent contradiction between the results of pathological observation and experimental investigation may be mentioned. On the one hand, pathological observation clearly teaches that a limited disease of the cord affects the conduction of volitional impulses much more distinctly than it does that of sensory impulses. A segment of the cord may be very largely diseased, causing a large or complete block to volitional impulses, and may yet serve to conduct sensory impulses, which, however, are in that case generally retarded as if the impulses were making progress upwards by a roundabout and difficult route. On the other hand, in the case of experiments after various sections of the cord, the recovery of voluntary power is generally more speedy and more complete than that of distinctly conscious sensations, even when both are primarily affected by the operation. The contradiction may partly, perhaps, be explained by the difficulty, in the case of animals, of any objective quantitative determination of sensation, but not wholly. Both facts point to the possibility of both sensory and volitional impulses making their way by changed paths under changed circumstances.

We may conclude our observations on this difficult but probably pregnant topic by the following statement. While we appear to have evidence that sensory and motor impulses are connected, at their entrance into and exit from the cord with complicated mechanisms, in which the gray matter undoubtedly, and possibly portions of the posterior and anterior columns, are involved, the paths along the cord are not clearly known. We have some reason to think that they pass largely along the lateral columns, but probably not in a direct straightforward manner, the whole cord being functionally a series of mechanisms, for which the white matter supplies commissural connections. And the view that the paths may shift according to circumstances is not without a certain support.

As was stated above, after unilateral section of the spinal cord, the sensation on the same side below the injury, so far from being diminished or lost, has, in a certain number of cases, though by no means always, been observed to be increased; the parts are then said to suffer from hyperæsthesia. Since the hyperæsthesia appears immediately after the operation, it cannot be due to any

inflammatory process. Nor can it be explained as simply the result of the increased supply of blood to the peripheral terminations of the sensory nerves, caused by the section involving vaso-motor tracts; since the simple section of a vaso-motor tract, as when the cervical sympathetic is divided, does not give rise to hyperæsthesia. Nor can we explain it as due to a one-sided hyperæmia of the spinal cord itself, for we have no evidence that such a state of things is brought about. Since it lasts for a very considerable time it cannot be due to any passing exciting effect of the operation. It has been suggested that section, in such cases, has removed previously existing influences, which descending the cord exercised an inhibitory action on the generation of sensory impulses, more particularly of those more complex impulses which we have supposed to arise in the local mechanism of gray matter with which the posterior roots are connected. In other words, this one-sided exaltation of sensation may be compared to the general increase of reflex action which occurs in the spinal cord after removal of the brain. But we cannot enter into the full discussion of this matter here.

Much discussion has arisen on the question whether the spinal cord itself is irritable towards stimuli other than nervous—that is, whether it can be excited by electric and other stimuli applied directly to it. Undoubtedly, the cord, as a whole, is irritable; if two electrodes be plunged into it, and a current sent through it, muscular movements, arterial constriction, and other results, follow. But, in such a case, the current may fall into nerve-roots, which are as irritable, at least, as nerve-trunks. But even if the nerve-roots be eliminated, the white matter, at least, is irritable; for it has been found that movements result when the anterior columns are isolated for some way down and stimulated with an electric current. With regard to the gray matter, it has been maintained that though it will convey both motor and sensory impulses, it cannot originate them. It has accordingly been spoken of as *kinesodic* and *œsthesodic*, as simply affording paths for motor and sensory impulses. But the arguments urged in support of this view cannot be regarded as conclusive.

CHAPTER VI.

THE BRAIN.

[*The Physiological Anatomy of the Brain.*

THE brain is that portion of the cerebro-spinal axis which is situated within the cranium. It consists of a number of ganglionic collections of nervous matter, which are intimately connected with each other by intercommunicating fibres, and with the general system by the sensory and motor nerves. The mass of the brain substance is formed by the cerebrum, cerebellum, pons Varolii, and medulla oblongata.

The *medulla oblongata* (Figs. 227, 228, and 229) is continuous below with the spinal cord, and above with the pons Varolii. It is situated obliquely, pointing downwards and backwards, and rests upon the basilar groove of the occipital bone. It is divided anteriorly and posteriorly into two portions by the anterior and posterior median fissures, which are continuations of the same fissures in the spinal cord. The halves are symmetrical and marked by grooves, dividing each of them into four smaller portions, which from before backwards are: the *anterior pyramids, lateral tracts, restiform bodies*, and *posterior pyramids*.

The *anterior pyramids* are continuous with the anterior columns of the cord, and are composed principally of fibres of the anterior columns, and partly of fibres of the lateral tracts and posterior columns of both sides. The fibres from the opposite side are received through four or five decussating bands which cross in the median line. (Fig. 227.) These bands are formed by fibres from the lateral tracts, of fibres from the anterior columns, and of fibres from the posterior columns. The *lateral tracts* are continuous with the lateral columns of the cord; each has resting upon it a small oval mass of nervous matter called the *olivary body*. This body consists of white matter externally and contains a gray nucleus, the *corpus dentatum*. Running from the anterior columns and curving around the lower end of the olivary body is a narrow band of fibres called the *fibræ arciformes*. The *restiform bodies* are the largest of the four portions, and are continuous with the posterior columns of the cord; they diverge as they ascend and form the inferior peduncles of the cerebellum. (Fig. 231.) The *posterior pyramids* are small narrow cords (fasci-

culi graciles), which are situated one on each side of the posterior median fissure, and separated from the restiform bodies by slight grooves. These bodies also diverge with the restiform bodies, and become blended with them.
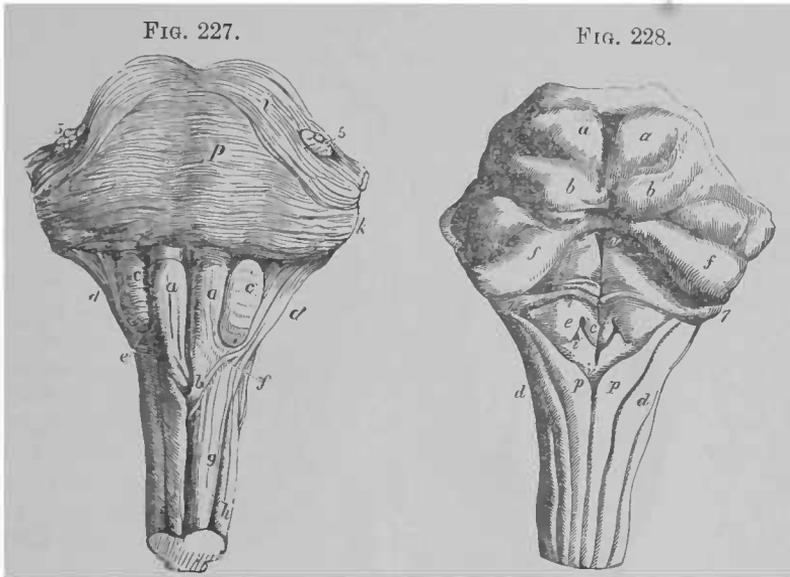
FIG. 227.—View of the Anterior Surface of the Pons Varolii and Medulla Oblongata. *a a*, anterior pyramids; *b*, their decussation; *c c*, olivary bodies; *d d*, restiform bodies; *e*, arciform fibres; *f*, fibres described by Solly as passing from the anterior column of the cord to the cerebellum; *g*, anterior column of the spinal cord; *h*, lateral column; *p*, pons Varolii; *i*, its upper fibres; 5 5, roots of the fifth pair of nerves.

FIG. 228.—View of the Posterior Surface of the Pons Varolii, Corpora Quadrigemina, and Medulla Oblongata. The peduncles of the cerebellum are cut short at the side. *a a*, the upper pair of corpora quadrigemina; *b b*, the lower; *f f*, superior peduncles of the cerebellum; *c*, eminence connected with the nucleus of the hypoglossal nerve; *e*, that of the glosso-pharyngeal nerve; *i*, that of the vagus nerve; *d d*, restiform bodies; *p p*, posterior pyramids; *c*, groove in the middle of the fourth ventricle, ending below in the calamus scriptorius; 7 7, roots of the auditory nerves.

The fibres of the anterior pyramids are distributed to the cerebrum and cerebellum. Of the cerebral fibres, some pass directly through the pons Varolii; others join fibres from the olivary body to form the olivary fasciculus. The cerebellar fibres pass beneath the olivary body, and are distributed to the cerebellum. The fibres of the lateral tracts run in three directions. The internal form the greater portion of the decussating bands, and a part of the anterior pyramids. The middle ascend in the floor of the fourth ventricle, and join with fibres of the restiform bodies and posterior pyramids to form the *fasciculi teretes,* which are located one on each side of the median fissure.

The external fibres join with the fibres of the restiform bodies,
and pass to the cerebellum. The restiform bodies receive fibres
from both the anterior and lateral columns, and after entering
the pons divide into two portions: the inner joins the fibres of
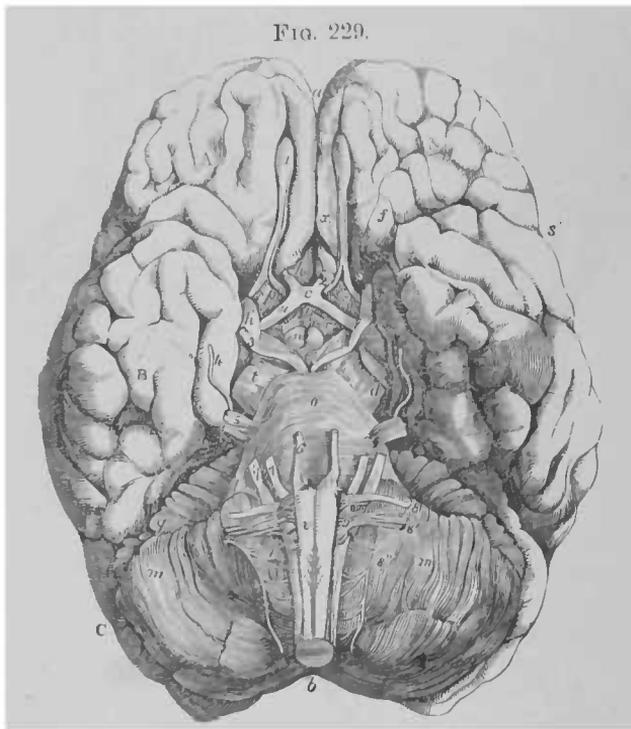
FIG. 229.

A, anterior; B, middle; C, posterior lobe of cerebrum. a, the forepart of the great longi-
tudinal fissure; b, notch between hemispheres of the cerebellum; c, optic commissure; d, left
peduncle of cerebrum; e, posterior perforated space; e to i, interpeduncular space; ƒ ƒ′, con-
volution of Sylvian fissure; h, termination of gyrus uncinatus behind the Sylvian fissure;
i, infundibulum; l, right middle crus or peduncle of cerebellum; m m, hemispheres of cere-
bellum; corpora albicantia; o, pons Varolii, continuous at each side with middle crura of
cerebellum; p, anterior perforated space; q, horizontal fissure of cerebellum; r, tuber
cinereum; s s′, Sylvian fissure; t, left peduncle or crus of cerebrum; u u, optic tracts; v, medulla
oblongata; x, marginal convolutions of the longitudinal fissure. 1 to 9 indicate the several
pairs of cerebral nerves, numbered according to the usual notation, viz., 1, olfactory nerve;
2, optic; 3, motor nerve of eye; 4, pathetic; 5, trifacial; 6, abducent nerve of eye; 7, audi-
tory, and 7′, facial; 8, glosso-pharyngeal; 8′, vagus, and 8″, spinal accessory nerve.

the posterior pyramids, and are traced in the fasciculi teretes;
the outer fibres are distributed to the cerebellum and form its
inferior peduncle. The fibres of the posterior pyramids are con-
tinued up to the cerebrum through the fasciculi teretes or to the

cerebellum. The outer fibres of the restiform bodies and posterior pyramids diverge as they ascend in the medulla (Fig. 228), and form the postero-lateral boundaries of a lozenge-shaped space, which is called the *fourth ventricle*. The ventricle (Fig. 231) is bounded antero-laterally by two bands of matter extending from the cerebellum to the cerebrum, called the *processus e cerebello ad testes*. The floor is formed by the posterior surface of the pons Varolii and medulla oblongata; the roof is formed by a band of gray matter, the *valve of Vieussens*, which stretches across between the processus e cerebello ad testes, and by the under surface of the cerebellum. In the portion of the floor of the fourth ventricle, corresponding to the point of divergence of the posterior pyramids and restiform bodies, is a part which, from its resemblance to the point of a pen, is called the *calamus scriptorius* (Fig. 231).

In the lower part of the medulla, the gray substance is arranged as it is in the spinal cord. Approaching upwards it is increased in quantity and becomes mixed with white fibres. The gray commissure is exposed in the floor of the fourth ventricle; the posterior cornua become expanded, and form the *tuberculo cinero* of Rolando, which appear at the surface of the medulla oblongata between the lateral tracts and restiform bodies. Beneath the floor of the ventricle are a number of special deposits of gray matter, with which are connected the roots of origin of all the cranial nerves, with the exception of the optic and olfactory. On each side of the median fissure is a longitudinal eminence, the *fasciculus teretes*. On the lower part of the floor are a number of transverse lines, the *lineæ transversæ;* these are fibres of the auditory nerves, which emerge from the median fissure (Fig. 231).

The *pons Varolii* or mesocephalon (Figs. 227, 229) is composed of gray and white matter, and serves as a medium of communication between the medulla oblongata and the cerebrum and cerebellum; also, connecting the two hemispheres of the cerebellum by transverse commissural bands. Its posterior surface forms the upper part of the floor of the fourth ventricle; the anterior surface rests upon the basilar groove of the occipital bone. Recent writers speak of the pons Varolii as being constituted only of the transverse fibres connecting the hemispheres of the cerebellum, and of what is commonly known as the pons Varolii, as the *tuber annulare.*

The *crura cerebri* (Fig. 230) are two bands of white fibrous matter, which extend from the pons Varolii to the under surface of each cerebral hemisphere, where they run to the corpora striata and optic thalami, or directly to the cerebral cortex. In the interior of each band is a gray body, called the *locus niger*,

...

which separates the fibres of each crus into two layers; the superficial or anterior layer is called the *crusta*, and is composed of fibres coming from the anterior columns, and anterior portion of

FIG 230.
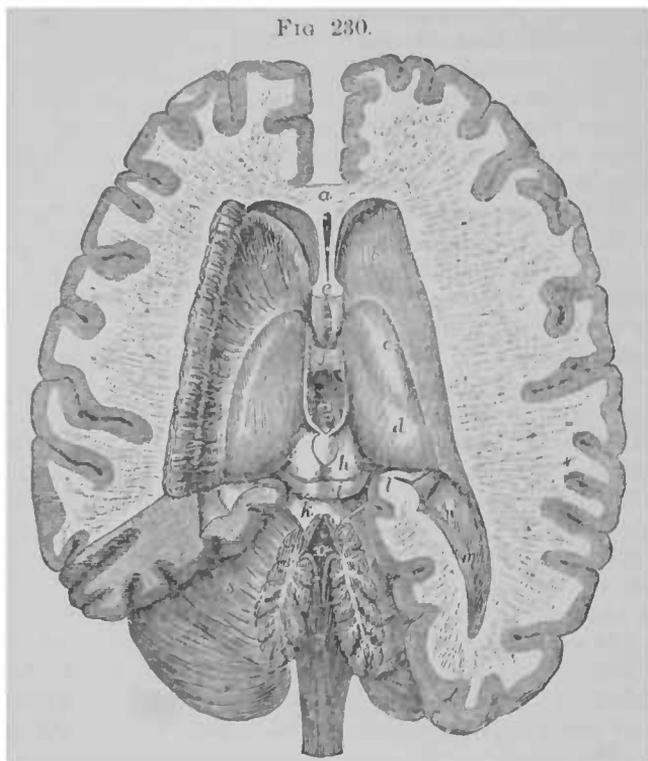
DISSECTION OF BRAIN, FROM ABOVE, EXPOSING THE THIRD, FOURTH, AND FIFTH VENTRICLES, WITH THE SURROUNDING PARTS. ½:

a, anterior part, or *genu* of corpus callosum; *b*, corpus striatum; *b'*, the corpus striatum of left side, dissected so as to expose its gray substance; *c*, points by a line to the tænia semicircularis; *d*, optic thalamus; *e*, anterior pillar of fornix divided—below they are seen descending in front of the third ventricle, and between them is seen part of the anterior commissure, in front of the letter *e* is seen the slit-like fifth ventricle, between the laminæ of the septum lucidum; *f*, soft or middle commissure; *g* is placed in the posterior part of the third ventricle, immediately behind the latter are the posterior commissure (just visible) and the pineal gland, the two crura of which extend forwards along the inner and upper margins of the optic thalami; *h* and *i*, the corpora quadrigemina; *k*, superior crus of cerebellum; close to *k* is the valve of Vieussens, which has been divided so as to expose the fourth ventricle; *l*, hippocampus major and corpus fimbriatum, or tænia hippocampi; *m*, hippocampus minor; *n*, eminentia collateralis; *o*, fourth ventricle; *p*, posterior surface of medulla oblongata; *r*, section of cerebellum; *s*, upper part of left hemisphere of cerebellum exposed by the removal of part of the posterior cerebral lobe. After HIRSCHFELD and LEVEILLE.

the lateral columns, and of fibres from the posterior columns which decussated at the anterior pyramids; the deep or posterior

layer is called the *tegmentum*, and is composed of fibres from the lateral tracts, posterior columns and olivary fasciculi, and from the cerebellum. The fibres of the crura in their course to the cortex of the cerebrum run through or beside four large ganglia, the corpora striata and optic thalami (Fig. 230). These are called the "basal ganglia." They are embedded in the cerebral substance, and are composed of both white and gray matter. The *corpora striata* lie anterior and external to the optic thalami; their external surface is gray, and they present in a transverse section a striated appearance, being composed of alternating layers of gray and white substance. Each ganglia is composed essentially of two nuclei; the largest is the *lenticular* or extra-ventricular nucleus; the smaller is the *caudate* or intraventricular nucleus (Fig. 233). Running upwards between the lenticular nucleus and the optic thalamus behind, and the lenticular nucleus and caudate nucleus in front, is a band of white matter which is called the *internal capsule*. External to the lenticular nucleus is a second band called the *external capsule*. The *optic thalami* are two oblong bodies situated posterior and internal to the corpora striata; each resting upon and embracing the corresponding crus cerebri. Externally they are composed of white matter, and internally of both white and gray matter.

The anterior fibres or *crusta* of the crus cerebri run to the corpus striatum of its own side; the posterior fibres or *tegmentum* run to the optic thalamus. Of these fibres some probably terminate in the ganglia, while others are continued on to different parts of the cerebral cortex, either through the basal ganglia or the capsules above referred to.

The *corpora quadrigemina* or optic lobes (Figs. 228, 230) are situated below the posterior border of the corpus callosum and above the aqueduct of Sylvius. These bodies are four in number, and are placed in pairs; the anterior pair, which is the largest, is called the *nates;* the posterior pair is called the *testes.* They both consist of gray and white matter, and are connected on each side with the optic thalami and optic tracts by bands of nervous matter called *brachia.* Those connecting the nates with the thalamus are called the anterior brachia; those connecting the testes, the posterior brachia. The corpora quadrigemina receive fibres from the cerebellum through the processus ad testes, from the olivary fasciculi and the optic tracts and third nerves.

The *corpora geniculata* are two small bodies situated on each side, external to the corpora quadrigemina, and beneath and posterior to the optic thalamus. They are called from their situations the internal and external. The internal and testes, and the external and nates, are jointly connected with the optic tracts.

The *cerebellum* (Fig. 231) or lesser brain rests in the inferior occipital fossæ. It consists of two lateral hemispheres, which are joined together by a central lobe, the vermiform processes. The hemispheres are also connected with each other by the transverse commissural band of the pons Varolii. This band is called the *middle peduncle*. The cerebellum is connected to the cerebrum by the *processus e cerebello ad testes*, which are called the *superior peduncles* (Fig. 231), and below with the medulla
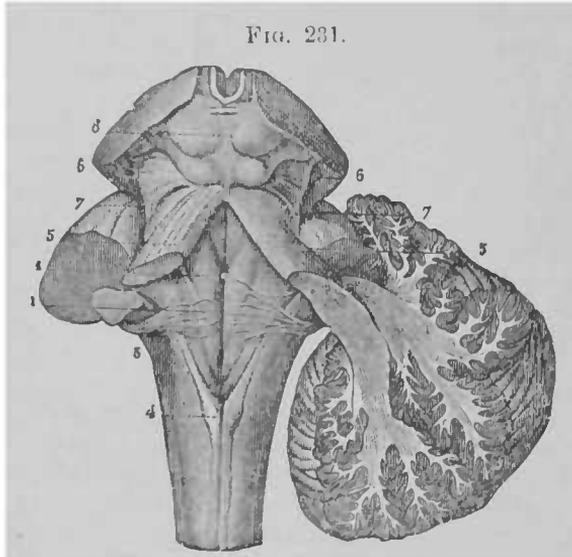
FIG. 231.

VIEW OF CEREBELLUM IN SECTION AND OF FOURTH VENTRICLE, WITH THE NEIGHBORING PARTS. FROM SAPPEY.

1, median groove of fourth ventricle, ending below in the *calamus scriptorius*, with the longitudinal eminences formed by the *fasciculi teretes*, one on each side ; 2, the same groove, at the place where the white streaks of the auditory nerve emerge from it to cross the floor of the ventricle ; 3, inferior peduncle of the cerebellum, formed by the restiform body ; 4, posterior pyramid, above this is the calamus scriptorius ; 5, superior peduncle of cerebellum, or processus e cerebello ad testes ; 6 6, fillet to the side of the crura cerebri ; 7 7, lateral grooves of the crura cerebri ; 8, corpora quadrigemina. After HIRSCHFELD and LEVEILLE.

oblongata by the *inferior peduncles*. The cerebellum is composed of both white and gray matter, and if a vertical section be made through the middle of one of the hemispheres in an antero-posterior direction, the interior will be seen to consist of white matter, in which is embedded a gray mass called the *corpus dentatum*. The surface of the white central matter is covered by a number of projecting laminæ, each of which has a secondary or tertiary laminæ projecting from it. The laminæ consist of a central white matter which is covered with gray matter, and on

account of the peculiar foliated appearance which they present in a transverse section have been called *arbor vitæ*.

The *cerebrum* constitutes the great mass of the brain substance. It is partially divided into two hemispheres by the longitudinal fissure, which divides it completely anteriorly and posteriorly, but only partially so in the median line, where the fissure is interrupted by a broad transverse commissural band called the *corpus callosum*.

The surface of the hemispheres is marked by rounded ridges or *convolutions*, which are separated from each other by fissures called *sulci*. The convolutions are very complicated and tortuous in their course, but they possess sufficient individuality in their arrangement to enable them to be differentiated and named. Each hemisphere is divided into five lobes : the *frontal, parietal, spheno temporal, occipital,* and *central* lobe, or island of Reil. The fissure of Sylvius in running from the under surface of the brain passes upwards and backwards, and divides into two branches, the superior and longitudinal. Anterior to the fissure is situated

FIG. 232.
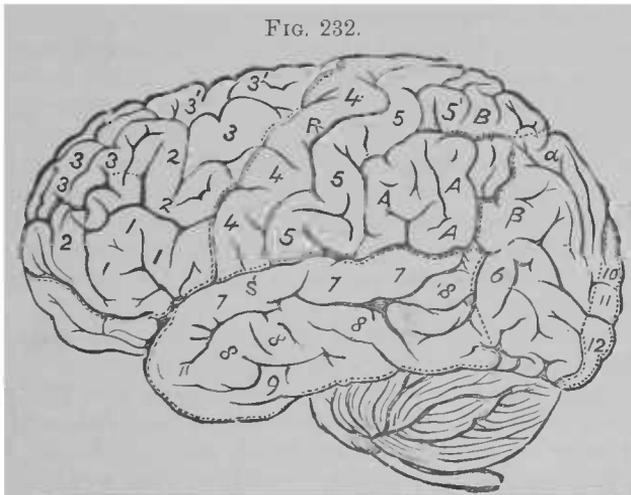
BRAIN OF MAN.

1, the inferior or third frontal convolution ; middle or second frontal ; 3, superior or first frontal ; 4, anterior central ; 5, posterior central ; *A*, supramarginal ; *B, a,* superior parietal ; ,3, *b,* angular convolution ; 7, superior or first spheno-temporal ; 8, middle or second spheno-temporal ; 9, inferior or third spheno-temporal ; 10, 11, 12, occipital convolutions ; *R,* fissure of Rolando ; *S,* fissure of Sylvius

the *frontal* lobe; the *parietal* lobe is separated from the frontal lobe by the fissure of Rolando, and from the *spheno-temporal,* which is below it, by the longitudinal branch of the fissure of Sylvius ; behind both of these is the *occipital* lobe. The *central* lobe, or island of Reil, lies within the fissure of Sylvius. Each

of these lobes consists of a number of recognized convolutions. The first convolution is called the superior or first frontal (Fig. 232, 3), and lies along the margin of the great longitudinal fissure; the inferior or third frontal convolution (1) is situated just above the fissure of Sylvius, and curves around the superior branch of the fissure; the middle or second frontal (2) is situated between these two, from which it is separated by the superior and inferior frontal fissures. The anterior central (4) is separated from the posterior central (5) by the fissure of Rolando; it communicates with the first and third frontal convolutions. The posterior central (5) is continuous above with the upper parietal (B) convolution. The supramarginal convolution (A) lies below the upper parietal and back of the posterior central. It curves around the extremity of the longitudinal branch of the fissure of Sylvius, and then running downwards and forwards forms the superior or first spheno-temporal (7). This convolution then curves backwards and forms the middle or second spheno-temporal (8), then continuing upwards forms an angular curvature, and is called the angular or posterior parietal convolution (β, b). Below the middle spheno-temporal is the inferior or third spheno-temporal (9); this forms the lower border of the spheno-temporal lobe. The occipital convolutions (10, 11, 12) are not well exhibited in a lateral view. A very important convolution, the *gyrus fornicatus*, curves around the upper part of the corpus callosum. This convolution commences in front of the anterior perforated space, curves around over the corpus callosum, and then winding around downwards and forwards embracing the crus, passes forwards as the *gyrus uncinatus*, and at its anterior aspect becomes sharply curved to form the *subiculum cornu Ammonis*.

The cerebrum is composed of both white and gray matter. The latter is found for the most part as constituting the cortex of the organ, where it covers the convolutions and dips down in the sulci. It is about two or three mm. in thickness, and consists of a number of superposed lamina of nerve-cells and very fine nerve-fibres, which are embedded in a matrix called the *neuroglia*. These cells are of rounded and irregular forms, and in the middle layers are of a pyramidal shape, with their bases generally looking towards the centre of the organ. The nerve-fibres are extremely fine, and, according to Kölliker, measure from about one to two mmm. in diameter. The prolongations of the cells are probably continuous with the axis-cylinders of the medullated nerve-fibres, which run to the central parts of the brain; or with prolongations of other cells, thus forming intercommunications.

In the interior of the cerebrum are several parts which are

here worthy of mention. The third ventricle is an open space filled with fluid, which is bounded laterally by the optic thalami; above by the velum interpositum, which is a reflection inwards and forwards of the pia mater through a transverse fissure below the posterior border of the corpus callosum. The floor is formed by nervous matter which closes the interpeduncular space; posteriorly it is bounded by the posterior commissure. Below the commissure is an opening, which is the canal leading to the fourth ventricle, called the *aqueduct of Sylvius*. Extending across the ventricle are three commissures: the anterior, middle, and posterior. The anterior passes through the corpora striata to each of the hemispheres. The middle (gray commissure) and posterior extend between the optic thalami. (Fig. 230.)

The lateral ventricle is bounded above by the corpus callosum; internally by the septum lucidum, which separates it from its fellow on the opposite side; below, principally by the corpus striatum, optic thalamus, and a band of white nervous matter, the fornix, which is continuous posteriorly with the corpus callosum. Extending outwards from each lateral ventricle are horn-shaped cavities or cornua. The anterior extends outwards, curving round the corpus striatum and running into the frontal lobe. The middle extends into the spheno-temporal lobe, passing behind the optic thalamus, then curving around the crus cerebri, and running deep into the lobe. In the floor of this cornu are three parts, which are here worthy of notice: the hippocampus major, pes hippocampi, and pes accessorius. (Fig. 230.) The *hippocampus major* is an elongated rounded white eminence, which courses the floor of the ventricle, ending in an irregular enlarged extremity, the pes hippocampi. This body is continuous with the gyrus fornicatus, and is curved upon itself, so that the white matter is external. The pes accessorius, or eminentia collateralis (Fig. 230), is a white eminence situated between the hippocampus major and the hippocampus minor of the posterior cornu. The posterior cornu extends downwards and backwards into the occipital lobe. On its floor is an eminence called the hippocampus minor. Many other parts of interest are referred to, and shown in the accompanying cuts.

The distribution of the fibres in the brain is one of great physiological interest. According to Meynert,[1] the cells of the same convolution are connected through their polar prolongations with each other; by arcuate fibres with the cells of different convolutions (Fig. 233, *CCH*); and with the convolutions of the opposite side by fibres passing the most part through the corpus callosum. To the corpus striatum fibres of the corona radiata

[1] Carpenter's Physiology, 1876, p. 896 et seq.

(CR) run from the whole area of the cortex to the lenticular body; others, the striæ corneæ S C, run from the temporal lobe to the anterior part of the corpus striatum; others run to the olfactory bulb (O). To the optic thalamus, fibres proceed from the frontal lobe, passing between the lenticular and caudate

Fig. 233.
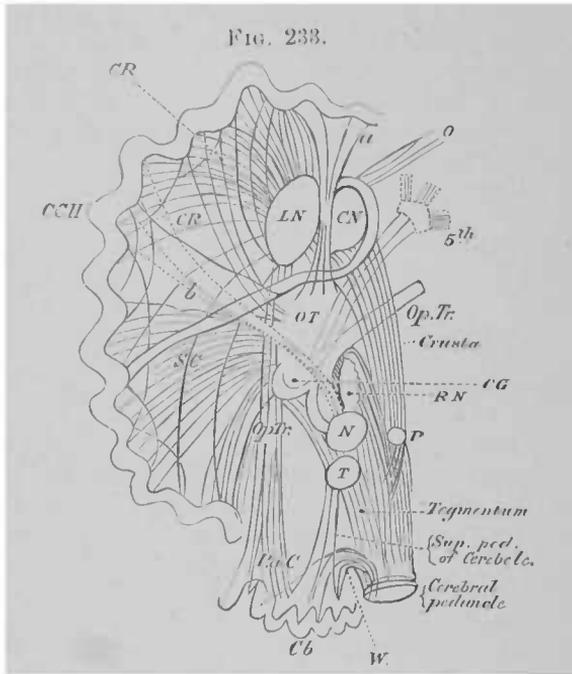
CCH, cortex of the cerebral hemispheres, the convolutions of which are seen to be connected by accurate connecting fibres; Cb, cortex of cerebellum; CR, corona radiata, consisting of fibres extending from the cortex cerebri to LN and CN, the lenticular and caudate nuclei of the corpus striatum, and to OT, the optic thalamus. The posterior extremity of the optic thalamus presents two enlargements, the corpus geniculatum externum and internum, which is seen to be connected with the optic tracts. The letters Op Tr. are placed on a band of fibres that are believed to run directly from the cortex cerebri to the cortex cerebelli; SC, stria cornea, or tænia semicircularis; RN, red nucleus of tegmentum; N, nates; T, testis; P, pineal gland; b, fibres passing directly into the tegmentum from the cortex cerebri; Pa C, the band of fibres to the right of these letters are part of the superior peduncle of the cerebellum.

nuclei (a), and from the temporal lobes, walls of the fissure of Sylvius, the gyrus fornicatus, and optic tracts. A special band ($Op. Tr.$) is supposed to run from the cortex to the cerebellum. The course of many other special fibres has been referred to in previous pages, or will be referred to hereafter.]

Sec. 1.—On the Phenomena Exhibited by an Animal Deprived of its Cerebral Hemispheres.

A frog from which the cerebral lobes have been removed, even though all the rest of the brain has been left intact, seems to possess no volition. The apparently spontaneous movements which it executes are so few and seldom that it is much more rational to attribute those which do occur to the action of some stimulus which has escaped observation, than to suppose that they are the products of a will acting only at long intervals and in a feeble manner.

By the application however of appropriate stimuli, such an animal can be induced to perform all the movements which an entire frog is capable of executing. It can be made to swim, to leap, and to crawl. When placed on its back, it immediately regains its natural position. When placed on a board, it does not fall from the board when the latter is tilted up so as to displace the animal's centre of gravity: it crawls up the board until it gains a new position in which its centre of gravity is restored to its proper place. Its movements are exactly those of an entire frog except that they need an external stimulus to call them forth. They inevitably follow when the stimulus it applied; they come to an end when the stimulus ceases to act. By continually varying the inclination of a board on which it is placed, the frog may be made to continue crawling almost indefinitely; but directly the board is made to assume such a position that the body of the frog is in equilibrium, the crawling ceases; and if the position be not disturbed the animal will remain impassive and quiet for an almost indefinite time. When thrown into water, the creature begins at once to swim about in the most regular manner, and will continue to swim till it is exhausted, if there be nothing present on which it can come to rest. If a small piece of wood he placed on the water the frog will when it comes in contact with the wood crawl upon it, and so come to rest. Such a frog, if its flanks be gently stroked, will croak; and the croaks follow so regularly and surely upon the strokes that the animal may almost be played upon like a musical instrument. Moreover, the movements of the animal appear to be influenced by light; if it be urged to move in any particular direction, it seems to avoid in its progress objects casting a strong shadow. In fact, even to a careful observer the difference between such a frog and an entire frog which was simply very stupid or very obstinate, would appear slight and unimportant except in one point, viz., that the animal without its cerebral hemispheres was obedient to every stimulus, and that each stimulus evoked an appropriate movement, whereas with the

entire animal it would be impossible to predict whether any result at all, and if so what result would follow the application of this or that stimulus. Both are machines; but the one is a machine and nothing more, the other is a machine governed and checked by a dominant volition.

Now such movements as crawling, leaping, swimming, and indeed, to a greater or less extent, all bodily movements, are carried out by means of coördinate nervous motor impulses, influenced, arranged, and governed by coincident sensory or afferent impulses. We have already seen that muscular movements are determined by the muscular sense; they are also directed by means of sensory impulses passing centripetally along the sensory nerves of the skin, the eye, the ear, and other organs. Independently of the afferent impulses, which acting as a stimulus *call forth* the movement, all manner of other afferent impulses are concerned in the generation and coördination of the resultant motor impulses. Every bodily movement such as those of which we are speaking is the work of a more or less complicated nervous mechanism, in which there are not only central and efferent, but also afferent factors. And, putting aside the question of consciousness, with which we have here no occasion to deal, it is evident that in the frog deprived of its cerebral hemispheres all these factors are present, the afferent no less than the central and the efferent. The machinery for all the necessary and usual bodily movements is present in all its completeness. The share therefore which the cerebral hemispheres take in executing the movements of which the entire animal is capable, is simply that of *putting this machinery into action*. The relation which the higher nervous changes concerned in volition bear to this machinery is not unlike that of a stimulus. We might almost speak of the will as an intrinsic stimulus. Its operations are limited by the machinery at its command. The cerebral hemispheres in their action can only give shape to a bodily movement by throwing into activity particular parts of the nervous machinery situated in the lower encephalic structures; and precisely the same movement may be initiated in their absence, by applying such stimuli as shall throw precisely the same parts of that machinery into the same activity.

Very marked is the contrast between the frog which, though deprived of its cerebral hemispheres, still retains the optic lobes, cerebullum, and medulla oblongta, and one which possesses a spinal cord only. The latter when placed on its back makes no attempt to regain its normal position; in fact, it may be said to have completely lost its normal position, for even when placed on its feet it does not stand with its forefeet erect, as does the other animal, but lies flat on the ground. When thrown into

water, instead of swimming it sinks like a lump of lead. When pinched, or otherwise stimulated, it does not crawl or leap forwards; it simply throws out its limbs in various ways. When its flanks are stroked it does not croak; and when a board on which it is placed is inclined sufficiently to displace its centre of gravity it makes no effort to regain its balance, but falls off the board like a lifeless mass. Though, as we have seen, there is in all parts of the spinal cord of the frog a large amount of coördinating machinery, it is evident that a great deal of the more complex machinery of this kind, especially all that which has to deal with the body as a whole, and all that which is concerned with equilibrium and is specially governed by the higher senses, is seated not in the spinal cord but in the brain, including the medulla oblongata; and apparently a great deal of this more complex machinery is concentrated in the optic lobes. The point however to which we wish now to call special attention is that the nervous machinery required for the execution, as distinguished from the origination, of bodily movements even of the most complicated kind, is present after complete removal of the cerebral hemispheres, though these movements are such as to require the coöperation of highly differentiated afferent impulses.

Our knowledge of the phenomena presented by the bird or mammal from which the cerebral hemispheres have been removed is not so exact as in the case of the frog. Under such circumstances movements apparently spontaneous in character are more common with the bird or mammal than with the frog. This might be expected, seeing that the more complicated brain of the former affords, even in the absence of the cerebral hemispheres, much more opportunity for the origination of stimuli within the nervous system itself, and for the play of stimuli however originating, than does that of the latter. It would be hazardous to regard such apparently spontaneous movements as indications of volition, and indeed it seems *a priori* improbable that the will should be confined to the cerebral hemispheres in the frog, and yet so to speak diffused among other parts of the brain in the more highly differentiated bird or mammal. On the other hand, when the cerebral hemispheres are bodily removed by the knife, the portions of the brain left behind are so profoundly affected by the "shock" of the operation, are for a while so obviously in an abnormal condition, that no just deductions can then be made as to what are their normal functions. And the animals generally die before they have entirely recovered from these immediate effects of the operation.

In the case of the bird, it has been found possible to keep the creature alive for months, after apparently complete removal of the hemispheres, and the following phenomena have then been

observed. The bird is able to maintain a completely normal posture, and will balance itself on one leg, after the fashion of a bird which has in a natural way gone to sleep. In fact, its appearance and behavior are strikingly similar to those of a bird sleepy and stupid. Left alone in perfect quiet, it will remain impassive and motionless for a long, it may be for an almost indefinite time. When stirred it moves, shifts its position ; and then on being left alone returns to a natural, easy posture. Placed on its side or its back it will regain its feet ; thrown into the air, it flies with considerable precision for some distance before it returns to rest. It frequently tucks its head under its wings, and at times may be seen to clean its feathers and to pick up corn or to drink water presented to its beak. It may be induced to move not only by ordinary stimuli applied to the skin, but also by sudden sharp sounds, or flashes of light ; and it is evident that its movements are to a certain extent guided by visual sensations, for in its flight it will, though imperfectly, avoid obstacles. Save that all clear signs of distinct volition are absent, that all satisfactory indications of intelligence are wanting, and that the movements are on the whole clumsy, resembling rather those of a stupid drowsy bird than those of one quite wide awake, there is very little to distinguish such a bird from one in full possession of its cerebral hemispheres.

In a mammal, during the few hours which intervene between the sudden removal of the whole of both hemispheres and death, very much the same phenomena may be observed. The rabbit, or rat, operated on can stand, run, or leap ; placed on its side or back it at once regains its feet. Left alone, it remains as motionless and impassive as a statue, save now and then when a passing impulse seems to stir it to a sudden but brief movement. Such a rabbit will remain for minutes together utterly heedless of a carrot or cabbage-leaf placed just before its nose, though if a morsel be placed in its mouth it at once begins to gnaw and eat. When stirred, it will with perfect ease and steadiness run or leap forward ; and obstacles in its course are very frequently, with more or less success, avoided. It will often follow by movements of the head a bright light held in front of it (provided that the optic nerves and tracts have not been injured during the operation), and starts when a shrill and loud noise is made near it. When pinched it cries, often with a long and seemingly plaintive scream. Evidently its movements are guided and may be originated by tactile, visual, and auditory *sensations*.[1]   But there is

Here we come upon a difficulty, which we shall meet with again in the present chapter. Are we justified in speaking of "sensation" in cases where we have reason to think that consciousness is absent, or where, as in the present instance, we have no evidence to show whether consciousness is present or not?

no satisfactory evidence that it possesses either visual or other *perceptions*, or that the sensations it experiences give rise to ideas. Its avoidance of objects depends not so much on the form of these as on their interference with light. No image, whether pleasant or terrible, whether of food or of an enemy, produces an effect on it, other than that of an object reflecting more or less light. And though the plaintive character of the cry which it gives forth when pinched suggests to the observer the existence of passion, it is probable that this is a wrong interpretation of a vocal action; the cry appears plaintive simply because, in consequence of the completeness of the reflex nervous machinery and the absence of the usual restraints, it is prolonged. The animal is able to execute all its ordinary bodily movements, but in its performances nothing is ever seen to indicate the retention of an educated intelligence. With the removal of that part of the brain which lies between the hemispheres and the medulla a large number of these coördinate movements disappear. The animal can no longer balance itself, it lies helpless on its side, and though various movements of a complex character, including cries, may be produced by appropriate stimuli, they are much more limited than when these cerebral structures are intact.

When in a dog, the cerebral convolutions are removed piecemeal at several operations, the animal may be kept alive and in good health for a long time, many months at least, though these parts of the brain have been reduced to very small dimensions. In such a case the indications of volition are much more prominent and numerous. We do not wish now to discuss whether the residues of volition and of intelligence then observed are to be ascribed to the small portion of the cerebral hemispheres still left, or whether they result from the working of other parts of the brain. To do this we should have to attempt to define with greater exactness than we have hitherto done, the meaning of the words "volition" and "intelligence;" and should probably in the end come to the conclusion that the discussion is a barren one. The more we study the phenomena exhibited by animals possessing a part only of their brain, the closer we are pushed to

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In treating of the senses we called attention to the fact that we must suppose in the case, for instance of vision, the visual peripheral organ to be connected with a visual central organ in such a way that the sensory impulses originating in the former become modified in the latter before they affect consciousness. In the peripheral organ and along the nerve of sense, the affection of the nervous tissue may be spoken of as a sensory impulse; but after the affection has traversed the central organ and become modified it is no longer a simple sensory impulse. We must then either call it a sensation irrespective of whether any change of consciousness intervenes or no, or we must give it a new name. Not wishing to introduce a new name, we have ventured to use the word "sensation" in a sense which neither affirms nor denies the coexistence of consciousness.

the conclusion that no sharp line can be drawn between volition
and the lack of volition, or between the possession and absence
of intelligence.   Between the muscle-nerve preparation at the
one limit, and our conscious willing selves at the other, there is
a continuous gradation without a break ; we cannot fix on any
linear barrier in the brain or in the general nervous system, and
say "beyond this there is volition and intelligence, but up to this
there is none."

This however is not the question with which we are now deal-
ing.   What we want to point out is, that in the higher animals,
including mammals, as in the frog, after the removal of the
cerebral hemispheres (or rather of the cerebral convolutions, for
interference with the corpora striata and optic thalami is apt to
induce disorders of which we shall speak presently), even
though volition and intelligence appear to be largely, if not
entirely, lost, the body is still capable of executing all the or-
dinary movements which the animal in its natural life is wont
to perform in spite of these movements necessitating the coöpera-
tion of various afferent impulses ; and that therefore the nervous
machinery for the execution of these movements lies in some part
of the brain other than the cerebral hemispheres.   We have
reasons for thinking that it is situated in the structures forming
the middle or hind brain.

SEC. 2.—THE MECHANISMS OF COORDINATED MOVEMENTS.

When in a pigeon the horizontal membranous circular canal
of the internal ear is cut through, the bird is observed to be
continually moving its head from side to side.   If one of the
vertical canals be cut through, the movements are up and down.
The peculiar movements may not be witnessed when the bird is
perfectly quiet, but they make their appearance whenever it is
disturbed, or attempts in any way to stir.   When one side only
of the head is operated on, the condition after a while passes
away.   When the canals of both sides have been divided, it
becomes much exaggerated, lasts longer, and sometimes re-
mains permanently.   And it is then found that these peculiar
movements of the head are associated with what appears to be a
complete want of coördination of all bodily movements.   If the
bird be thrown into the air, it flutters and falls down in a help-
less and confused manner ; it appears to have totally lost the
power of orderly flight.   If placed in a balanced position, it may
remain for some time quiet, generally with its head in a peculiar
posture ; but directly it is disturbed, the movements which it
attempts to execute are irregular and fall short of their purpose.

It has great difficulty in picking up food and in drinking; and in general its behavior very much resembles that of a person who is exceedingly dizzy.

It can hear perfectly well, and therefore the symptoms cannot be regarded as the result of any abnormal auditory sensations, such as "a roaring" in the ears. Besides, any such stimulation of the auditory nerve as the result of the section, would speedily die away, whereas these phenomena may be permanent.

The movements are not occasioned by any partial paralysis, by any want of power in particular muscles or groups of muscles. Nor on the other hand are they due to any uncontrollable impulse; a very gentle pressure of the hand suffices to stop the movements of the head, and the hand in doing so experiences no strain. The assistance of a very slight support enables movements otherwise impossible or most difficult, to be easily executed. Thus, though when left alone the bird has great difficulty in drinking or picking up corn, it will continue to drink or eat with ease if its beak be plunged into water, or into a heap of barley; the slight support of the water or of the grain being sufficient to steady its movements. In the same way, it can, even without assistance, clean its feathers and scratch its head, its beak and foot being in these operations guided by contact with its own body.

In mammals (rabbits) section of the canals produces a loss of coördination similar to that witnessed in birds; but the movements of the head are not so marked, peculiar oscillating movements of the eyeballs (nystagmus), differing in direction and character according to the canal or canals operated upon, becoming however very prominent. In the frog no deviations of the head are seen, but there is, as in other animals, a loss of coördination in the movements of the body.

Injury to the bony canals alone is insufficient to produce the symptoms; the membranous canals themselves must be divided or destroyed.

How are we to explain these remarkable phenomena? Let us for a while turn aside to ourselves and examine the coördination of the movements of our own bodies. When we appeal to our own consciousness we find that our movements are governed and guided by what we may call a sense of equilibrium, by an appreciation of the position of our body and its relations to space. When this sense of equilibrium is disturbed we say we are dizzy, and we then stagger and reel, being no longer able to coördinate the movements of our bodies or to adapt them to the position of things around us. What is the origin of this sense of equilibrium? By what means are we able to appreciate the position of our body? There can be no doubt that this appreciation is

in large measure the product of visual and tactile sensations; we recognize the relations of our body to the things around us in great measure by sight and touch; we also learn much by our muscular sense. But there is something besides these. Neither sight nor touch nor muscular sense would help us when, placed perfectly flat and at rest on a horizontal rotating table, with the eyes shut and not a muscle stirring, we attempted to determine whether the table and we with it were moved or no, or to ascertain how much it and we were turned to the right or to the left. Yet under such circumstances we are not only conscious of a change in our position but some observers have been able to pass a tolerably successful judgment as to the angle through which they have been moved. What are the data on which such a judgment can be formed? It is possible that the mere displacement of blood or of the more fluid parts of the tissues in various regions of the body, by giving rise to affections of general sensibility, may contribute to these data; but the peculiar features of the semicircular canals suggest that these are special agents in this matter. The three canals are, as we know, placed in the head in planes nearly at right angles to one another. Hence the pressure of the endolymph on the walls of the canal (including the maculæ of the ampullæ) in any given position of the head, and variations of that pressure due to movements of the head, or the movements of the endolymph within the canals accompanying movements of the head, would be different in the three canals; a sonorous wave on the other hand would affect all the ampullæ equally. If we suppose that the pressure of the endolymph or variations in that pressure, or the movements of the endolymph can give rise to afferent impulses which, though passing up to the brain along the auditory nerve, are not of the nature of auditory impulses, we appear to have the data for which we are seeking; for it is quite possible to conceive that the impulses thus generated in the ampullæ by movements of the head, should by becoming transformed into sensations enter into the judgment which we form of the movements which have given rise to them.

But if ampullar sensations, if we may so call them, thus enter into our appreciation of the position of our body and thus form, in part, the basis of our sense of equilibrium, it is obvious that when these are absent or deranged, the sense of equilibrium will be affected and the coördination of movements interfered with. And it has been urged that the phenomena attendant on injury to the semicircular canals are due either to the absence of normal or to the influence of abnormal ampullar sensations. There are however difficulties in the way of giving a satisfactory explanation of these phenomena. If, as some observers state, both auditory

nerves may be completely and permanently severed, without any effect on the coördination of movements, it is obvious that the incoödination which follows upon section of the auditory canals is due to some irritation set up by the operation and not to the absence of any normal impulses passing up from those organs to the brain, to the lack of what we called just now ampullar sensations. But if the effects are those of irritation, it is difficult to understand how they can, as according to certain observers they certainly do, become permanent. It has, however, been strongly urged that in such cases of permanent incoördination, the operation has set up secondary mischief in the brain, in the cerebellum for instance, and that the permanent effects are really due to the disease going on here; and we have reason as we shall see to think that the cerebellum is concerned in the coördination of movements. But the matter is one on which it does not as yet seem possible to make a dogmatic statement.

We compared the condition of a pigeon after injury to the semicircular canals to that of a person who is dizzy, and, indeed, one great characteristic of vertigo or dizziness is an inability on the part of the subject to maintain a due equilibrium; he cannot coördinate his movements properly or adapt them to the circumstances around him, and, in consequence, staggers and reels. Vertigo may be brought about in various ways. It may be the result simply of unusual and powerful visual sensations, such as those produced by water falling rapidly from a great height, or by objects moving swiftly across the field of vision. It may arise from changes taking place in the brain itself, and is a common symptom of many maladies and of the action of many poisons. As is well known, a most severe vertigo may be at once produced by rapidly rotating the body; and a very curious form may be induced by passing an electric constant current of adequate strength through the head from ear to ear. All cases of vertigo, however produced, have this common subjective feature, that one or more of the sets of sensations which form the basis of our appreciation of the relation of our body to external things disagree, and are in conflict with, the rest of the sensations which go to make up the same appreciation. Thus, in the vertigo after rapid rotation of the body, while we seem to see the whole world whirling round us, this conclusion is contradicted by other sensations. Corresponding to this subjective feature of vertigo is the objective feature of the failure of motor coördination; and there can be no doubt that the two are connected together as cause and effect. The exact manner in which the vertigo is developed—i. e., the sequence and relation of the various factors of it—will naturally vary according to the nature of the exciting cause, and the course of events appears to be not only different

in different forms, but in many cases complex. When vertigo comes on from rapidly rotating the body with the eyes open, an element of discord is introduced by the eyeballs not keeping pace with the movements of the head, but following irregularly, executing the oscillatory movements known as nystagmus, movements which continue after the body has come to rest, and then give rise to the false sensation that external objects are moving rapidly. But in this vertigo of rotation there are other factors at work, for the dizziness comes on, though less readily, when the eyes are kept shut all the time. It has been suggested that false ampullar sensations arise from the rotation of the body exciting the semicircular canals; and the form of vertigo, which is the salient symptom of the so-called Ménière's malady, has been ascribed to disease of the semicircular canals. But it must be remembered that the canals are frequently diseased without any vertigo appearing; and if, as some observers state, vertigo by rotation may be readily induced in rabbits after section of both auditory nerves, it is clear that the semicircular canals can have little share in this form of vertigo. And, indeed, even admitting this as a contribution to the total effect, it seems probable that changes in the brain due to the displacement of the blood, or even of the brain-substance itself, caused by the too rapid rotation, are at work. It is difficult otherwise to explain the unconsciousness which may ensue if the rotation be rapid and long-continued; and the vertigo resulting from various poisons seems to be distinctly of central origin.

Whether we accept the view of ampullar sensations just discussed or not, and whatever be the exact share which false ampullar sensations take in the causation of vertigo, this at all events is clear, that afferent impulses of various kinds so far contribute to the building up of the coördinating mechanisms that changes in these impulses tend to throw the mechanisms into disorder, or at least to impair their proper working. It is not necessary that these afferent impulses should directly affect consciousness (or, to speak more correctly, should affect that complete consciousness which is associated with volition), and so develop into distinct perceptions. We have seen that a bird from which the cerebral hemispheres have been removed is perfectly able to fly; and that, therefore, the coördinating nervous mechanism necessary for flight is situated in the parts of the brain lying behind the cerebral hemispheres. We have also dwelt on the fact that all the chief coördinating mechanisms of the frog lie in the hind parts of the brain; yet in the frog, as in the bird, and, we may add, as in the mammal, injury to the hinder parts of the brain produces loss of coördination, whether the hemispheres be present or not. Now, we have no satisfactory reasons for either

asserting or denying that what we call consciousness—*i. e.*, a distinct consciousness similar to our own consciousness, exists in animals deprived of their cerebral hemispheres. When signs of volition are present, we may safely take these signs as indications of consciousness also; but we are not justified in saying that all consciousness is absent when satisfactory signs of volition are wanting. We cannot form any just judgment on the matter without some more trustworthy and objective tokens of consciousness than we at present possess. But what we may safely assert is, that the coördinating mechanism, the retention of which is so striking a feature of an animal deprived of its cerebral hemispheres, is constructed out of divers afferent impulses of various kinds arriving at the coördinating centre from various parts of the body, that, in fact, the coördination taking place at the centre is the adjustment of efferent to afferent impulses. Many, if not all, of these afferent impulses are such that in the presence of consciousness they would give rise to perceptions and ideas; but we have no reason for thinking that the complete development of the afferent impulse into a perception or an idea is always necessary to the carrying out of coördination. We may say that we have a sense of equilibrium by means of the semicircular canals, and when that sense is deranged, we feel giddy and cannot stand. We have no reason, however, for thinking that the failure to keep upright is due to the *feeling* of giddiness, in the sense of being a direct result of the condition of the consciousness. On the contrary, since the peculiar movements characteristic of vertigo may take place in the absence of consciousness without the vertigo being actually felt, we may with security assert that the failure to stand upright and the feeling of giddiness are both concomitant effects of the same disarrangement of the coördinating mechanism.

It cannot be too much insisted upon that for every bodily movement of any complexity afferent impulses are as essential as the executive efferent impulses. Our movements, as we have already urged, are guided not only by the muscular sense, but also by contact sensations, auditory sensations, visual sensations, and visual perceptions (for the remarks made above concerning the relations of the coördinating mechanism to consciousness do not exclude the possibility of consciousness affecting the mechanism, indeed, not only may perceptions enter into the causation of vertigo, but even an imaginary idea may be the sole exciting cause of this condition); and when we say "they are guided," we mean that without the sensations the movements become impossible. In studying vision we saw repeatedly that the movements of the eyes were directly dependent on vision, and every ball-room affords abundant evidence of the ties between

sensations of sound and motions of the limbs.   So essential, in fact, are afferent impulses to the development of complex bodily movements, that we are almost justified in considering every such movement in the light of a reflex action made up of afferent and efferent impulses and central actions, and set going by the influence of some dominant afferent impulse, or by the direct action of those nervous changes, whose psychical correlative is what we call the will, on the centre itself.   All day long and every day multitudinous afferent impulses, from eye, and ear, and skin, and muscle, and other tissues and organs, are streaming into our nervous system ; and did each afferent impulse issue as its correlative efferent motor impulse, our life would be a prolonged convulsion.   As it is, by the checks and counterchecks of cerebral and spinal activities, all these impulses are drilled and marshalled, and kept in hand in orderly array till a movement is called for ; and thus we are able to execute at will the most complex bodily manœuvres, knowing only why, and unconscious or but dimly conscious *how*, we carry them out.

We have ventured to use the phrase "coördinating centre," but it must be understood that we have no right to attach more than a general meaning to the words.   We cannot, at present at least, define such a centre in the same way that we can the vaso-motor or respiratory centre.   When the optic lobes as well as the cerebral hemispheres are removed from the frog, the power of balancing itself is lost ; when such a frog is thrown off its balance by inclining the plane on which it is placed, it falls down.   The special coördinating mechanism for balancing must, therefore, in this animal be situated in the optic lobes ; but after removal of these organs, the animal is still capable of a great variety of co-ordinate movements : unlike a frog retaining its spinal cord only, it can swim and leap, and when placed on its back immediately regains the normal position.   The cerebellum of the frog is so small, and in removing it injury is so likely to be done to the underlying parts, that it becomes difficult to say how much of the coördination apparent in a frog possessing cerebellum and medulla is to be attributed to the former or to the latter ; probably, however, the part played by the former is small.   In the mammal, as we have stated, removal of the whole middle and hind brain does away with the most marked of these coördinating mechanisms.   Removal of the pons Varolii alone has the same effect.   Injury to, or disease of, the more superficial parts of the corpora quadrigemina or of the cerebellum, does not appear to influence the movements of the body at large to any striking extent ; but there are many pathological cases, as well as experimental observations, tending to associate the coördinating mechanisms of which we are speaking with the deeper parts

of the cerebellum. It would be hazardous, in the present state of our knowledge, to make any definite statement concerning the share taken by these several cerebral structures in the various coördinations.

Forced Movements.

All investigators who have performed experiments on the brain, have observed as the result of injury to various parts of it remarkable compulsory movements. One of the most common forms is that in which the animal rolls incessantly round the longitudinal axis of its own body. This is especially common after section of one of the crura cerebri, more particularly of the external and superior parts, or after unilateral section of the pons Varolii, but has also been witnessed after injury to the medulla oblongata and corpora quadrigemina. Sometimes the animal rotates towards and sometimes away from the side operated on. Another form is that in which the animal executes "circus movements"—i. e., continually moves round and round in a circle, sometimes towards and sometimes away from the injured side. This may be seen after several of the above-mentioned operations, but is perhaps particularly common after injuries to the corpora striata and optic thalami. There is a variety of the circus movement said to occur frequently after lesions of the nates, in which the animal moves in a circle, with the longitudinal axis of its body as a radius, and the end of its tail for a centre. And this form, again, may easily pass into a simply rolling movement. In yet another form, the animal rotates over the transverse axis of its body, tumbles head over heels in a series of somersaults; or it may run incessantly in a straight line backwards or forwards until it is stopped by some obstacle. These latter forms of forced movements are frequently seen after injury to the corpora striata, even when a very limited portion of their gray matter is affected. Lastly, many, if not all, these various forced movements may result from injuries which appear to be limited to the cerebral cortex.

Attempts have been made to explain the rotatory movements by reference to unilateral paralysis or to spasm of various muscles of the body caused by the cerebral injury; and in the case of the "circus" movements with partial hemiplegia, which follow upon injury to the corpora striata or other parts, the explanation that the animal in progressing forward naturally bears on its paralyzed or weak side seems a valid one; but the movements may frequently be witnessed in the complete absence of either paralysis or spasm, and cannot, therefore, be always so explained. On the other hand, if the views urged just now concerning the nature of the coördinating mechanisms of the brain are true, it is

evident that they afford a general explanation of the phenomena, though our present knowledge will not permit us to explain the genesis of each particular kind of movement. Such gross injuries as are involved in dividing cerebral structures, or in injecting corrosive substances into the midst of cerebral organs, must of necessity, either by irritation or otherwise, seriously affect the transmission not only of afferent impulses in their cerebral course, but also of central impulses, inhibitory and the like, passing from one part of the brain to another; and must, therefore, seriously affect the due working of the general coördinating mechanisms. The fact that an animal can, at any moment, by an effort of its own will, rotate on its axis or run straight forwards, shows that the nervous mechanism for the execution of those movements is ready at hand in the brain, waiting only to be discharged; and it is easy to conceive how such a discharge might be affected either by the substitution of some potent intrinsic afferent impulse for the will or by some misdirection of the volitional impulses. Persons who have experienced similar forced movements as the result of disease, report that they are frequently accompanied, and seem to be caused, by disturbed visual or other sensations; thus, when they suddenly fall forward, they say that they do so because the ground in front of them appears to sink away beneath their feet. Without trusting too closely to the interpretations the subjects of these disorders give of their own feelings, we may at least conclude that the disorderly movements are in many cases due, not to any paralytic or other failing of the simple muscular instruments of the nervous system, but to a disorder of the coördinating mechanism, which in many cases is itself the result of disordered sensory impulses. And this view is supported by the fact that many of these forced movements are accompanied by a peculiar and wholly abnormal position of the eyes, which alone might, perhaps, explain many of the phenomena.

Sec. 3.—The Functions of the Cerebral Convolutions.

Using the word cerebral hemisphere for brevity's sake to denote the cortical substance of the cerebrum (for we have no reason to think that the fibres of the white matter serve for any other than conducting functions, and it is advisable to keep apart the consideration of the corpora striata), we have endeavored to show that in respect to function a broad line separates these structures from the rest of the brain. We have seen reason to think that will and intelligence are associated with the former, while the latter are concerned in elaborating and coördinating afferent and efferent impulses in such a way as to furnish a complicated

nervous machinery, of which the former makes use in carrying out the voluntary and intelligent movements of the body. It is not uncommon to speak of the cerebral hemispheres as "the seat of" will and intelligence. Such a phrase is, however, open to objection. It suggests that if the cerebral hemispheres could be kept alive quite isolated from the rest of the brain, the processes of volition and intelligence, though unable to manifest themselves by any outward show, would still go on. But we are not in a position to accept, without hesitation, such an assumption. All we know is that the existence of volition and intelligence are dependent on the connection of the cerebral cortex with the rest of the brain. When that connection is broken, they disappear ; and it may be that what we call volition and intelligence are the product of both the cerebral hemispheres and other parts of the brain working together by virtue of their connections, and ceasing so to work when the connections fail ; on the other hand, it may be that they are generated in the former alone, and that the connections only serve to allow the former to make use of the machinery of the latter. Our present knowledge will not allow us to decide between these two views; meanwhile, it will be well not to consider the latter as the only possible one.

With this preliminary caution, we may now proceed to inquire whether we can attribute different functions to different parts of the cerebral cortex. All the older observers, Flourens and others, agreed that when the cerebral cortex was gradually removed, piece by piece or slice by slice, no obvious effects manifested themselves, either in the intelligence or volition of the animal, when the first small portions were taken away ; but that, as the removal was repeated, the animal became more and more dull and stupid, until at last both intelligence and volition seemed to be entirely lost. It has been frequently observed that in case of wounds of the skull large portions of the brains of men might be removed without any marked effect on the psychical condition of the patients. The brain when exposed was found not to be sensitive ; and ordinary stimuli applied to the surface of the convolutions of animals failed in the hands of most experimenters to produce any clearly recognizable effect. Hence, it became very common to deny the existence of any localization of functions in the convolutions of the hemisphere, and to speak of the brain as "acting as a whole," whatever that might mean. On the other hand, pathological observation seemed clearly to show that diseased conditions limited to different areas of the convolutions, produced different effects. It was found that in the case of circumscribed lesions confined to parts of the cerebral cortex, the effects, whether in the way of paralysis or of convulsive movements, were frequently confined to certain regions of the

body, or were even limited to particular groups of muscles. One set of phenomena in particular spoke very strongly in favor of definite convolutions—*i. e.*, definite parts of the cerebral cortex having definite functions. In certain cases of cerebral disease, the patient is unable to speak at all, or speaks imperfectly or incorrectly. It is obvious that the failure to speak or to speak properly may be brought about in various ways; the fault may be simply in the tongue or hypoglossal nerve, or it may lie in one or other of the series of central and cerebral processes which issue in coördinate impulses being sent to the organs of speech. Using the word aphasia, as is usually done, in its general sense, to denote the partial or complete loss of articulate speech due to cerebral causes, we may say that aphasia was found to be so closely associated with disease of a definite part of the brain, viz., the posterior portion of the third frontal convolution, Fig. 235 (9) (10), as to afford almost irresistible proof that this particular part of the brain must be specially connected with the faculty of speech. Moreover, the disease occurs in so great a majority of cases on one side of the brain only, namely, the left (aphasia being frequently a symptom accompanying right hemiplegia, or paralysis of the right side of the body, the disease in such cases affecting other parts of the brain as well), as to suggest the idea that in the act of speech, one side of the brain only is used. On this point, however, we must not dwell now; we cannot here discuss the question of unilateral cerebral activity, or the exact nature of the failings which lead to the loss of, or to errors in, speech, or with what particular link or links in the chain of cerebral events leading to speech, whether mainly afferent or mainly efferent ones, this portion of the cortex is associated; we simply quote these cases of aphasia, as affording proof of the localization of function in the cerebral cortex.

For a while then the teachings of pathology and experiment were contradictory; but continued experimental inquiry showed that the former were in the right. Hitzig and Fritsch were the first to show that the local application of the constant galvanic current to particular convolutions and to particular parts of convolutions gave rise to definite coördinate movements of various groups of muscles. Thus, while the stimulation of one spot (Fig. 234) caused movements in the muscles of the neck, another caused extension with adduction of the foreleg, a third movements of the hindleg, a fourth movements of the eye and other parts of the face. In fact, they and Ferrier, who, using chiefly the interrupted or faradic current, repeated and extended their observations, were able to map out the convolutions of the front and middle parts of the hemisphere of the dog (Figs. 234, 235), cat, monkey (Figs. 235, 236), and other animals, into a

number of precisely limited areas, the stimulation of each area producing a distinct and limited movement, while stimulation of a large surface produced general convulsions. The movements were so precise that they answered each to the spot stimulated almost as completely as a note answers to a key struck on the piano. A somewhat similar relationship has also been observed between various regions of the cortex and the secretion of saliva, the beat of the heart, the condition of the pupil, the action of vaso-motor nerves, and other organic functions.

FIG. 234.
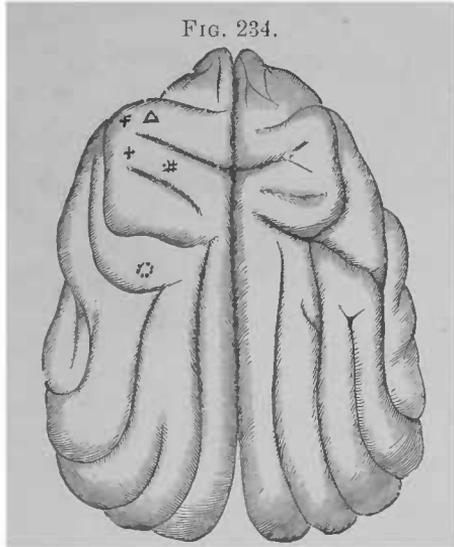
THE AREAS OF THE CEREBRAL CONVOLUTION OF THE DOG, ACCORDING TO HITZIG AND FRITSCH.

(1) △ The area for the muscles of the neck.

(2) ⊢ The area for the extension and adduction of the forelimb.

(3) + The area for the flexion and rotation of the forelimb.

(4) ⇌ The area for the hindlimb.

Running transversely towards and separating (1) and (2) from (3) and (4) is seen the *crucial sulcus*.

(5) ⊘ The facial area.

These experiments, which have not only been confirmed by many observers, but may, with due care, be successfully repeated by any one, clearly show, in spite of some discordance among various authors as to the exact position and extent of the several "areas," that there is a connection between electric stimulation of certain areas of the brain-surface and certain bodily movements. The areas in question have been spoken of by some authors as "motor centres." Such a term is, however, undesirable, since it suggests that the brain-surface in a given area is largely occu-

pied in giving rise to the coördinate nervous impulses which carry out the movement resulting from stimulation of the area; whereas, as we have already seen from the behavior of an animal deprived of its cerebral hemispheres, coördination is effected in parts of the brain other than the surface of the cerebral hemi-

Fig. 285.
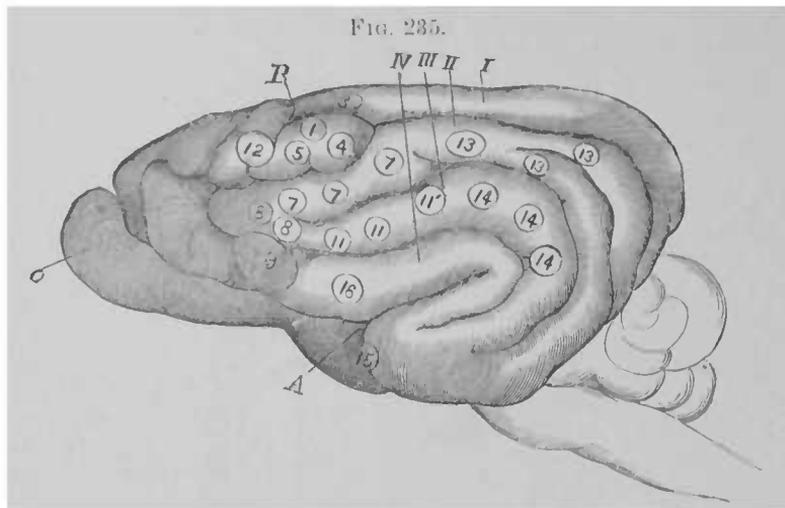
THE AREAS OF THE CEREBRAL CONVOLUTIONS OF THE DOG, ACCORDING TO FERRIER.

O, the olfactory lobe; A, the fissure of Sylvius; B, the crucial sulcus. Stimulation by the interrupted current of the areas indicated by the several circles produces the following results:

(1) The hindleg is advanced as in walking

(3) Lateral or wagging motion of the tail.

(4) Retraction and adduction of the opposite forelimb.

(5) Elevation of the shoulder of, and extension forwards of, the opposite forelimb.

(7) Closure of the opposite eye caused by combined action of the orbicular and zygomatic muscles.

(8) Retraction and elevation of the opposite angle of the mouth.

(9) The mouth is opened and the tongue moved, sometimes barking is produced

(11) Retraction of the angle of the mouth.

(12) Opening of the eyes and dilation of the pupils; the eyes and then the head turning to the opposite side.

(13) The eyeballs move to the opposite side.

(14) Pricking or sudden retraction of the opposite ear.

(15) Torsion of the nostril on the same side.

(16) Elevation of the lip and dilation of the nostril.

spheres; and all that the areas in question do is to make use in some way or other of these lower coördinating mechanisms.

As will be seen from an inspection of the figures the areas, stimulation of which gives rise to definite movements, are distributed over a part only of the surface of the hemispheres. Over large tracts of the surface electric stimulation gives rise to no movements at all. It has been supposed that the stimulation

of these parts gives rise to various psychical states, of such a nature that they do not manifest themselves by any movements as do the psychical states brought about by stimulation of the so-called motor areas ; and hence these tracts have been supposed to be composed of so-called " sensory " centres, a term even more objectionable than " motor " centres.

FIG. 236.
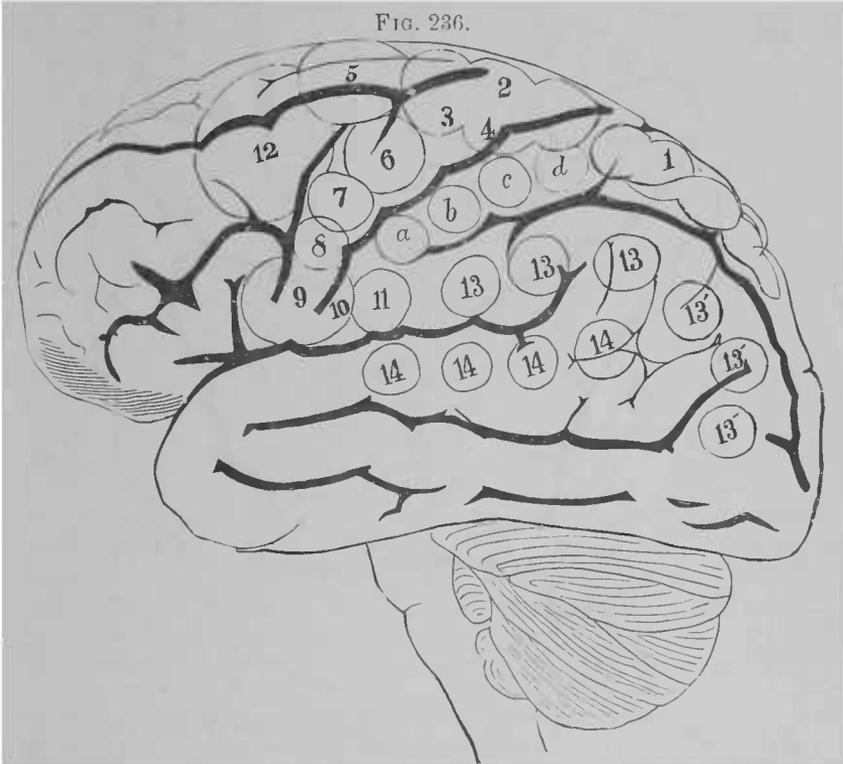
FIGS. 236 AND 237.—SIDE AND UPPER VIEWS OF THE BRAIN OF MAN, WITH THE AREAS OF THE CEREBRAL CONVOLUTIONS, ACCORDING TO FERRIER.

The figures are constructed by marking on the brain of man, in their respective situations, the areas of the brain of the monkey as determined by experiment, and the description of the effects of stimulating the various areas refers to the brain of the monkey.

(1) (On the posterior-parietal [superior parietal] lobule.) Advance of the opposite hindlimb, as in walking.

(2), (3), (4) (Around the upper extremity of the fissure of Rolando.) Complex movements of the opposite leg and arm, and of the trunk, as in swimming.

(*a*), (*b*), (*c*), (*d*) (On the postero-parietal [posterior central] convolution.) Individual and combined movements of the fingers and wrist of the opposite hand. Prehensile movements.

(5) (At the posterior extremity of the superior frontal convolution.) Extension forward of the opposite arm and hand.

(6) (On the upper part of the antero-parietal or ascending frontal [anterior central] convolution.) Supination and flexion of the opposite forearm.

FIG. 237.
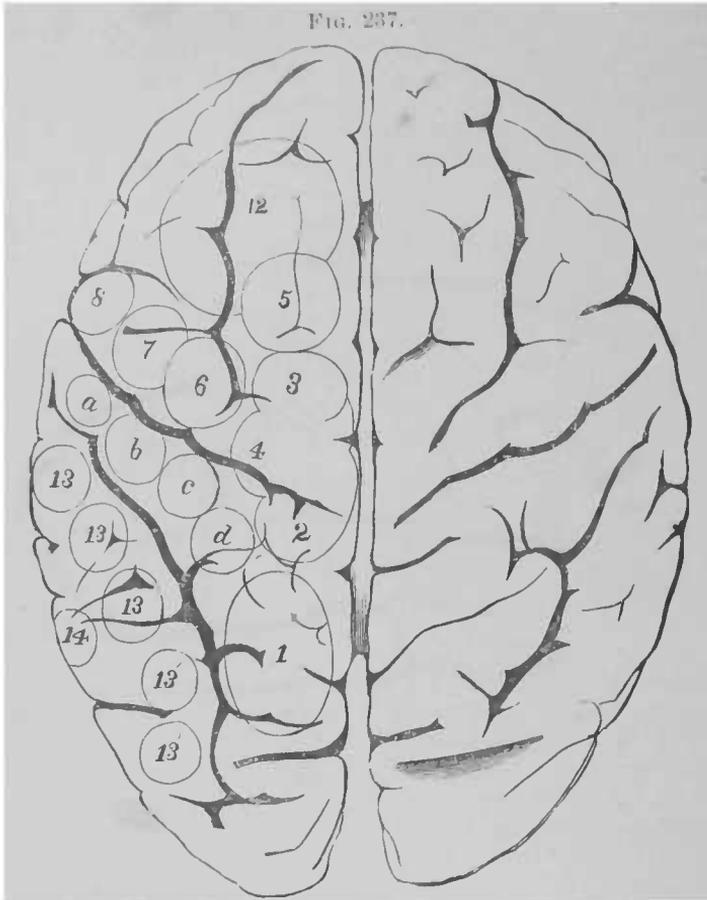
(7) (On the median portion of the same convolution.) Retraction and elevation of the opposite angle of the mouth by means of the zygomatic muscles.

(8) (Lower down on the same convolution.) Elevation of the ala nasi and upper lip with depression of the lower lip on the opposite side.

(9), (10), (At the inferior extremity of the same convolution, Broca's convolution.) Opening at the mouth with (9) protrusion and (10) retraction of the tongue; region of aphasia, bilateral action.

(11) (Between (10) and the inferior extremity of the postero-parietal convolution.) Retraction of the opposite angle of the mouth, the head turned slightly to one side.

(12) (On the posterior portions of the superior and middle frontal convolutions.) The eyes open widely, the pupils dilate, and the head and eyes turn towards the opposite side.

(13), (13'), (On the supra-marginal lobule and angular gyrus.) The eyes move towards the opposite side with an upward (13) or downward (13') deviation. The pupils are generally contracted. (Centre of vision.)

(14) On the infra-marginal or superior [first] temporo-sphenoidal convolution.) Pricking of the opposite ear, the head and eyes turn to the opposite side, and the pupils dilate largely. (Centre of hearing.)

Ferrier, moreover, places the centres of taste and smell at the extremity of the temporo-sphenoidal lobe, and that of touch in the gyrus uncinatus and hippocampus major.

Confining ourselves, for the present, to the areas, stimulation of which produces movements, the question naturally presents itself, Do events of importance take place in the gray matter itself when stimulated, or is it that either by stimulation of the fibres of the white matter, or by simple escape downwards of the current employed as a stimulus, the parts below, such as the corpora striata, are stimulated, and that the shaping of the movements according to the locality operated on is effected in these lower parts and not at the surface itself? On this point considerable controversy has taken place. On the one hand, it seems clear that localization of function—that is to say, the occurrence of definite movements as the result of stimulation of definite parts—may take place in the regions of the brain below the cortex, since the appropriate movements follow upon stimulation of the several cortical areas, when the gray matter has been removed, or rendered functionally incapable by treatment with acids and the like, or separated functionally from the white matter below by an incision parallel with the surface; and definite movements have been even obtained by stimulation of definite parts of the surface of the corpora striata. On the other hand, we have adequate evidence that when movements in a muscle or group of muscles are produced by stimulation of an area of the surface of the cerebrum, the movements differ in character, for instance in the length of the latent period, the form of the muscle curves, etc., according as the stimulus is applied to the intact cortex or to the underlying white matter. Further, the irritability of the gray matter, falling and rising with the condition of the animal, is much more variable than is that of the white matter; and, while under certain circumstances, stimulation of the gray matter is apt to give rise to general epileptiform convulsions, stimulation of the white matter rarely, if ever, produces such an effect. Without discussing the matter any more fully, we may say that the preponderating evidence seems clearly in favor of the view that when the gray matter is stimulated, some events of an important kind do take place in the gray matter itself; in other words, we have evidence of a localization of function in the cortex, inasmuch as when a given area of the cortex is stimulated the movements in a definite group of muscles which result are, in part at least, due to changes taking place in the gray matter itself of that area.

If such is the case, if events of importance having an especial connection with certain muscles result from the stimulation of a given area, it is only reasonable to conclude that in actual life more or less similar events, having similar relations to the muscles, take place in the area from time to time. Further, it seems also reasonable to suppose that these events are of such a kind

that the area may be regarded as a "point d'appui" by which will and intelligence are brought to bear on the muscles corresponding to the area. We may very fairly imagine that when a dog wills to extend the fore-limb, the cerebral changes are of such a kind that eventually processes are set up in the gray matter of the area for extension of the fore-limb similar to those which arise from stimulation of the area. But if this be the case, then removal of the area ought permanently to remove also, from the dominion of the will, the muscles employed in extension of the limb; the chain of events leading down from the inception of the voluntary effort to the actual contraction of the appropriate muscles ought to be broken in the link constituted by the events occurring in the cortical area; the dog ought thereafter to be unable to extend his fore-limb by any direct effort of the will. The results of experiment, however, show that this is not the case. Immediately after the operation by which the area is removed, more or less paralysis, it is true, may be observed in the corresponding muscles. But this soon passes away, and complete power over the muscles may be regained. The temporary paralysis seems to be a sort of inhibitory effect due to the injury caused by the operation; and, though the experiment confirms the view that some special connection exists between the cortical area and the appropriate group of muscles, it disproves the view that the area serves as a direct instrument of the will. Nor can we take refuge in the idea that some other area has taken up vicariously the duties of the lost area. This is disproved by the observations of many inquirers which go to show that not only many different parts of the brain, but a very large portion of the whole brain, may be removed without any clear and definite paralysis of any group of muscles being occasioned. In the experiments of Goltz, which we shall mention directly, the loss of a large mass of the cerebral convolutions diminishes the movements of the body, inasmuch as it curtails the general action of the intelligent will which brings them about, but does not withdraw any particular set of muscles from the influence of the, so to speak, shortened will which is left to the animal. Indeed, we have reason to think that when in such operations directed solely to the removal of the cerebral convolutions, paralysis of any particular group of muscles occurs, mischief must unwittingly have been done to other parts of the brain.

What then can we conclude as to the nature of the events which take place in the several cortical areas? To this question unfortunately no clear answer can yet be given; for the results of different inquirers are so far irreconcilably opposed.

On the one hand, one observer (Munk) states that the removal

of a certain area in the posterior lobes produces no other effect whatever but blindness. He further states that removal of small portions of the area leads to partial blindness—that is, to the formation so to speak of artificial blind spots in the field of vision corresponding to the spots of cerebral cortex removed ; so that the retinal image may be conceived of as projected, as it were, on to the "visual area" of the cerebral convolutions. Munk has moreover been led, for reasons which we cannot enter into here, to believe that removal of part of this area (the circumferential part) leads to what may be called "absolute blindness," *i. e.*, the inability to gain conscious sensations of the images falling on the retina, whereas removal of another part (the central part) leads to what may be called "psychical blindness," *i. e.*, the inability to form an intelligent comprehension of the visual impressions received. The latter, he maintains, may eventually be recovered from by processes which may be crudely spoken of as the deposition of new visual experiences in the visual area. We cannot discuss these results in detail here, but we may add that Munk has similarly been led from his experiments to conclude that the rest of the cerebral surface may be parcelled out into auditory, olfactory, tactile, etc., areas, in fact that all the sensory impulses which stream upon the living body are projected as sensations on to the cerebral convolutions in definite order, being there elaborated into perceptions and experiences, this reception and elaboration being the special work of the cerebral cortex. And one author (Schiff) has from the first maintained that the cortical "motor" areas associated with movements in particular regions of the body, have to do with the tactile sensations arising in those regions, and that the movements arising from stimulation of the areas are tactile reflex actions started in the cortex of the brain instead of in the periphery of the body.

On the other hand, another observer (Goltz) maintains that the whole of the posterior lobes may be removed without affecting vision any more directly than does the removal of the anterior or middle lobes. In fact this author in his latest, as in his earlier researches, insists most strongly that he can no more obtain distinct evidence of localization in reference to vision or other sensations than in reference to movements. When in a dog the lesions are slight the recovery from imperfections of vision, of the other senses, and of general sensibility which follow immediately on the operation, may be complete. When a larger portion of brain is removed, whatever be the region of the hemisphere acted on, certain peculiar imperfections of sight and other sensations, corresponding to the psychical blindness spoken of just now as observed by Munk, become striking, and may

remain permanent. In the case of vision the salient character of this imperfection is, that though the animal evidently can see, and uses his sight successfully in avoiding obstacles and guiding his movements, yet what he sees does not produce its usual effect on him; he obviously fails to recognize many things, and has become indifferent to scenes which formerly affected him strongly. Thus, a dog from which portions of the cerebral hemispheres have been removed, fails to recognize his food by sight; when he is threatened with the whip, he is not cowed; when the hand is held out for his paw he makes no response; and though before the operation he became violently excited when the laboratory servant dressed in a fantastic garb was presented to him, he remains after the operation perfectly indifferent to the same image. Another striking character of this imperfection of vision is that recovery from it to a considerable extent is, under certain circumstances, possible by means of educational exercise; the dog, which at first could not recognize his food by sight and was indifferent to the whip, learns after a while to know the one and to respect the other. It would be hazardous, however, to insist upon the view that in such a case the failure was of distinctly psychical origin, due to the want of intelligent power fully to appreciate the crude sensations. It might be that the sensations were themselves imperfect, and unable to give rise to sufficiently definite perceptions, all things possibly appearing to the dog as if seen through a gauze with all their colors washed out. With such an imperfect vision a dog might readily fail to recognize meat by sight and might easily regard with unconcern any figure however fantastically dressed.

According then to the views advocated by Goltz, barring some possible difference in the extent to which the intellect or the emotions are respectively affected according to the part of the brain operated on, removal of the brain gives no evidence as to any part of the mind (using that word in a wide sense) being connected with any particular part of the cerebral cortex. According to the views advocated by Munk, all the sensations which form the basis of psychical activity, are very definitely associated with distinct areas of the convolutions; and nearly all those, Ferrier and others, who have urged the doctrine of localization of function in the cerebral cortex have been led to entertain conceptions more or less similar to those of Munk. The time is not yet ripe to decide dogmatically between these conflicting views, though it appears to us that, of the two, the former one is the nearer the truth. All the more so since there are some reasons for thinking that in those operations which appear to be confined to the cortex and the white matter immediately beneath this, damage is not unfrequently done to more central parts of

the brain, such as the corpora striata and optic thalami; and it is quite possible that where blindness becomes a prominent symptom after these operations, the immediate cause of that blindness is not in the cortex but in the optic thalami.

But if we accept Goltz's conclusions, there still remains at least an apparent contradiction between these and the conclusions we reached just now concerning the results of stimulation of the surface; but this we must leave for further inquiries to clear up.

Before leaving the subject of the cerebral convolutions we wish to call attention to certain remarkable results which have been observed to follow upon stimulation of the cerebral cortex, under various circumstances, more particularly in different stages of the influence of narcotic drugs such as morphia. In certain stages of narcotism by morphia, the dose required varying according to the individual, but generally being large, the irritability of the cortex is diminished; currents which previously readily produced contractions in the muscles corresponding to the area stimulated, now produce little or none at all; and, indeed, the cortex may be thus brought to such condition that even very strong currents produce no movements at all. In such cases, movements may, at times at all events, be brought about by removing the cortex and applying the electrodes directly to the underlying white matter, thus showing that the morphia produces its effects, in part at least, by acting directly on the cortex itself. From this we gain an additional argument in favor of the independent irritability of the cortex.

On the other hand, in certain stages of the action of morphia the irritability of the cortex is not diminished, but on the contrary increased. It is well known that an animal under the influence of morphia frequently manifests an increase of reflex excitability, being, for instance, remarkably sensitive, and readily responding to the stimuli of sounds and noises; and a similar exaltation has been observed in reference to the influence of electric stimuli applied to the cortical areas. At times this increased excitability may become so developed that the application of even a moderate stimulus leads to epileptiform convulsions, lasting for some considerable time. Not unfrequently, indeed, experiments of this kind have to be suspended on account of the appearance of these convulsions. When any particular "motor area" is being stimulated the convulsive contractions generally appear first in the appropriate group of muscles and thence spread first over the same side and then over the other side of the body until sometimes the whole frame is convulsed. When the cortex is removed, and the electrodes are applied directly to the subcortical white matter, these convulsions are not nearly so readily produced, and when they appear are not

exactly of the same character, being generally limited to one side of the body. It would thus appear that the convulsions, though carried out by the nervous machinery of the lower parts of the brain, and more especially perhaps by the so-called "convulsive centre" in the medulla oblongata, originate and to a large extent are fashioned by changes in the cerebral cortex; and, though this is a matter into which we must not go more fully here, pathological and clinical observations similarly tend to show that epilepsy itself, in certain cases at all events, is the product of an abnormal action of the cerebral convolutions.

From what has been said in previous sections, more particularly in reference to the reflex actions of the spinal cord (p. 592) and coördinating mechanisms (p. 734), the reader will be prepared for the observation that the phenomena of these convulsions suggest the idea that they arise not so much from a positive increase in the explosive, discharging energy of the central nervous mechanisms, as from a withdrawal of certain normal restraining inhibitory influences. We have already more than once insisted that almost any event in the central nervous system is to be regarded not as the result of the activity of some one isolated nervous machine, but as the outcome of various conflicting processes, some positive, tending to bring out the event, others negative, offering a resistance or bringing inhibitory influences to bear. And it would seem that this is even more true perhaps of the cerebral convolutions than of any other part of the nervous system. Such a view is at all events strongly supported by some observations lately made by Heidenhain. If in an animal under morphia, the contractions in a muscle resulting from the stimulation of the appropriate "motor area," by a current of known strength, be recorded, the sciatic nerve then divided or torn or otherwise irritated, and the motor area again stimulated with the same strength of current, the contractions will be much less in height, and the latent period will be much longer. This, of course, is nothing more than an instance of somewhat ordinary inhibition. But, in certain stages of the influence of morphia, the following remarkable result makes its appearance. If a subminimal stimulus be found—that is, a current of such intensity that applied to a motor area, it will produce no movement, but if increased ever so slightly will give a feeble contraction of the appropriate muscles—it may be observed that a slight stimulus, such as gently stroking the skin over the muscles in question, or, indeed, some other part of the body, will render the previous subminimal stimulus effective, and so call forth a movement. Thus, if the area experimented on be that connected with the lifting of the forepaw, and the subminimal stimulus be applied to the area at intervals, after several ineffec-

tive applications, a gentle stroke or two over the skin of the paw will lead to the paw being lifted the next time the stimulus is applied to the area. On the other hand, in certain other stages of the influence of morphia, the convolutions and the rest of the nervous system are in such a condition that the application of even a momentary stimulus to an area leads to a long-continued tonic contraction of the appropriate muscles. Under these circumstances, a gentle stimulus, such as stroking the skin, or blowing on the face, applied immediately after the application of the electric stimulus to the area, suddenly cuts shorts the contraction, and brings the muscles at once to rest and normal flaccidity. Thus, according to the condition of the central nervous system (and in these instances the effect appears to be dependent largely though not wholly on the condition of the cerebral cortex) the same kind of stimulus, and, indeed, we might almost say the same stimulus, will lead now to exaltation, now to inhibition of a nervous action. We must not dwell on these matters any further, though we might point out the interesting even if partial light which they throw on the phenomena known as Hypnotism. We have introduced them chiefly to emphasize the view that the nervous system is not to be considered as a collection of isolated organs, each fulfilling its functions independently of its fellow, but as a large machine, integrated into a whole, the constituent parts of which are in almost all its actions acting and reacting on each other in various ways. So much so does this appear to be the case, that the secondary influences, often of the kind called inhibitory, of outlying parts prove as important to the due function of any particular structure as its own more direct action.

SEC. 4.—THE FUNCTIONS OF OTHER PARTS OF THE BRAIN.

If the views just expressed are true, then it is clear that the proper method to study the brain is to trace out a cerebral operation along its chain of events rather than to seek to attach readily definable functions to the cerebral anatomical components.

We may, therefore, be permitted to summarize very briefly what can be fairly placed under this heading.

Corpora Striata and Optic Thalami.—These two bodies, often spoken of as "the basal ganglia," are undoubtedly the great means of communication between the cerebral hemispheres on the one hand, and the crura cerebri on the other. Though some fibres appear to pass from the crura by or through the ganglia to the cerebral convolutions without being connected with the nerve-cells of those ganglia, the great mass of the peduncular fibres

are probably connected with the superficial gray matter of the hemispheres in an indirect manner only, the lower or anterior fibres (*crusta*) passing first into the corpora striata, and the upper or posterior fibres (*tegmentum*) into the optic thalami. This anatomical disposition would lead us to suppose that these bodies have important functions in mediating between the psychical operations of the cerebral convolutions on the one hand, and the sensori-motor machinery of the middle and hind brain on the other; and the separate courses taken by the peduncular fibres would further lead us to expect that the functions of the corpora striata differ fundamentally from those of the optic thalami.

When in the human subject a lesion occurs involving both these bodies, on one side of the brain, the result is a loss of sensation in, and voluntary power over, the opposite side of the body and face, a so-called hemiplegia, which may be absolutely complete without any impairment whatever of the intellectual faculties. The will and the psychical power to receive impressions are present in their entirety, but neither efferent nor afferent impulses can make their way to or from the peripheral organs and the cerebral convolutions. The injury to the basal ganglia blocks the way. In the great majority of cases, the anæsthesia (or loss of sensation) and akinesia (or loss of movement) are absolutely confined to the opposite side of the body; and the cases in which a lesion of the basal ganglia of one side of the brain affects the same side of the body or both sides, must be regarded as exceptional, and explicable as the results of the action of one side of the brain on the other side either of the brain or of some region of the cerebro-spinal axis. The results of experiments on animals agree entirely with the general experience of pathologists, that lesions of the corpora striata and optic thalami produce their effects on the opposite side of the body. Whatever be the view taken concerning the decussation of sensory and motor impulses in the spinal cord (see p. 705), it must be admitted that both kinds of impulses cross over completely somewhere during their transmission to and from the basal ganglia and the peripheral organs.

When, however, we have admitted that these bodies act, as it were, the part of middlemen between the cerebral convolutions and the rest of the brain, we have gone almost as far as facts will support us. We are not at present in a position to state dogmatically what is the nature of the mediation which either body respectively effects. A very tempting hypothesis is one which suggests that the corpora striata are concerned in the downward transmission and elaboration of efferent volitional impulses, and the optic thalami in a similar upward transmission

and elaboration of afferent sensory impulses; and there are many facts which may be urged in favor of this view.

The evidence in this matter afforded by pathology is, perhaps, the most consistent, but not wholly so. A number of cases may be cited to show not only that lesions of a corpus striatum may be accompanied by akinesia without anæsthesia, but that lesions of an optic thalamus may cause anæsthesia without actual akinesia—that is, without any further interference with the execution of voluntary movements than is occasioned by the loss of the coördinating sensations. Of these two classes of cases, the latter is the more valuable, since all clinical experience shows that any lesion more readily interferes with volitional movements than with the reception of sensory impressions. Convulsions are not common when the lesions are confined to these bodies; but when witnessed they can generally be referred to the corpora striata rather than to the optic thalami; like the paralysis, the convulsions are generally limited to the opposite side of the body, though feeble movements may occasionally be seen on the same side as well. But it would be dangerous to trust too much to evidence of this kind; for numerous cases have been recorded where an injury apparently confined to one corpus striatum has had as part of its results anæsthesia of the opposite side of the body; and others where disease apparently confined to an optic thalamus has caused loss of movement as well as of sensation.

The evidence obtained by means of experiments on animals is still more discordant. Some observers have found that stimulation, either mechanical or electrical, of the corpora striata gives rise to convulsive movements, while stimulation of the optic thalami does not; and have seen in these results a confirmation of the view we are discussing. Such a confirmation is, at best, a feeble one, and, moreover, is not supported by the results of all observers. Some observers again have found that removal or destruction by the injection of corrosive substances, of both nuclei lenticulares (the extra-ventricular portions of the corpora striata) leads to a suppression of voluntary movements almost as complete as if both hemispheres were removed, whereas after removal or destruction of both nuclei caudati (intra-ventricular portions of the same bodies) voluntary movements still persist; and it has been affirmed that the removal or destruction of the optic thalami may with care be effected without the animal appearing any the worse. In the absence of more exact knowledge, it is useless to attempt to form any clear judgment; and the view we stated above as to the motor functions of the corpora striata and sensory functions of the optic thalami may be allowed to stand as neither definitely disproved nor satisfactorily proved,

and as in any case affording an inadequate expression of the part played by these masses in the general work of the brain. Two points we may venture to call attention to, which, as far as they go, may be used as arguments in support of the above view. Almost all observers agree that after injuries to the corpora striata, more particularly after one-sided or after partial injuries, and especially after injuries of the nuclei caudati, forced movements, such as those of which we spoke on p. 735, are very apt to make their appearance. With regard to the optic thalami, on the other hand, there is an agreement both of experimental and pathological evidence in favor of the view (which, as the very name of the bodies shows, is an old one) that these structures are, in some way or other, concerned in vision. Where the optic thalami are directly involved in an injury to or disease of the brain, blindness, or, at least, some imperfection of vision is a frequent result; and there are reasons for thinking that in some, at all events, of the cases where blindness has resulted from removal of the cerebral cortex of the hinder part of the hemispheres, the optic thalami have been either directly or secondarily affected.

Corpora Quadrigemina.—We have already seen that the centre of coördination for the movements of the eyeballs (p. 639), and that for the contraction of the pupil (p. 593), lie in the neighborhood of the upper or anterior pair of the corpora quadrigemina. These two centres are associated together in such a way that when the eyeballs are voluntarily directed inwards and downwards, as for near vision, the pupils are at the same time contracted; and when the eyeballs are directed upwards, and return to parallelism, the pupils are dilated to a corresponding extent; when both eyeballs are moved together sideways the pupils remain unchanged. We have seen (p. 639) that the various movements of the eyeballs may be brought about by direct stimulation of particular parts of the anterior corpora quadrigemina, and are then also accompanied by the appropriate changes in the pupils. The association therefore of the movements of the pupil and of the ocular muscles is not simply psychical in nature, but is dependent on the close connection of their respective centres. From the fact of the movements of the eyeball and pupil being so readily and variously excited by stimulation of the anterior corpora quadrigemina, it has been inferred that the centres for these movements lie in those bodies; it would appear, however, that what may be called the real or immediate centres of these movements lie beneath the corpora quadrigemina, in the front part of the floor of the aqueduct of Sylvius, and therefore are affected in a indirect manner only when the corpora quadrigemina are stimulated.

It was long ago observed that unilateral extirpation of the corpora quadrigemina in mammals or of the optic lobes in birds produced blindness in the opposite eye ; and the same result has been gained by many subsequent observers. We have seen moreover that both frogs, birds, and mammals continue to receive and within limits to react upon visual impressions after the total removal of the cerebral hemispheres. From these facts we infer that visual sensory impulses become transformed into visual sensations in the corpora quadrigemina ; or, in other words, that these nervous structures are centres of sight. But they are so in a limited sense only. We have seen that destruction or injury of the cerebral hemispheres profoundly affects vision ; even admitting that in such cases the results may be in part at least due to concomitant failures in the optic thalami, we may still venture to say that in the absence of the cerebral convolutions, a crude vision, devoid of distinct visual perceptions, is probably all that is possible. The processes constituting distinct and perfect vision, in fact, begin in the retina, are partially elaborated in the corpora quadrigemina, and further developed in the optic thalami, but do not become perfected until the cerebral convolutions have been called into operation. Anatomical considerations lead us to suppose that the anterior pair of the corpora quadrigemina are alone connected with the optic tract, and so with the external corpus geniculatum and optic thalamus. Hence, we may infer that it is the anterior pair alone which are thus concerued in vision, and that the posterior pair have some other function.

In those animals (*ex. gr.*, rabbits) in which unilateral destruction of the corpora quadrigemina entails blindness of the opposite eye, and yet does not affect at all the visual sensory impulses, originating in the eye of the same side, it is obvious that complete decussation of the sensory impulses must take place before the centre is reached. The question, however, whether the decussation of fibres (and consequently of impulses) in the optic chiasma is complete or incomplete, whether the optic tract of one side is the continuation of the fibres in the optic nerve of the opposite side exclusively, or whether it is composed of representatives of the optic nerves of both sides, is one which has been much debated, both from an anatomical and a physiological standpoint. In the case of mammals the evidence goes to show that in some kinds of animals (rabbits) the decussation is complete, but in others (dogs) more or less incomplete. In man a peculiar affection of vision, which may be spokeu of under the general name of hemiopia, is a frequent symptom of diseases of the brain. In this affectiou portions of the field of vision are wanting ; thus, a patient sometimes can see nothing in the right half or the upper half of the fields of vision of both eyes ; look-

ing at a man or a house he can only see half the object, the left half or the lower half as the case may be. Hemiopia of both eyes has been observed in cases in which disease was apparently limited to one side of the brain; and these cases, added to other evidence, lead to the conclusion that in man the decussation is incomplete.

Many observers have noticed that injury or removal of the corpora quadrigemina on one side frequently caused forced movements, and that removal of the whole mass led to great want of coördination. These results are quite in harmony with the fact mentioned above (p. 725) concerning the coördinating functions of the optic lobes in frogs. But at present we have no exact knowledge concerning the nature of the coördination, and what relations are borne in this respect by the corpora quadrigemina to the cerebellum, crura cerebri, and pons Varolii.

Various observers have witnessed as the result of stimulation of the corpora quadrigemina movements of the several parts of the alimentary canal, and of the urinary bladder, changes in blood-pressure, and alterations in the working of the respiratory mechanism, indicating that these bodies have a special connection with the centres (in the medulla oblongata and spinal cord respectively) concerned in carrying on these movements.

Cerebellum.—We have already referred to the cerebellum as being probably concerned in the coördination of movements. It was long ago observed that when a small portion of the cerebellum was removed from a pigeon, the animal's gait became unsteady; when larger portions were taken away its movements became much more disorderly, and when the whole of the organ was removed an almost total loss of coördination supervened. When the portion removed was small, the disorderly movements which at first appeared eventually vanished, but when a large portion was removed the loss of coördination became permanent. Subsequently observers have obtained similar results in other animals; and it has in general been found that lateral or unsymmetrical lesions and incisions produce a greater effect than those which are median or symmetrical. Section of the middle peduncle on one side almost invariably gives rise to a forced movement, the animal rolling rapidly round its own longitudinal axis; the rotation is generally though not always towards the side operated on; and is accompanied by nystagmus—*i. e.*, by peculiar rolling movements of the eyes suggestive of vertigo; frequently one eye is moved in one direction—*ex. gr.*, inwards and downwards, and the other in a different or opposite direction—*ex. gr.*, outwards and upwards. As we have already said, the permanent effects which follow upon injury to the semicircular canals, have been attributed by some to secondary mischief

being set up in the cerebellum. The clinical evidence is discordant, for though unsteadiness of gait has been frequently witnessed in cases of cerebellar disease, many histories have been recorded in which extensive disease, amounting at times to almost complete destruction, of the cerebellum has existed without any obvious disturbance of the coördination of movements. Still the experimental evidence is so strong, that we must consider the cerebellum as an important organ of coördination, though we are unable at present to define its functions more exactly.

In this connection we may observe that the history of the development of the spinal cord (see p. 703) tends to connect a definite portion of the lateral columns of the spinal cord with the cerebellum; but the meaning of this connection is obscure.

Attempts have been made to connect the cerebellum with the sexual functions; but there is no satisfactory evidence of any such relation. As we shall see later on, the nervous centres connected with the sexual and generative organs are seated, in the case of dogs at least and probably of all animals, in the lumbar spinal cord; and all or nearly all sexual phenomena may be witnessed in animals, in which the lumbar spinal cord has been isolated by section from the rest of the cerebro-spinal system. Galvanic stimulation of the cerebellum produces no change in the generative organs, and when erection of the penis is caused by emotions, the tract connecting the cerebral convolutions with the erection-centre in the spinal cord must be supposed to pass straight along the crura cerebri and medulla, for it has been observed that stimulation of these parts in the dog will produce erection.

Crura Cerebri and Pons Varolii.—Though from the gray matter, abundant in both these organs, we may infer that they possess important functions, we hardly know more concerning them than that the former serve as the great means of communication between the spinal cord and the higher parts of the brain, and that both are intimately connected with the coördination of movements, since either forced or disorderly movements are the frequent results of section of either of them; and, as we have seen, the possession of these parts, in the absence of the cerebral hemispheres, and even of the corpora striata and optic thalami, is sufficient to carry out the most complex bodily movements.

Since the paralysis of the face seen in cases of hemiplegia from disease of one corpus striatum, is on the same side as that of the limbs, it follows that the impulses proceeding along the cranial nerves cross over like those of the spinal nerves; and when the nucleus of origin of such a nerve as the facial is stimulated on one side, the movements which result are on the opposite side. Hence, when paralysis of the face occurs on the opposite side to

that of the body, it may be inferred that the injury or disease has affected the cranial nerve (or nerves) in a part of its course before decussation has taken place; and pathological observations support this view, unilateral disease or injury of the pons Varolii not infrequently involving the facial nerve of the same side in its comparatively superficial course before decussation has taken place, and so causing paralysis of the muscles of the same side of the face as the disease, and the opposite side to the paralysis of the limbs. It is probable that the decussation which we have seen to take place partly in the spinal cord, is gradually completed as the impulses pass through the medulla and pons Varolii. There does not appear to be adequate support for the view of those who maintain that volitional impulses cross suddenly and completely at the decussation of the pyramids.

Medulla Oblongata.—We have so often spoken of this link between the brain and the spinal cord, that it is hardly necessary here to do more than recall the fact, that the majority of the "centres" for various organic functions are situated in it.

These we may briefly recapitulate as follows: The respiratory centre with its neighboring convulsive centre. The vaso-motor centre. The cardio-inhibitory centre. The diabetic centre, or centre for the production of artificial diabetes. The centre for deglutition. The centre for the movements of the œsophagus and stomach, with its allied vomiting centre. The centre for reflex excitation of the secretion of the saliva, with which may be associated the centre through which the vagus influences the secretion of pancreatic juice, and possibly of the other digestive juices.

In the frog, as we have urged, p. 724, the medulla is undoubtedly largely concerned in the coördination of movements, and it is exceedingly probable that in the mammal also a considerable portion of work of this kind falls to its lot.

Sect. 5.—On the Rapidity of Cerebral Operations.

We have already seen (p. 698) that a considerable time is taken up in a purely reflex act, such as that of winking, though this is perhaps the most rapid form of reflex movement. When the movement which is executed in response to a stimulus involves mental operations a still longer time is needed; and the interval between the application of the stimulus and the commencement of the muscular contraction varies according to the nature of the mental labor involved.

The simplest case is that in which a person makes a signal immediately that he perceives a stimulus—*e. g.*, closes or opens a

galvanic circuit the moment that he feels an induction shock applied to the skin, or sees a flash of light, or hears a sound. By arrangements similar to those employed in measuring the velocity of nervous impulses, the moment of the application of the stimulus and the moment of the making of the signal are both recorded on the same travelling surface, and the interval between them is carefully measured. This interval, which has been called "the reaction period," consists of three portions : (1) the passage of afferent impulses from the peripheral sensory organ to the central nervous system, including the possible latent period of the generation of the impulses in the sensory organ ; (2) the transformation, by the operations of the central nervous system, of the afferent into efferent impulses ; and (3) the passage of the efferent impulses to the muscles, including the latent period of the muscular contractions. If the time required for the first and third of these events be deducted from the whole, the "reduced reaction period," as it may be called, gives the time taken up exclusively by the operations going on in the central nervous system.

The reaction period, both reduced and unreduced, varies according to the nature and disposition of the peripheral organs stimulated. The reaction period of vision has long been known to astronomers. It was early found that when two observers were watching the appearance of the same star, a considerable discrepancy existed between their respective reaction periods ; and that the difference, forming the basis of the so-called "personal equation," varied from time to time according to the personal conditions of the observers.

In general it may be said that tactile sensations produced by the stimulus of an electric shock applied to the skin, are followed by a shorter reaction period than are auditory sensations, while the period of these is in turn shorter than that of visual sensations produced by luminous objects ; on the other hand, the shortest period of all is that of visual sensations produced by direct electrical stimulation of the retina. Roughly speaking, we may say that the reaction period of physiological time is for feeling $\frac{1}{7}$th, for hearing $\frac{1}{6}$th, and for sight $\frac{1}{5}$th of a second. But even with the same stimulus, the reaction period will vary according to circumstances, such as the time of year, weather, etc., and according to the condition of the individual, previous practice, fatigue, and the like.

The calculations involved in "reducing" the reaction period are obviously open to much error ; in general, the reduced reaction period may be said to be less than $\frac{1}{10}$th of a second, that is to say, an intelligent person takes about this time to perceive and to will.

The reaction period just given belongs to cases where a single stimulus is used, and all that the person experimented on has to do is to perceive the stimulus, and to make an effort in accordance. If, however, the stimulus, instead of being applied to a part of the body determined by previous arrangement, as, for instance, to the left foot, were applied either to the left or the right foot, without the person being told which it was to be, and it was arranged that he should make a signal when the left foot, but not when the right foot was stimulated, additional mental exertions would be necessary; and it is found that in such a case the reaction period is considerably prolonged. The difference between a simple reaction period, and one in which a mental decision has to be carried out before the voluntary effort to make the signal is initiated, gives the time required for a person to "make up his mind" in accordance with the nature of the sensation which he receives; this is found to be, roughly speaking, from $\frac{1}{5}$th to $\frac{1}{20}$th of a second.

Sec. 6—The Circulation in the Brain.

The supply of blood to the brain seems at first sight not to correspond to the importance of this the chief organ of the body. In the rabbit it would appear that not much more than one per cent. of the total quantity of the blood of the body is present at any one time in the brain, a quantity distinctly less than that which is found in the kidneys; and of the total weight of the organ, the weight of blood in the brain at any one time amounts to about five per cent., being about the same as in the muscles, whereas in the kidney it amounts to nearly twelve per cent., and in the liver to as much as nearly thirty per cent. Making every allowance for the relative small size and functional importance of the rabbit's brain, the blood-supply of even the human brain must still be small. In other words, the metabolism of the brain-substance is of importance, not so much on account of its quantity as of its special qualities.

We have seen (p. 431), in speaking of respiration, that when the brain is exposed, the quantity of blood in the brain, and so the total volume of the brain, rises and falls, in a conspicuous manner, with the respiratory movements. And observations by the plethysmographic method, a portion of the skull being removed for the purpose, or advantage being taken of a natural deficiency, have shown the existence of more rapidly repeated movements, of a swelling and shrinking synchronous with and due to the beats of the heart, as well as of variations, larger and slower than the respiratory undulations, and brought about by

various causes, such as the position of the head in relation to the trunk, movements of the limbs, modifications of the respiratory movements, and apparently phases of activity of the brain itself, as in waking and sleeping.

In certain respects the circulation in the brain is peculiar. The skull forms a fairly complete inextensible envelope, presenting a strong contrast to the extensible elastic capsules which invest such organs as the spleen and kidney. As a consequence of this, when at any time an extra quantity of blood is sent from the heart to the brain, room must be made for it by the increased exit of the fluids already present. For any pressure on the brain-substance beyond a certain limit is injurious to its welfare and activity, as is seen in certain maladies, where blood passing by rupture of the bloodvessels out of its normal channels remains effused on the surface of the brain or elsewhere, and thus taking up the room of the proper brain-substance leads, by "compression," as it is called, to paralysis, loss of consciousness, or death. Within the limits of the normal cerebral circulation, the characteristic venous sinuses serve to regulate the internal pressure; they form temporary reservoirs from which a comparatively large quantity of blood can be rapidly discharged from the cranium, the flow from the sinuses being greatly assisted by the inspiratory movements of the chest.

The arterial supply of the brain, as a whole, is undoubtedly regulated by vaso-motor nerves, and in all probability the special distribution of blood to the various parts of the brain is determined by the same agents. When the head is suddenly shifted from the erect to a hanging position, there must be a tendency for the blood to accumulate in the cranial cavity, and, conversely, when the head is suddenly shifted from a hanging to an erect position, there must be a tendency for the supply of blood within the cranium to be for a while less than normal. Either change of position, and especially, perhaps, the latter, would thus lead to cerebral disturbances which would in ourselves be revealed by affections of our consciousness. That a perfectly healthy, and especially young, organism whose vaso-motor mechanisms are at once effective and delicately responsive, can pass swiftly from one position of the head to the other without inconvenience, whereas those in whom the vaso-motor mechanisms by age or otherwise have become imperfect are giddy when they attempt such rapid changes, is in itself adequate evidence of the importance of the vaso-motor arrangements of the brain. But our information concerning this matter is at present of a very vague and general character. As yet we have no detailed knowledge, and are especially ignorant as to how far special

parts of the brain are supplied with independent vaso-motor mechanisms.

Many writers have insisted on the mechanical importance of the cerebro-spinal fluid. By the foramen of Majendie at the apex of the roof of the fourth ventricle, the fluid within the various ventricular cavities of the brain is continuous with the fluid in the subarachnoid labyrinth of the spinal cord. And it has been argued that when an extra quantity of blood is driven into the skull, the transference of a corresponding quantity of cerebro-spinal fluid through the foramen of Majendie, from the cranium into the spinal canal, the walls of which are less rigidly complete, prevents any injurious intracranial compression. Experimental evidence, however, as far as it goes, does not lend any very great support to this view; and though removal of the fluid by aspiration is said to lead to hemorrhage from the pia mater and to various nervous disorders, the value of the cerebro-spinal fluid depends in all probability more on its physiological properties as lymph, than on its mechanical properties as a mere fluid.

SEC. 7.—THE CRANIAL NERVES.

Though we have incidentally dwelt on the functions of all these nerves, it may be as well to recapitulate them somewhat briefly, giving at the same time a very general outline of their physiological anatomy.

1. *Olfactory* (Nerve of Smell).—[The olfactory tracts are prolongations of the cerebral substance. According to the observations of Henle and Meynert, each tract arises in a tubercular eminence, which is situated in the posterior inferior portion of the anterior cerebral lobe, internal to and connected with the island of Reil. These eminences are called the "optic tubercles," and are connected with each other by commissural fibres. The olfactory tracts are composed of both white and gray matter; the former occupies the inferior and lateral portions. Each tract (Fig. 213) terminates in an oblong ganglion, which is called the olfactory bulb. The bulb rests upon the cribriform plate of the ethmoid bone, and in this position gives off the nervous filaments which constitute what are, strictly speaking, the true olfactory nerves. The distribution of these nerves has been referred to in previous pages.]

2. *Optic* (Nerve of Sight).—[The optic tracts arise from the corpora quadrigemina and geniculata and the optic thalami. The fibres have been traced to the crura cerebri, and the anterior portion of the floor of the aqueduct of Sylvius. The optic tracts

(Fig. 229) run forward beneath the cerebrum, and when they reach the olivary process of the sphenoid bone unite to form the optic commissure or chiasm. The optic nerves arise from the

Fɪɢ. 238.

Inter-Retinal

To OPTIC N.
of same side

Inter-Cerebral
of opposite side
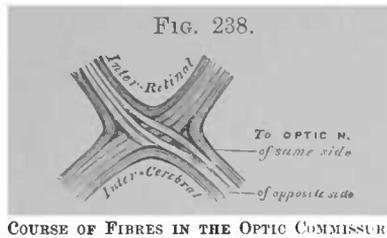
COURSE OF FIBRES IN THE OPTIC COMMISSURE.

anterior part of the commissure, enter the orbit through the optic foramina, pierce the external coats of the eyeball, and become expanded to form the retinæ.

Within the commissure the fibres of the optic tract pursue divergent courses. Some of the fibres decussate; others continue to the retina on the same side; others cross over to the opposite side and return to the optic thalamus, and thus form inter-cerebral or commissural fibres between the optic thalami; other fibres (inter-retinal) probably run through one optic nerve across to the other between the retinæ.]

3. *Oculo-motor.*—[The oculo-motor nerves arise from the crura cerebri immediately anterior to the pons Varolii (Fig. 229). The fibres of each nerve have their deep origin in a gray nucleus in the floor of the aqueduct of Sylvius. This nucleus is continuous with the nucleus in which the root of the fourth nerve originates, and is, therefore, often spoken of as the common nucleus of the two nerves. Each nucleus is connected with the opposite side of the brain by fibres which pass through the corpus striatum of the opposite side, and decussate beneath the floor of the aqueduct of Sylvius. Some of the fibres from the corpora striatum probably remain on the same side without decussating.

From its superficial point of origin this nerve passes along the cavernous sinus, receiving some sensory filaments from the fifth. It enters the orbit through the sphenoidal fissure (Fig. 239).]

Motor nerve to the levator palpebræ superioris and all the muscles of the eye, except the obliquus superior and the rectus externus. Efferent nerve for the contraction of the pupil and for the muscles of accommodation. Hence, when the nerve is divided or otherwise paralyzed, the upper eyelid falls (ptosis); the eye, which is turned outwards, is capable of partial movements only, viz., such as can be produced by the rectus externus and obliquus superior; when the head is moved, the eye moves with it, the inferior oblique not being able to execute the usual

compensating movements of the eyeball; the pupil is dilated, and the eye cannot accommodate for near distances. The root of the nerve shows recurrent sensibility, due to fibres from the fifth, but is otherwise a purely motor nerve.

[FIG. 239.
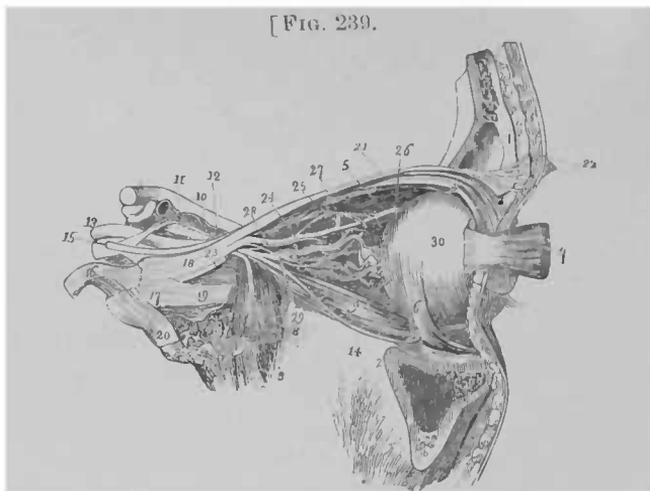
THE NERVES OF THE ORBIT SEEN FROM THE OUTER SIDE.

1, section of the frontal bone; immediately behind the numeral is the frontal sinus, and, in front, the integument; 2, the superior maxillary bone, the section in front of the numeral exhibits the maxillary sinus; 3, part of the sphenoid bone; 4, the levator palpebræ and superior rectus muscles; 5, the superior oblique muscle; 6, the inferior oblique muscle; 7, the ocular half of the external rectus muscle drawn forwards; 8, the orbital half of the external rectus muscle turned downwards. On this muscle the sixth nerve is seen dividing into branches; 9, the inferior rectus muscle; 10, the optic nerve; 11, the internal carotid artery emerging from the cavernous sinus; 12, the ophthalmic artery; 13, the third nerve; 14, the branch of the third nerve to the inferior oblique muscle. Between this and the sixth nerve (8) is seen the branch which supplies the inferior rectus, its branch to the ophthalmic ganglion is seen proceeding from the upper side of the trunk of the nerve, at the bottom of the orbit; 15, the fourth nerve; 16, the trunk of the fifth nerve; 17, the Gasserian ganglion; 18, the ophthalmic nerve; 19, the superior maxillary nerve; 20, the inferior maxillary nerve; 21, the frontal nerve; 22, its division into branches to supply the integument of the forehead; 23, the lachrymal nerve; 24, the nasal nerve, the small nerve seen in the bifurcation of the nasal and frontal nerve is one of the branches of the upper division of the third nerve; 25, the nasal nerve passing over the internal rectus muscles to the anterior ethmoidal foramen; 26, the infra-trochlear nerve; 27, a long ciliary branch of the nasal, another long ciliary branch is seen proceeding from the lower aspect of the nerve; 28, the long root of the ophthalmic ganglion, proceeding from the nasal nerve, and receiving the sympathetic root, which joins it at an acute angle; 29, the ophthalmic ganglion, giving off from its forepart the short ciliary nerves; 30, the globe of the eye.]

4. *Trochlear* or *Pathetic.*—[The trochlearis or patheticus nerve is the smallest of all the cranial nerves. This nerve arises from the upper surface of the valve of Vieussens, behind the corpora quadrigemina (Fig. 229). The larger proportion of fibres run

transversely across the valve of Vieussens, and decussate with those of the nerve of the opposite side; other fibres remain on the same side as the nerve. These fibres have their origin in a gray nucleus situated in the floor of the aqueduct of Sylvius, immediately behind, and adjoining the nucleus of the oculo-motor nerve; and also in a nucleus which is located near the nucleus of the fifth nerve in the upper part of the floor of the fourth ventricle. It passes along the cavernous sinus, and enters the orbit through the sphenoidal fissure (Fig. 239).]

Motor nerve to the obliquus superior. When the nerve is paralyzed, no marked difference is observed in the position of the eye, but the patient sees double when he attempts to look straight forward or towards the paralyzed side; the images, however, coalesce when he turns his head to the sound side. When the head is moved from side to side, the eye moves with it, the usual compensating movement of the eye which accompanies the movements of the head failing in consequence of the superior oblique not acting. It is a purely motor nerve, but receives recurrent fibres from the fifth.

5. *Trigeminus.*—[The fifth or trigeminus is the largest of the cranial nerves. It arises from the side of the pons Varolii (Fig. 229) by two roots, which are separated by a narrow band of fibres. The anterior or smaller root is motor; the posterior root is sensory. The fibres have their deep origin principally in a gray nucleus in the extreme side of the floor of the fourth ventricle, and immediately behind the nuclei of the oculo-motorius and patheticus nerves. Some of the fibres terminate in the nuclei or decussate with those of the opposite side; others have been traced through the superior peduncle of the cerebellum of the same side to the tubercula quadrigemina. These nerves run forwards from their superficial point of origin to the Gasserian ganglion (Fig. 240), which rests on the petrous portion of the temporal bone. At this point the sensory root spreads out in the ganglion; but the motor root passes by, forming no connection with it. The sensory fibres pass through the ganglion, being reinforced by fibres from the ganglionic cells, and form three branches or trunks: the ophthalmic, superior maxillary, and inferior maxillary. The two former are sensory; the latter is joined by the motor root, and is, therefore, both sensory and motor. The ophthalmic branch enters the orbit through the sphenoidal fissure. The superior maxillary passes through the foramen rotundum into the spheno-maxillary fossa, where it sends off a tract to the spheno-palatine ganglion, then passes through a groove in the floor of the orbit, and emerges at the infra-orbital foramen. The inferior maxillary division passes through the

foramen ovale, then gives off several branches to the otic ganglion, and passes on to its points of distribution.]

A mixed efferent and afferent nerve, with distinct motor and sensory roots, the latter bearing the ganglion of Gasser.

Efferent Fibres. Motor fibres to the muscles of mastication, temporal, masseter, two pterygoids (mylo-hyoid, anterior belly of

[Fig. 240.
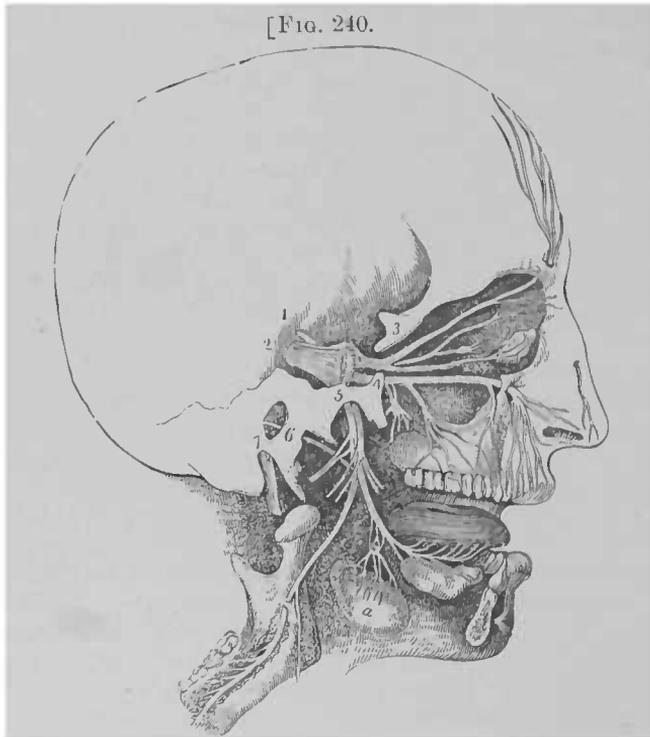
GENERAL PLAN OF THE BRANCHES OF THE FIFTH PAIR (after a sketch by CHARLES BELL) ⅓.

1, lesser root of the fifth pair ; 2, greater root passing forward into the Gasserian ganglion; 3, placed on the bone above the ophthalmic nerve, which is seen dividing into the supra-orbital, lachrymal, and nasal branches, the latter connected with the ophthalmic ganglion; 4, placed on the bone close to the foramen rotundum, marks the superior maxillary division, which is connected below the spheno-palatine ganglion, and passes forwards to the infra-orbital foramen ; 5, placed on the bone over the foramen ovale, marks the submaxillary nerve, giving off the anterior auricular and muscular branches, and continued by the inferior dental to the lower jaw; and by the gustatory to the tongue ; a, the submaxillary gland, the submaxillary ganglion placed above it in connection with the gustatory nerve ; 6, the chorda tympani ; 7, the facial nerve issuing from the stylo-mastoid foramen.]

digastric), to the tensor palati and tensor tympani ; vaso-motor fibres to various parts of the head and face ; secretory fibres to the lachrymal gland, and, according to some authors, to the parotid and submaxillary glands by fibres joining the facial.

Trophic (?) fibres to eye, nose, and other parts of the face. Efferent fibres for the dilation of the pupil.

Afferent Fibres. General nerve of sensation of the skin of head and face, and of the mucous membrane of the mouth, except the back part of the tongue, the posterior pillars of the fauces, and a large part of the pharynx, these parts being supplied by the glossopharyngeal and vagus; the back of the head is chiefly supplied by branches from the cervical nerves, and the external meatus and concha are supplied chiefly by the auricular branch of the vagus. Nerve of special sense of taste for the front part of the tongue.

6. *Abducens.*—[The abducens nerve emerges from the brain at the posterior border of the pons Varolii (Fig. 229). The fibres have their principal source of origin in a gray nucleus in the widest part of the floor of the fourth ventricle near the median line. The nerve, after emerging from the brain, passes along the cavernous sinus, where it receives filaments from the sympathetic and sensory filaments from the ophthalmic branch of the fifth. It then passes through the sphenoidal fissure to the external rectus muscle of the eye.]

Motor nerve to the rectus externus. When the nerve is divided or otherwise paralyzed, the eye is turned inwards. It probably receives recurrent sensory fibres from the fifth. It is also joined by fibres coming from the cervical sympathetic; when this latter nerve is divided in the neck, the action of the muscle is said to be weakened.

7. *Facial.*—[The facial nerve arises from the groove between the olivary and restiform bodies, just below the pons Varolii (Fig. 229). The fibres have their deep origin principally in a gray nucleus in the floor of the fourth ventricle, which is a common seat of origin for both the facial and abducens nerves. The facial fibres arise from the external portion of the nucleus, and the abducens arises from the internal portion, so that they form a sort of loop, being apparently continuous with each other through the nucleus. Some of the fibres extend from the nucleus to the brain on the same side; others decussate freely in the median line with fibres coming from the opposite nucleus, and run to the nucleus or are continued up to the brain on the opposite side to which they originated.

The facial nerve, after it emerges from the brain, passes in company with the auditory nerve into the internal auditory meatus. Then leaving the auditory nerve, it enters the aqueductus Fallopii and makes its exit through the stylo-mastoid foramen. It then spreads out between the lobules of the parotid gland, its branches diverging like a fan, and is distributed principally to the muscles of the face (Fig. 241).]

Motor nerve to the muscles of the face; hence, nerve of expression. Supplies also stylohyoid, posterior belly of the digastric, buccinator, stapedius, muscles of the external ear, platysma, some muscles of the palate, viz., the levator palati and probably others. Secretory nerve of submaxillary and parotid gland.

[Fig. 241.
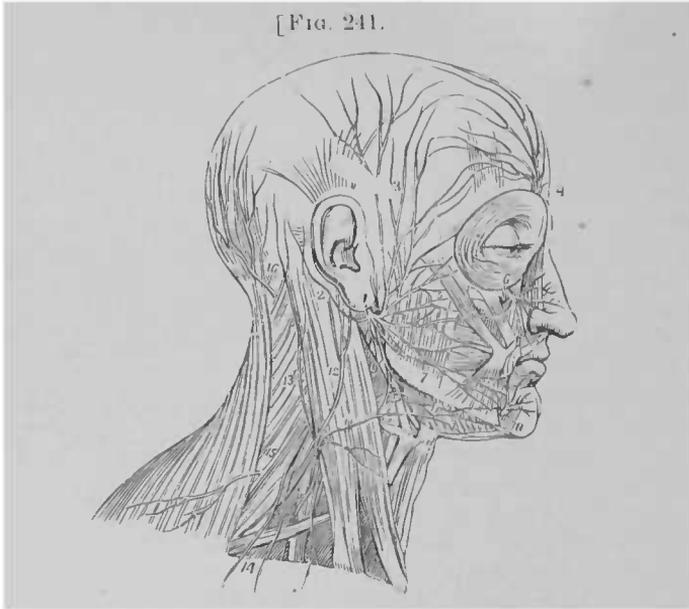
THE DISTRIBUTION OF THE FACIAL NERVE, AND THE BRANCHES OF THE CERVICAL PLEXUS.

1, the facial nerve, escaping from the stylo-mastoid foramen, and crossing the ramus of the lower jaw, the parotid gland has been removed in order to show the nerve more distinctly; 2, the posterior auricular branch, the digastric and stylo-mastoid filaments are seen near the origin of this branch; 3, temporal branches, communicating with (4) the branches of the frontal nerve; 5, facial branches, communicating with (6) the infra-orbital nerve; 7, facial branches, communicating with 8, the mental nerve; 9, cervico-facial branches, communicating with (10) the superficialis colli nerve, and forming a plexus 11) over the submaxillary gland. The distribution of the branches of the facial in a radiated direction over the side of the face, constitutes the pes anserinus; the auricularis magnus nerve, one of the ascending branches of the cervical plexus; 13, the occipitalis minor, ascending along the posterior border of the sterno-mastoid muscle; 14, the superficial and deep descending branches of the cervical plexus; 15, the spinal accessory nerve, giving off a branch to the external surface of the trapezius muscle; 16, the occipitalis major nerve, the posterior branch of the second cervical.]

Receives afferent, possibly efferent, fibres from trigeminus and also from vagus. It is said by some to contain vaso-motor fibres for the tongue and side of the face. The effects of paralysis of the facial, from the inability of the orbicularis to close the eye, the drawing of the face to the sound side, and the smoothness of the paralyzed side, are very striking.

8. *Auditory Nerve.*—[The auditory nerve arises by two roots from the posterior median fissure of the medulla oblongata, below the lower border of the pons Varolii. (Fig. 229.) In the floor of the fourth ventricle, below its widest part, are a number of transverse white striæ. (Fig. 231.) These are the fibres of the posterior root, which arise from a gray nucleus beneath them, which is connected with the white substance of the cerebellum. These fibres pass outwards, winding around the restiform body. The deep or anterior root is traced to the borders of the calamus scriptorius, and into the cerebellum especially. This root passes inwards around the restiform body to meet the other root, and thus embraces this part of the medulla. Some of the fibres decussate in the floor of the fourth ventricle.

This nerve accompanies the facial into the internal auditory meatus, and at the bottom of it divides into the cochlear and vestibular branches, which supply the internal ear. The cochlear branch is distributed to the cochlea; the vestibular branch to the sacculi and semicircular canals. Within the meatus the auditory nerve receives several filaments from the facial.]

Special nerve of hearing; afferent nerve for impulses other than auditory proceeding from the semicircular canals.

9. *Glosso-pharyngeal.*—[The glosso-pharyngeal nerve arises by four or five bundles of fibres from the upper part of the medulla oblongata, posterior to the olivary body. (Fig. 229.) These fibres have their deep origin in a nucleus, which is situated below and beneath the nucleus of the auditory nerve. The nucleus of the glosso-pharyngeal is a continuation of the same series of cells which give origin to the spinal accessory and pneumogastric nerves. The nerve makes its exit from the cranium through the jugular foramen in company with the pneumogastric and spinal accessory nerves. In its passage the nerve presents two ganglia on its trunk, the *jugular* and *petrosal.* From the petrosal ganglion fibres arise which connect the nerve with the pneumogastric, facial, and sympathetic nerves. It sends a special branch to the ear, called the tympanic branch. It divides into two principal branches, one of which is distributed to the pharynx and parts immediately surrounding; the other going to the tongue. (Fig. 242.)]

Motor nerve for levator palati, azygos uvulæ, stylo-pharyngeus, constrictor faucium medius; the motor functions of this nerve have been disputed. Special nerve of taste for the back of the tongue. General nerve of sensation for the root of the tongue, the soft palate, the pharynx (being here associated with the vagus), the Eustachian tube, and the tympanum.

10. *Pneumogastric. Vagus.*—[The pneumogastric nerve arises by ten or twelve bundles of fibres behind the olivary body and

below the point of origin of the glosso-pharyngeal nerve. (Fig. 229.) These fibres have their deep origin in a gray nucleus, which is situated below the nucleus of the glosso-pharyngeal, with its upper portion projecting somewhat above it. The nucleus is exposed in the floor of the ventricle. The fibres proceed from the nucleus downwards and outwards through the medulla oblongata, and emerge at the point above stated. It makes its exit from the cranium through the jugular foramen. Before its exit the trunk presents a gangliform enlargement (ganglion jugulare), through which it receives fibres from the spinal accessory (accessory portion), facial, glosso-pharyngeal, and sympathetic. After its exit it presents a second enlargement (ganglion inferius), through which it is connected with the spinal accessory (accessory portion), hypoglossal, loop of the first and second cervical, and sympathetic nerves.]

Efferent Fibres. Motor nerve for the muscles of the pharynx, for the movements of the œsophagus, of the stomach, of the intestines, for the muscles of the larynx, possibly for the plain muscular fibres of the trachea and bronchial divisions. Vasomotor fibres for lungs. Inhibitory nerve of the heart. Trophic fibres for lungs and heart.

Afferent Fibres. Sensory nerve of the respiratory passages, and of the pharynx, œsophagus, and stomach. Afferent nerve, augmenting and inhibiting, of the respiratory centre, afferent inhibitory nerve (depressor branch) of the medullary vaso-motor centre, afferent nerve producing salivary secretion, inhibiting pancreatic secretion. It is stated that in the rabbit the vagus may be easily dissected into two strands, an outer one containing the afferent, and an inner one containing the efferent fibres.

11. *Spinal Accessory.*—[The spinal accessory nerve arises by eight or ten filaments from the lateral tract of the cord, below the point of origin of the pneumogastric. The spinal accessory nerve consists of two portions, the *accessory* and *spinal.* (Fig. 229.) The accessory portion joins the pneumogastric nerve, as has been previously stated. The fibres have their deep origin in a gray nucleus, in the lower part of the medulla and upper part of the spinal cord, which is continuous above with the nucleus of the pneumogastric, and below with the remains of the anterior cornu. The nerve makes its exit from the cranium through the jugular foramen.]

Motor nerve to the sterno-mastoid and trapezius muscles. It receives recurrent sensory fibres from the cervical nerves. Part of the spinal accessory blends with the pneumogastric, and the efferent effects (such as the movements of the larynx, pharynx, etc., and cardiac inhibition) of the united trunk seem to be largely due to the spinal accessory fibres contained in them. It
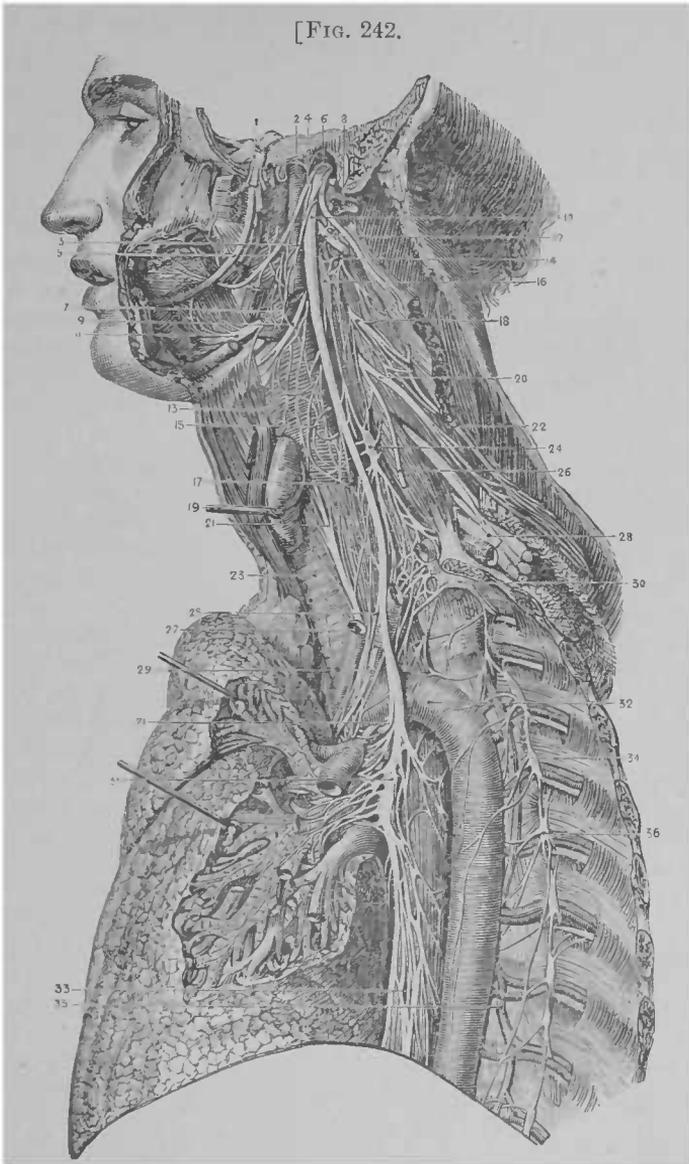
DISTRIBUTION OF THE PNEUMOGASTRIC OR TENTH PAIR OF NERVES ON THE LEFT SIDE.
After HIRSCHFELD and LEVEILLE.

1, Gasserian ganglion of fifth nerve ; 2, internal carotid artery ; 3, pharyngeal branch of pneumogastric ; 4, glosso-pharyngeal nerve ; 5, lingual nerve (fifth) ; 6, spinal accessory nerve ; 7, middle constrictor of pharynx ; 8, internal jugular vein (cut) ; 9, superior laryngeal nerve ; 10, ganglion of trunk of pneumogastric nerve ; 11, hypoglossal nerve (cut) on hyoglossus ; 12, ditto (cut), communicating with eighth and first cervical nerves ; 13, external

is stated, however, that division of the spinal accessory before it joins the pneumogastric, does not entirely do away with either swallowing or the movements of the larynx. In the movements of the œsophagus and stomach, brought about by the vagus acting as an efferent nerve, the accessory fibres seem to have no share. The cardiac inhibitory fibres seem to be distinctly of accessory origin.

12. *Hypoglossal.*—[The hypoglossal nerve arises by twelve or fifteen bundles from the groove between the anterior pyramid and the olivary body, in a line corresponding to the antero-lateral groove in the cord. The fibres have their deep origin in an elongated gray nucleus situated in the floor of the fourth ventricle at its inferior part, near the median line and internal to the nucleus of the spinal accessory, pneumogastric, and glossopharyngeal nerves. The nerve makes its exit from the cranium through the anterior condyloid foramen.]

Motor nerve for the muscles of the tongue, and for all the muscles connected with the hyoid bone except the digastric, stylohyoid, mylo-hyoid, and middle constrictor of the pharynx; it also supplies the sterno-thyroid. It receives sensory fibres from the fifth and vagus, and is also connected with the three upper cervical nerves as well as with the sympathetic.

CHAPTER VII.

SPECIAL MUSCULAR MECHANISMS.

[*The Physiological Anatomy of the Larynx.*

THE larynx is a membrano-cartilaginous chamber, broader above than below, and situated in the anterior median portion of the neck. It consists of a number of cartilages, which are

Fig. 243.
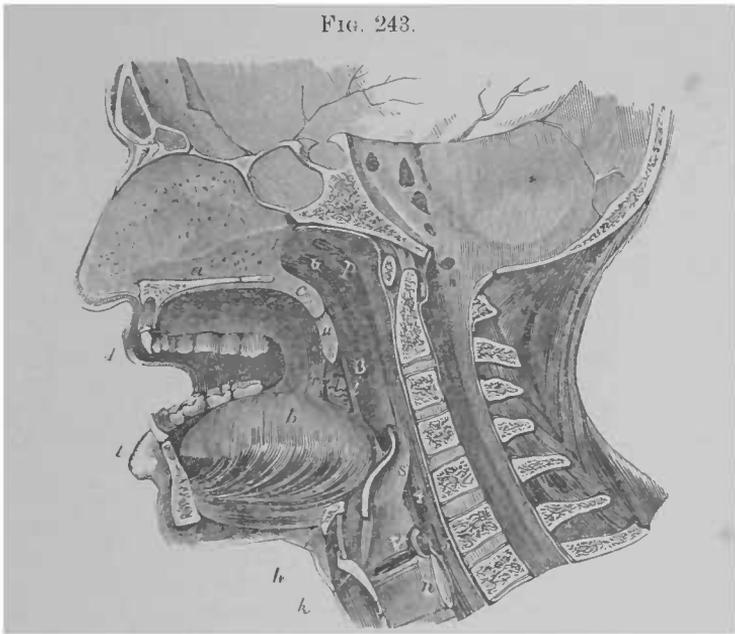
MEDIAN SECTION OF MOUTH, NOSE, PHARYNX, AND LARYNX.

a, septum of nose, below it, section of hard palate; *b*, tongue; *c*, section of velum pendulum palati; *d*, *d*, lips; *u*, uvula; *r*, anterior arch or pillar of fauces; *i*, posterior arch; *t*, tonsil; *p*, pharynx; *h*, hyoid bone; *k*, thyroid cartilage; *n*, cricoid cartilage; *ə*, epiglottis; *v*, glottis; 1, posterior opening of the nares; 3, isthmus faucium; 4, superior opening of larynx; 5, passage into œsophagus; 6, mouth of right Eustachian tube.

articulated with each other, connected by ligaments, moved by a number of muscles, and lined by a mucous membrane.

The principal cartilages are the thyroid, cricoid, the two arytenoid, and the epiglottis.

The thyroid cartilage is the largest and consists of two quadrilateral plates of alæ, which are continuous with each other in front, where they form the prominence called the pomum Adami. The posterior borders of the thyroid cartilage serve as a point of attachment of the stylo-pharyngeus and palato-pharyngeus muscles. The upper part of each of these borders terminates in a superior cornu, which articulates with the hyoid bone; the lower portion terminates in the inferior cornu, which articulates with the cricoid cartilage. The upper border between the cornua is connected with the hyoid bone by the thyro-hyoid membrane. The lower border is connected with the cricoid cartilage by the thyro-cricoid membrane at the median line, and at the sides by the crico-thyroid muscles.

The cricoid cartilage is situated below the thyroid cartilage with its broad portion posteriorly. At the upper part of its broad portion are two smooth surfaces on which the arytenoid cartilages articulate.

The arytenoid cartilages are pyramidal in form and articulate on the upper surface of the cricoid. Each cartilage has an external, posterior, and internal (median) surface, an apex and a base. The apex is pointed backwards and inwards, and is surmounted by a small cartilaginous tubercle, called the cartilage of Santorini (Fig. 246). The base, which articulates with the cricoid cartilage, presents at its external internal angle a projection called the *processus vocalis*. At the posterior internal angle is a second projection, called the *processus muscularis*.

The superior opening of the larynx is formed anteriorly by the epiglottis, posteriorly by the apices of the arytenoid cartilages, and laterally by the aryteno-epiglottidean folds stretching between these points. The inferior opening corresponds to the inferior border of the cricoid cartilage. Between these points is the *cavity* of the larynx, which has stretching across its sides the vocal cords. The vocal cords consist of two pairs: the superior or false vocal cords are membrano-ligamentous bands, which extend from the receding angle of the thyroid to the external surfaces of the arytenoid cartilages; the inferior or true vocal cords (*chorda vocales*) are membrano-ligamentous bands which stretch across the cavity of the larynx from the receding angle of the thyroid to the processus vocales of the arytenoid cartilages. Between the borders of the true and false vocal cords is an elliptical opening, the *ventricle*, which leads to a space running upwards and behind the false vocal cords, called the *sacculus laryngis*. The mucous membrane lining this sac contains a great number of follicular glands, which discharge a mucous secretion for the purpose of lubricating the true vocal cords.

Between the true vocal cords is an opening which is called the

rima glottidis. The form of the glottis varies very much both in the inspiratory and expiratory acts, and in the act of phonation.

The muscles of the larynx are divided anatomically into the intrinsic and extrinsic. The former are nine in number, four of
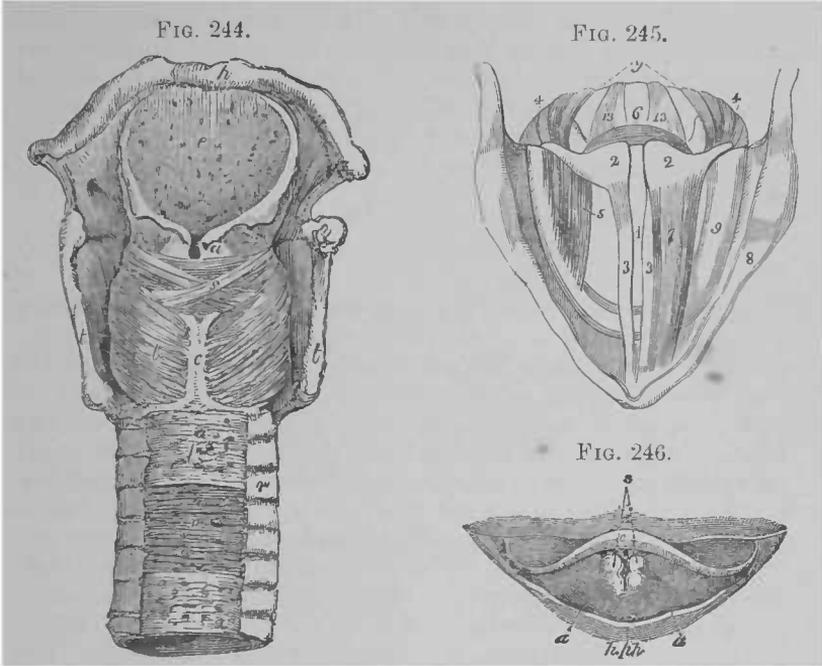
FIG. 244.—View of the Larynx and part of the Trachea from behind, with the Muscles Dissected. *h*, the body of the hyoid bone; *e*, epiglottis; *t*, the posterior borders of the thyroid cartilage; *c*, the median ridge of the cricoid; *u*, upper part of the arytenoid; *s*, placed on one of the oblique fasciculi of the arytenoid muscle; *b*, left posterior crico-arytenoid muscle; ends of the incomplete cartilaginous rings of the trachea; *l*, fibrous membrane crossing the back of the trachea; *n*, muscular fibres exposed in a part (from Quain's *Anatomy*).

FIG. 245.—View of the Larynx from above. 1, aperture of glottis; 2, arytenoid cartilages; 3, vocal cords; 4, posterior cricoarytenoid muscles; 5, lateral cricoarytenoid muscle of right side, that of left side removed; 6, arytenoid muscle; 7, thyroarytenoid muscle of left side, that of right side removed; 8, thyroid cartilage; 9, cricoid cartilage; 13, posterior crico-arytenoid ligament. With the exception of the arytenoid muscle, this diagram is a copy from Mr. Willis's figure.

FIG. 246.—View of the Upper Part of the Larynx as seen by means of the Laryngoscope during the Utterances of a Grave Note. *c*, epiglottis; *s*, the cartilages of Santorini; *a*, arytenoid cartilages; *z*, base of the tongue; *ph*, the posterior wall of the pharynx.

them being in pairs. They are the essential muscles concerned in the movements of the arytenoid cartilages and chorda vocales. Their points of origin and insertion are referred to on p. 776. The extrinsic muscles connect the larynx with adjacent parts,

and are for the most part concerned in the elevation and depression of the organ.

The larynx is lined with a mucous membrane which is continuous above with that lining the pharynx and mouth, and below with that lining the trachea. Above the chorda vocales it is lined with pavement epithelium, excepting at the lower anterior portion, where it is ciliated; below the chorda vocales the epithelium is of a ciliated columnar variety. The mucous membrane contains many mucous glands, which are pretty uniformly distributed; they are, however, very abundant in the part of the membrane lining the sacculus laryngis.]

Sec. 1.—The Voice.

A blast of air, driven by a more or less prolonged expiratory movement, throws into vibrations two elastic membranes—the *chordæ vocales.* These impart their vibrations to the column of air above them, and so give rise to the sound which we call the voice. Since the sound is generated in the vocal cords, we may speak of them and of those parts of the larynx which decidedly affect their condition as constituting the essential vocal apparatus; while the chamber above the vocal cords, comprising the ventricles of the larynx with the false vocal cords, the pharynx and the cavity of the mouth, the latter varying much in form, constitute a subsidiary apparatus of the nature of a resonance-tube, modifying the sound originating in the vocal cords. In the voice, as in other sounds, we distinguish: (1) Loudness. This depends on the strength of the expiratory blast. (2) Pitch. This depends on the length and tension of the vocal cords. Their *length* may be regarded as constant, or varying only with age. It consequently determines the range only of the voice, and not the particular note given out at any one time. The shrill voice of the child is determined by the shortness of the cords in infancy, and the voices of a soprano, tenor, and baritone are all dependent on the respective lengths of their vocal cords. Their *tension* is, on the contrary, variable; and the chief problems connected with the voice refer to variations in the tension of the vocal cords. (3) Quality. This depends on the number and character of the overtones accompanying any fundamental note sounded, and is determined by a variety of circumstances, chief among which is the physical quality of the cords.

The vocal cords, attached in front to the thyroid cartilage, end behind in the processus vocales of the arytenoid cartilages. Hence, a distinction has been drawn between the rima vocalis— *i. e.,* the opening bounded laterally by the vocal cords, and the

rima respiratoria, or space between the arytenoid cartilages behind the processus vocales; these names, however, are not free from objections. In quiet breathing (Fig. 247, *B*), the two form together a V-shaped space, which, as we have seen (p. 391), in

Fig 247.
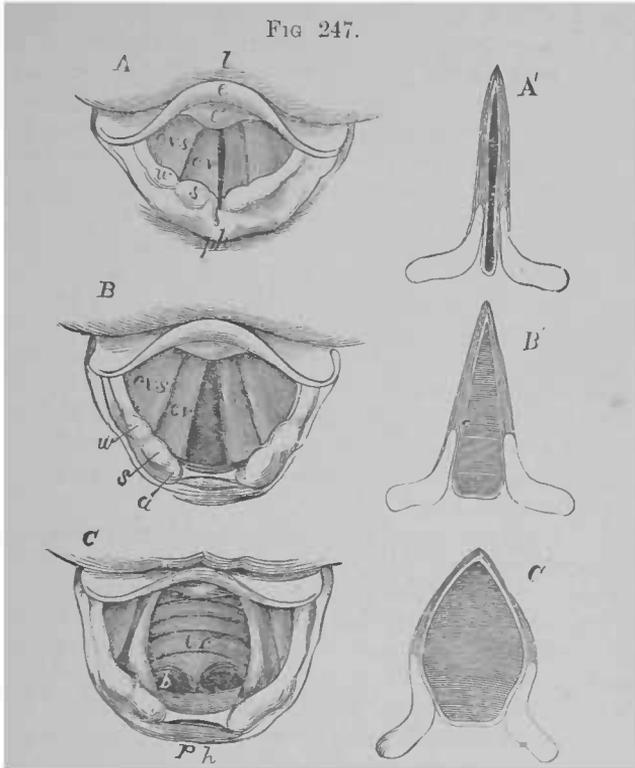
THE LARYNX AS SEEN BY MEANS OF THE LARYNGOSCOPE IN DIFFERENT CONDITIONS OF THE GLOTTIS. From Quain's *Anatomy*, after CZERMAK.

A, while singing a high note; *B*, in quiet breathing; *C*, during a deep inspiration. The corresponding diagrammatic figures *A'*, *B'*, *C'*, illustrate the changes in position of the arytenoid cartilages, and the form of the rima vocalis and rima respiratoria in the above three conditions.

l, the base of the tongue; *e*, the upper free part of the epiglottis; *e'* the tubercle or cushion of the epiglottis; *ph*, part of the anterior wall of the pharynx behind the larynx; *w*, swelling in the aryteno-epiglottidean fold caused by the cartilage of Wrisberg; *s*, swelling caused by the cartilage of Santorini; *a*, the summit of the arytenoid cartilage; *cv*, the true vocal cords; *cvs*, the false vocal cords; *tr*, the trachea with its rings; *b*, the two bronchi at their commencement.

deep inspiration is widened into a rhomboidal opening by the divergence of the processus vocales (Fig. 247, *C*). When a note is about to be uttered, the vocal cords are by the approximation of the processus vocales brought into a position parallel to each

other, and the whole rima is narrowed (Fig. 247, *A*). By their parallelism, and by the narrowness of the interval between them, the cords are rendered more susceptible of being thrown into vibration by a moderate blast of air. The problems we have to consider are, first, by what means are the cords brought near to each other or drawn asunder as occasion demands; and, secondly, by what means is the tension of the cords made to vary. We may speak of these two actions as narrowing or widening of the glottis, and tightening or relaxation of the vocal cords.

Narrowing of the Glottis.—The change of form of the glottis is best understood when it is borne in mind that each arytenoid cartilage is, when seen in horizontal section (Fig. 247), somewhat of the form of a triangle, with an internal or median, an external, and a posterior side, the processus vocalis being placed in the anterior angle at the junction of the median and external sides. When the cartilages are so placed that the processus vocales are approximated to each other, and the internal surfaces of the cartilages nearly parallel, the glottis is narrowed. When, on the contrary, the cartilages are wheeled round on the pivots of their articulations, so that the processus vocales diverge, and the internal surfaces of the cartilages form an angle with each other, the glottis is widened.

There are several muscles forming together a group, which has been called by Henle, the sphincter of the larynx. These are: (1) the *thyro-ary-epiglotticus*, proceeding from the inner surface of the thyroid cartilage, and from the arytenoid epiglottidean ligament, and sweeping round the outer ridge of the arytenoid cartilage of its own side to be inserted into the processus muscularis of the arytenoid cartilage of the other side; (2) the *thyro-arytenoideus externus*, passing from the reëntrant angle of the thyroid cartilage to be inserted into the outer edge of the arytenoid cartilage of the same side; (3) the *thyro-arytenoideus internus*, passing from the angle of the thyroid cartilage to the processus vocalis and outer side of the arytenoid cartilage; (4) the *arytenoideus (posticus)*, passing transversely from one arytenoid cartilage to another. All these muscles, when they act together, grasp round the glottis and tend to close it up; and each of them, acting alone, has, with the exception of the last-named (arytenoideus), the same effect. In addition to these, the *crico-arytenoideus lateralis*, which passes from the lateral border of the cricoid cartilage upwards and backwards to the outer angle of the arytenoid, by pulling this outer angle forwards throws the processus vocalis inwards, and so also narrows the glottis.

Widening of the Glottis.—The *crico-arytenoideus posticus* passing from the posterior surface of the cricoid cartilage to the outer angle of the arytenoid cartilage behind the attachment of

the lateral crico-arytenoideus, pulls back this outer angle, and so causing the processus vocalis to move outwards, widens the glottis. The *arytenoideus posticus*, acting alone, has a similar effect.

Tightening of the Vocal Cords.—The *crico-thyroideus* pulls the thyroid downwards and forwards, and so increases the distance between that cartilage and the arytenoids when the latter are fixed. Supposing, then, the arytenoideus and crico-arytenoideus posticus to fix the arytenoids, the effect of the contraction of the crico-thyroideus would be to tighten the vocal cords.

Slackening of the Vocal Cords.—This is effected by the whole sphincter group just mentioned, but more especially by the *thyro-arytenoidei externus* and *internus;* these acting alone, supposing the arytenoid cartilages to be fixed, would pull the thyroid cartilage upwards and backwards, and so shorten the distance between the processus vocales and that body.

Thus, almost every movement of the larynx is effected not by one muscle only, but by several, or at least by more than one, acting in concert. The movements which give rise to the voice are preëminently combined and coördinate movements. When we remember how a very slight variation in the tension of the vocal cords must give rise to a marked difference in the pitch of the note uttered, and yet what a multitude of fine differences of pitch are at the command of a singer of even moderate ability, it appears exceedingly probable that the various muscular combinations required to produce the possible variations in pitch are of such a kind that frequently a part only, possibly a few fibres only, of a particular muscle, may be thrown into contraction, while all the rest of the muscle remains quiet. Taking into view, moreover, the great range of pitch possessed by even common voices, as compared with the possible variations of tension of which the vocal cords in their natural length are capable, it has been suggested that some of the fibres of the thyro-arytenoideus internus, which, passing either from the thyroid or from the arytenoid, appear to end in the vocal cords themselves, may, by fixing particular points of the cords, so to speak, "stop" them; and by thus artificially shortening the length actually thrown into vibration, produce higher notes than the cords in their natural length are capable of producing. It has been also suggested that the processus vocales may overlap each other, and thereby shorten the length of cord available for vibration.

These various muscles are supplied by the vagus nerve, or rather by spinal accessory fibres running in the vagus trunk. The superior laryngeal is the afferent nerve supplying the mucous membrane, but it also contains the motor fibres distributed to the crico-thyroid muscle; hence, when this nerve is divided on one

side the corresponding vocal cord is relaxed and high notes become impossible. It is worthy of notice that this, the chief tensor, and therefore the most important, muscle of the larynx, has a separate and distinct nervous supply. According to some authors, the arytenoideus posticus also receives its nervous supply from this nerve; but this is denied by others.

The inferior laryngeal or recurrent branch supplies all the other muscles. When this nerve is divided the voice is lost, since the approximation and parallelism of the vocal cords can no longer be effected. When in a living animal both recurrent nerves are divided, the glottis is seen to become immobile and partially dilated, the vocal cords assuming the position in which they are found in the body after death, and which may be considered as the condition of equilibrium between the dilating and constricting muscles. During forcible inspiration, the glottis passes from this condition in the direction of more complete dilation; during forcible expiration, the change is one of constriction. When the peripheral portion of one recurrent nerve is stimulated, the vocal cord of the same side is approximated to the middle line; when both nerves are stimulated, the vocal cords are brought together and the glottis is narrowed. Though the nerve is distributed to both dilating and constricting muscles, the latter overcome the former when the nerve is artificially stimulated. In the complete closure of the glottis, which is so important a part of the act of coughing (p. 448), the group of muscles which we have spoken of as constituting a sphincter is thrown into forcible contractions by the recurrent laryngeal nerve.

Though fundamentally a voluntary act, the utterance of a given note is not effected by the direct passage of simple volitional impulses down to the laryngeal muscles. So complex and coördinate a movement as that of sounding even a simple and natural note requires a coördinating nervous mechanism in which, as in other complex muscular actions, afferent impulses play an important part. Auditory sensations, if not as important for an accurate management of the voice as are visual sensations for the movements of the eye, are yet of prime importance. This is recognized when we say that such and such a one, whose power over his laryngeal muscles is imperfect, "has no ear."

A person may speak or sing in two kinds of voice. In the one the sounds are full and strong, and the resonance chamber which is supplied by the trachea, bronchi, and indeed by the whole chest, is thrown into powerful and palpable vibrations; hence this voice is spoken of as the chest-voice. The other kind of voice, called the falsetto, is thin and poor, deals chiefly with high notes, and is not accompanied by the same conspicuous

vibrations of the chest. Much controversy has taken place as to the exact manner in which these two voices are respectively produced. The prevailing opinion teaches that in the chest-voice the vocal cords are somewhat thick, their substance being thrust inward towards the median line by the contraction of the thyroarytenoidei externi muscles, and the opening between them, sometimes so narrow as to be almost linear, extends along their whole length. In the falsetto voice, on the other hand, the vocal cords are said to be thin and membranous, and the note to be given forth by a vibration, not of the whole width of the cords as in the chest-voice, but of the extreme edges only, the lateral parts though not absolutely at rest vibrating with a different rhythm. Though the whole larynx in the falsetto voice is stretched in the antero-posterior direction and the vocal cords correspondingly elongated, the rima vocalis does not extend along their whole length; at their posterior part the cords are in contact, and indeed, according to some authors, the high falsetto notes are produced by a sort of "stopping" of the cords. The sense of effort which accompanies the falsetto voice indicates that the changes in the larynx which bring it about are effected by some special muscular manœuvres, as is also suggested by the fact that the ease with which falsetto notes can be uttered is readily increased by practice. The change from the chest to the falsetto voice is an abrupt one, and the combined range may be very extensive, as in the case of persons who can carry on a duet, singing alternately, for instance, in a tenor (chest) and a soprano (falsetto) voice.

The ventricles of Morgagni are apparently of use in giving the vocal cords sufficient room for their vibrations, and perhaps supply a secretion by which the vocal cords are kept adequately moist. The purpose of the false vocal cords is not exactly known. Some authors think that in the falsetto voice they are brought down into contact with, and thus serve to stop, the true vocal cords.

At the age of puberty, a rapid development of the larynx takes place, leading to a change in the range of the voice. The peculiar harshness of the voice when it is thus "breaking," seems to be due to a temporary congested and swollen condition of the mucous membrane of the vocal cords accompanying the active growth of the whole larynx. The change in the mucous membrane may come on quite suddenly, the voice "breaking," for instance, in the course of a night.

Sec. 2.—Speech.

Vowels.

Every sound, or every note (for all vocal sounds when considered by themselves are musical sounds), caused by the vibrations of the vocal cords, besides its loudness due to the force of the expiratory blast, and its pitch due to the tension of the cords, has a quality of its own, due to the number and relative prominence of the overtones which accompany the fundamental tone. Some of these features which make up the quality are imposed on the note by the nature of the vocal cords, but still more arise from various modifications which the relative intensities of the overtones undergo through the resonance of the cavity of the mouth and throat. Whenever we hear a note sounded by the larynx, we are able to recognize in it features which enable us to state that one or other of the "vowels" is being uttered. Vowel sounds are, in fact, only extreme cases of quality, extreme prominence of certain overtones brought about by the shape assumed by the buccal and pharyngeal passages and orifices, as the vibrations pass through them. Each vowel has its appropriate and causative disposition of these parts. When *i* (ee in feet) is sounded, the sounding-tube of the upper air-passages is made as short as possible, the larynx is raised and the lips are retracted, the whole cavity of the mouth taking on the form of a broad flask with a narrow neck. During the giving out of *e* (a in fat) the shape of the mouth is similar, but somewhat longer. For the production of *a* (as in father) the mouth is widely open, so that the buccal cavity is of the shape of a funnel with the apex at the pharynx. With *o*, the buccal cavity is again flask-shaped, with the mouth more closed than in *a*, but the lips, instead of being retracted as in *i* and *e*, are somewhat protruded, so that the sounding-tube is prolonged. The greatest length of the tube is reached in *u* (oo), in which the larynx is depressed and the lips protruded as much as possible. While the two latter vowels are being uttered, the general form of the buccal cavity is that of a flask with a short neck and a small opening, the orifice being smaller for *u* than for *o*.

Each of these various "vowel" forms of the mouth possesses a note of its own, one towards which it acts as a resonance chamber. Thus, if several tuning-forks of various pitch be held while sounding before a mouth which has assumed the particular form necessary for sounding U, it will be found that the resonance will be particularly great with the fork having the pitch of the bass *b*-flat. Similarly other and higher notes will be intensified

when the mouth is moulded to utter the other vowels. And it is the experience of singers, that each vowel is sung with peculiar ease on a note having a prominent overtone corresponding to the tone proper to the mouth when moulded to utter the .vowel. The precise nature of the vowel sounds is, however, still disputed.

As the vibrations are travelling through the pharyngeal and buccal cavities, the posterior nares are closed by the soft palate; and it may be shown, by holding a flame before the nostril, that no current of air issues from the nose when a vowel is properly said or sung. When the posterior nares are not effectually closed the sound acquires a nasal character. The same happens when the anterior nares are closed, as when the nose is held between the fingers, the nasal chamber then forming a cavity of resonance.

Consonants.

Vowels are, as their name implies, the only real vocal sounds; it is only on a vowel that a note can be said or sung. Our speech, however, is made up, not only of vowels, but also of consonants, *i. e.*, of sounds which are produced, not by the vibrations of the vocal cords, but by the expiratory blast being in various ways interrupted, or otherwise modified, in its course through the throat and mouth.

The distinction between the two is, however, not an absolute one, since, as we have seen, the characters of the several vowels depend on the form of the mouth, and in the production of some consonants (B, D, M, N, etc.) vibrations of the vocal cords form a necessary though adjuvant factor.

Consonants have been classified according to the place at which the characteristic interruption or modification takes place. Thus it may occur—

1. At the lips, by the movement or position of the lips in reference to each other or to the teeth, giving rise to *labial* consonants.

2. At the teeth, by the movement or position of the front part of the tongue in reference to the teeth or the hard palate, giving rise to *dental* consonants.

3. In the throat, by the movement or position of the root of the tongue in reference to the soft palate or pharynx, giving rise to *guttural* consonants.

Among the dentals, again, may be distinguished the dentals, commonly so called, such as T, the sibilants such as S, and the lingual L, all differing in the relative position of the tongue, teeth, and palate.

Consonants may also be classified according to the character of the movements which give rise to them. Thus they may be either *explosive* or *continuous*.

1. *Explosives.*—In these the characters are given to the sound by the sudden establishment or removal of the appropriate interruption. Thus, in uttering the labial P, the lips are first closed, then an expiratory current of air is driven against them, and upon their being suddenly opened, the sound is generated. Similarly, the dental T is generated by the sudden removal of the interruption caused by the approximation of the tip of the tongue to the front of the hard palate, and the guttural K by the sudden removal of the interruption caused by the approximation of the root of the tongue to the soft palate.

The labial B differs from P, inasmuch as it is accompanied by vibrations of the vocal cords (that is, a vowel sound is uttered at the same time), and these vibrations continue after the removal of the interruption. Hence, B is often spoken of as being uttered with voice, and P without voice; and D and G (hard) with voice bear the same relation to T and K without voice.

The *continuous* consonants may further be divided into

2. *Aspirates.*—In these the sound is generated by a rush of air through a constriction formed by the partial closure of the lips, or by the raising of the tongue against the hard or soft palate, etc. Thus, F is sounded when the lips are brought into partial, and not as in P and B into complete approximation, and a current of air is driven through the narrowed opening. F is uttered without any accompanying vibration of the vocal cords—*i. e.,* without voice. With voice it becomes V.

The sibilant S is formed by a rush of air past an obstruction caused by the partial closure of the teeth, the front of the tongue being depressed at the same time; and S accompanied with vibrations of the vocal cords becomes Z.

In Sh the dorsal surface of the tongue is raised so as to narrow the passage between that organ and the palate for a considerable portion of its length.

Th is formed by placing the tongue between the two partially open rows of teeth; and the hard and soft Th bear to each other the same relation as do P and B.

L is produced when the passage is closed in the middle by pressing the tip of the tongue against the hard palate and the air is allowed to escape at the sides of the tongue.

When the constriction in an aspirate is formed by the approximation of the root of the tongue to the soft palate, we have the guttural CH (as in loch) without voice, and GH (as in lough) with voice.

3. *Resonants or Nasals.*—In these, all of which must have vibrations of the vocal cords as a basis, the usual passage through

the mouth is closed either in a labial, dental, or guttural fashion, and the peculiar character is given to the sound by the nasal chambers acting as a resonance cavity. Thus, in M, the passage is closed by the approximation of the lips, in N by the approximation of the tongue to the hard palate, and in NG by the approximation of the root of the tongue to the soft palate.

4. The various forms of R are often spoken of as *vibratory*, the characteristic sounds being caused by the vibration of some or other of the parts forming a constriction in the vocal passage. Thus, the ordinary R is produced by vibrations of the point of the tongue elevated against the hard palate, the guttural R by the vibrations of the uvula or other parts of the walls of the pharynx ; and in some languages there seems to be an R produced by the vibrations of the lips.

H is caused by the rush of air through the widely open glottis. When, in sounding a vowel, the sound coincides with a sudden change in the position of the vocal cords from one of divergence to one of approximation, the vowel is pronounced with the *spiritus asper*. When the vocal cords are brought together before the blast of air begins, the vowel is pronounced with the *spiritus lenis*. The Arabic H is produced by closing the rima vocalis, the epiglottis and false vocal cords being depressed, and sending a blast of air through the rima respiratoria.

On many of the above points, however, there are great differences of opinion, the discussion of which, as well as of other more rare consonantal sounds, would lead us too far away from the purpose of this book. The following tabular statement must therefore be regarded as introduced for convenience only.

EXPLOSIVES.	*Labials,*	without voice	P.
	Labials,	with voice	B.
	Dentals.	without voice	T.
	Dentals,	with voice	D.
	Gutturals,	without voice	K (hard C).
	Gutturals,	with voice	G (hard).
ASPIRATES.	*Labials.*	without voice	F.
	Labials,	with voice	V.
	Dentals,	without voice	L S (soft C), Sh, Th (hard).
	Dentals,	with voice	Z, Zh (in *azure,* the French j), Th (soft).
	Gutturals,	without voice	CH (as in *loch*).
	Gutturals,	with voice,	GH (as in *lough*).
RESONANTS.	*Labial,*		M.
	Dental,		N.
	Guttural,		NG.
VIBRATORY.	*Labial,*	not known in European speech.	
	Dental,	R (common).	
	Guttural,	R (guttural).	

Whispering is speech without any employment of the vocal cords, and is effected chiefly by the lips and tongue. Hence, in whispering the distinction between consonants needing and those not needing voice, such as B and P, becomes for the most part lost.

SEC. 3.—LOCOMOTOR MECHANISMS.

The skeletal muscles are for the most part arranged to act on the bones and cartilages as on levers, examples of the first kind of lever being rare, and those of the third kind—where the power is applied nearer to the fulcrum than is the weight—being more common than the second. (Fig. 248.) This arises from the fact

FIG. 248.
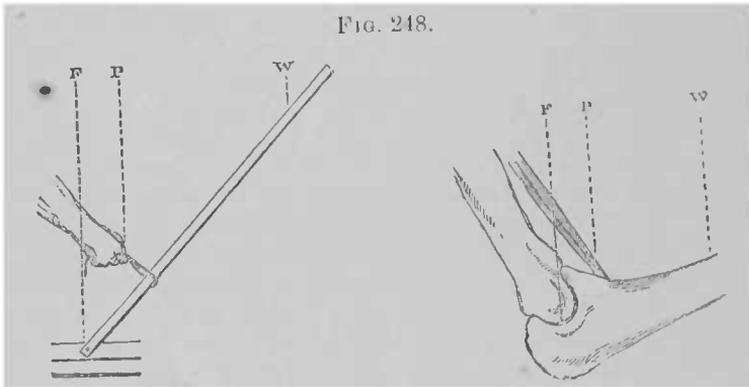
ILLUSTRATION OF THE THIRD KIND OF LEVER. F, fulcrum; P, power; W, weight.

that the movements of the body are chiefly directed to moving comparatively light weights through a great distance, or through a certain distance with great precision, rather than to moving heavy weights through a short distance. The fulcrum is generally supplied by a (perfect or imperfect) joint, and one end of the acting muscle is made fast by being attached either to a fixed point, or to some point rendered fixed for the time being by the contraction of other muscles. There are few movements of the body in which one muscle only is concerned; in the majority of cases several muscles act together in concert; nearly all our movements are coördinate movements. Where gravity or the elastic reaction of the parts acted on does not afford a sufficient antagonism to the contraction of a muscle or group of muscles, the return to the condition of equilibrium is provided for by the action either elastic or contractile of a set of antagonistic muscles: this is seen in the case of the face.

The *erect posture*, in which the weight of the body is borne by

the plantar arches, is the result of a series of contractions of the muscles of the trunk and legs, having for their object the keeping the body in such a position that the line of gravity falls within the area of the feet. That this does require muscular exertion is shown by the facts, that a person when standing perfectly at rest in a completely balanced position falls when he becomes unconscious, and that a dead body cannot be set on its feet. The line of gravity of the head falls in front of the occipital articulation, as is shown by the nodding of the head in sleep. The centre of gravity of the combined head and trunk lies at about the level of the ensiform cartilage, in front of the tenth dorsal vertebra, and the line of gravity drawn from it passes behind a line joining the centres of the two hip-joints, so that the erect body would fall backward were it not for the action of the muscles passing from the thighs to the pelvis, assisted by the anterior ligaments of the hip-joints. The line of gravity of the combined head, trunk, and thighs falls moreover a little behind the knee-joints, so that some, though little, muscular exertion is required to prevent the knees from being bent. Lastly, the line of gravity of the whole body passes in front of the line drawn between the two ankle-joints, the centre of gravity of the whole body being placed at the end of the sacrum; hence some exertion of the muscles of the calves is required to prevent the body falling forwards.

In *walking*, there is in each step a moment at which the body rests vertically on the foot of one, say the right leg, while the other, the left leg, is inclined obliquely behind, with the heel raised and the toe resting on the ground (Fig. 249). The left

[FIG. 249.
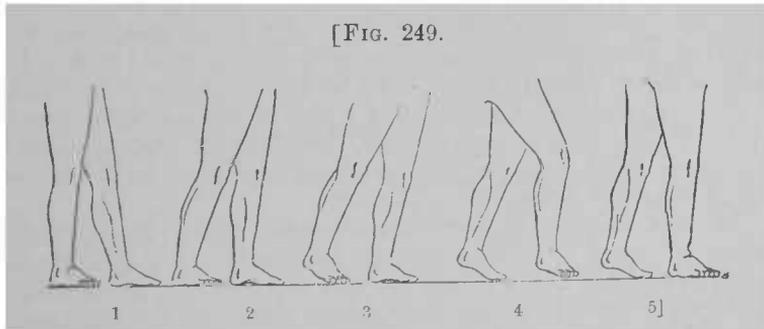
leg, slightly flexed to avoid contact with the ground, is then swung forward like a pendulum, the length of the swing or step being determined by the length of the leg; and the left toe[1] is

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[1] This indicates perhaps what should be done rather than the actual practice; most people put the heel to the ground first, the contact with the toe coming later.

brought to the ground.   On this left toe as a fulcrum, the body is moved forward, the centre of gravity of the body describing a curve, the convexity of which is upward, and the left leg necessarily becoming straight and rigid.   As the body moves forward, a point will be reached similar to that with which we supposed the step to be started, the body resting vertically on the left foot, and the right leg being directed behind in an oblique position. The movement on the left foot, however, carries the body beyond this point, and in doing so swings the right leg forward until it is the length of a step in advance of its previous position, and its toe in turn forms a fulcrum on which the body, and with it the left leg, is again swung forward.   Hence, in successive steps the centre of gravity, and with it the top of the head, describes a series of consecutive curves, with their convexities upwards, very similar to the line of flight of many birds.

Since in standing on both feet the line of gravity falls between the two feet, a lateral displacement of the centre of gravity is necessary in order to balance the body on one foot.   Hence, in walking the centre of gravity describes, not only a series of vertical, but also a series of horizontal curves, inasmuch as at each step the line of gravity is made to fall alternately on each standing foot.   While the left leg is swinging, the line of gravity falls within the area of the right foot, and the centre of gravity is on the right side of the pelvis.   As the left foot becomes the standing foot, the centre of gravity is shifted to the left side of the pelvis.   The actual curve described by the centre of gravity is therefore a somewhat complicated one, being composed of vertical and horizontal factors.   The natural step is the one which is determined by the length of the swinging leg, since this acts as a pendulum ; and hence the step of a long-legged person is naturally longer than that of a person with short legs.   The length of the step, however, may be diminished or increased by a direct muscular effort, as when a line of soldiers keep step in spite of their having legs of different lengths.   Such a mode of marching must obviously be fatiguing, inasmuch as it involves an unnecessary expenditure of energy.

In slow walking there is an appreciable time during which, while one foot is already in position to serve as a fulcrum, the other, swinging, foot has not yet left the ground.   In fast walking this period is so much reduced, that one foot leaves the ground the moment the other touches it ; hence there is practically no period during which both feet are on the ground together.

When the body is swung forward on the one foot acting as a fulcrum with such energy that this foot leaves the ground before the other, swinging, foot has reached the ground, there being an

interval during which neither foot is on the ground, the person is said to be *running*, not walking.

In jumping this propulsion of the body takes place on both feet at the same time; in hopping it is effected on one foot only.

The locomotion of four-footed animals is necessarily more complicated than that of man. ' The simple walk, such as that of the horse, is executed in four times, with a diagonal succession; thus, right foreleg, left hindleg, left foreleg, right hindleg. In the amble, such as that of the camel, the two feet of the same side are put down at one and the same time, this movement being followed by a similar movement of the other two legs; it corresponds therefore very closely to human walking. In the trot, which corresponds to human running, the two diagonally opposite feet are brought to the ground at the same time, and the body is propelled forwards on them. Concerning this, however, as well concerning the still more complicated gallop and canter, observers are not agreed, and much discussion has arisen.

The other problems connected with the action of the various skeletal muscles of the body are too special to be considered here.

BOOK IV

MANY of the individual constituent parts of the body are capable of reproduction—*i. e.*, they can give rise to parts like themselves; or they are capable of regeneration—*i. e.*, their places can be taken by new parts more or less closely resembling themselves. The elementary tissues undergo during life a very large amount of regeneration. Thus, the old epithelium scales which fall away from the surface of the body are succeeded by new scales from the underlying layers of the epidermis; old blood-corpuscles give place to new ones; worn-out muscles, or those which have failed from disease, are renewed by the accession of fresh fibres; divided nerves grow again; broken bones are united; connective tissue seems to disappear and appear almost without limit; new secreting cells take the place of the old ones which are cast off; in fact, with the exception of some cases, such as cartilage, and these doubtful exceptions, all those fundamental tissues of the body, which do not form part of highly differentiated organs, are, within limits fixed more by bulk than by anything else, capable of regeneration. That regeneration by substitution of molecules, which is the basis of all life, is accompanied by a regeneration by substitution of mass.

In the higher animals regeneration of whole organs and members, even of those whose continued functional activity is not essential to the well-being of the body, is never witnessed, though it may be seen in the lower animals; the digits of a newt may be restored by growth, but not those of a man. And the repair which follows even partial destruction of highly differentiated organs, such as the retina, is in the higher animals very imperfect.

In the higher animals the reproduction of the whole individual can be effected in no other way than by the process of sexual generation, through which the female representative element or

ovum is, under the influence of the male representative or sper-
matozoon, developed into an adult individual.

We do not purpose to enter here into any of the morphological
problems connected with the series of changes through which the
ovum becomes the adult being; or into the obscure biological
inquiry as to how the simple, all but structureless, ovum contains
within itself, in potentiality, all its future developments, and as
to what is the essential nature of the male action.   These prob-
lems and questions are fully discussed elsewhere; they do not
properly enter into a work on physiology, except under the view
that all biological problems are, when pushed far enough, physi-
ological problems.   We shall limit ourselves to a brief survey of
the more important physiological phenomena attendant on the
impregnation of the ovum, and on the nutrition and birth of the
embryo.

[*The Physiological Anatomy of the Organs of Generation.*

The female organs of generation are anatomically divided into
the internal and external organs.   The latter comprise the labia
majora and minora, the clitoris, the hymen, the meatus urinarius,
the vulvo-vaginal glands, and the mucous and sebaceous glands
which are distributed in the mucous membrane covering the
parts.   The external organs play a very subsidiary part in the
function of reproduction, and they will be passed by with this
brief notice.

The internal organs comprise the vagina, uterus, Fallopian
tubes, and ovaries.

The vagina is a musculo-membranous canal, about four to six
inches long, directed obliquely upwards and backwards, and ex-
tending from the hymen to the cervix uteri, where it is attached
at a point a short distance above the os uteri.   Its walls consist
of an external coat of longitudinal muscular fibres, a middle
erectile coat, and an internal mucous coat.   The mucous mem-
brane is continuous below with that covering the external geni-
tals, and above with the mucous membrane lining the uterus.
The anterior and posterior surfaces are marked by longitudinal
folds or raphe, from which a number of transverse folds are
given off.   This membrane is provided with mucous glands, and
is thickly covered with sensitive papillæ.

The uterus is a flattened, pyriform, muscular organ (Fig. 250).
Anatomically it is divided into the fundus, neck, and cervix.
The neck indicates the point of division between the lower con-
stricted portion, which is the cervix, and the upper expanded
portion, the fundus.   The cervix, which extends from the neck
to the end of the organ, projects into the vagina, at which point
it is marked by a transverse fissure, called the *os uteri.*

The cavity of the uterus is somewhat triangular in shape, and very much flattened antero-posteriorly. The inferior angle of the cavity is continuous with the canal running through the cervix to the vagina. The superior angles are called the cornua; at the bottom of each is an orifice of a Fallopian tube. The uterus is composed of three coats; a serous (formed by the peri-

FIG. 250.
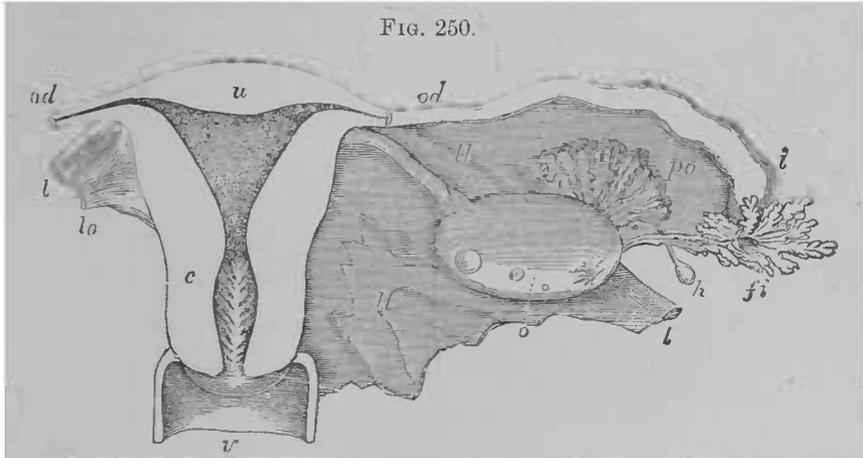
DIAGRAMMATIC VIEW OF THE UTERUS AND ITS APPENDAGES, AS SEEN FROM BEHIND
(from QUAIN). ½.

The uterus and upper part of the vagina have been laid open by removing the posterior wall; the Fallopian tube, round ligament, and ovarian ligament have been cut short, and the broad ligament removed on the left side; *u*, the upper part of the uterus; *c*, the cervix opposite the os internum; the triangular shape of the uterine cavity is shown, and the dilation of the cervical cavity with the rugæ, termed arbor vitæ; *v*, upper part of the vagina; *od*, Fallopian tube or oviduct; the narrow communication of its cavity with that of the cornu of the uterus on each side is seen; *l*, round ligament; *lo*, ligament of the ovary; *o*, ovary; *i*, wide outer part of the right Fallopian tube; *fi*, its fimbriated extremity; *po*, parovarium; *h*, one of the hydatids frequently found connected with the broad ligament.

toneum), a muscular, and a mucous coat. The mucous coat is continuous with that lining the Fallopian tubes and vagina. It is covered with columnar ciliated epithelium, and, if examined with a lens, the openings of the mucous follicles will be seen to be very profusely distributed over the surface. If a vertical section be made, as in Fig. 251, the tubules will be seen to be arranged perpendicularly to the surface, having a wavy course. In the impregnated uterus they become much swollen and enlarged. The mucous membrane lining the cervix, on account of its peculiar appearance, is called the *arbor vitæ uterinus*.

The Fallopian tubes (Fig. 250) are about four inches in length, and extend from the cornua of the uterus to the ovaries, where they end in enlarged expanded extremities, the margins of which

are covered by long slender processes, one of them being connected to the ovary. This portion of the tube is called the fimbriated extremity. The tubes are composed of a serous, muscular, and mucous layer. The mucous membrane is covered with ciliated columnar epithelium.

The ovaries (Fig. 250) are flattened, ovoidal bodies, which are situated one on each side of the uterus, and enclosed in the folds of the broad ligaments. They are each connected with the uterus by a ligament, and with the Fallopian tube by one of its fimbriæ. They each consist of a fibrous coat (*tunica albuginea*) which encloses the stroma of the organ. (Fig. 251.) The stroma is com-
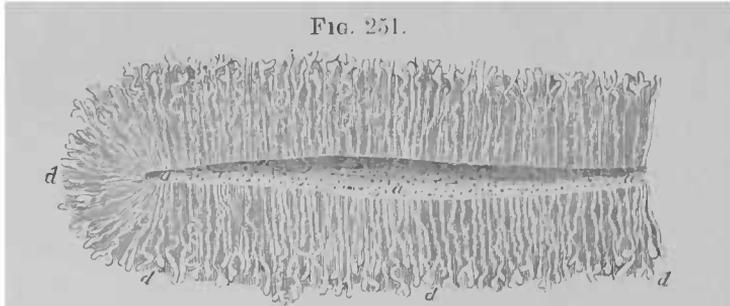
FIG. 251.

Section of the Lining Membrane of a Human Uterus at the Period of Commencing Pregnancy, showing the arrangements and other peculiarities of the glands, *d, d, d,* with their orifices, *a, a, a,* on the internal surface of the organ. Twice the natural size.

posed of a soft vascular fibrous tissue, having embedded in it a number of small bodies, called Graafian vesicles, which are in divers stages of development. These vesicles commence their development in the deeper portions of the ovary, and as they approach maturity gradually make their way to the surface, where they project as prominences, and their capsule finally rupturing, discharge their contents into the Fallopian tube. Each vesicle consists of an external coat formed by the ovary, an internal coat or capsule, and within this a layer of cells, which constitutes the *membrana granulosa*. The interior of the vesicle consists of an albuminous fluid, in which is suspended the ovule.

The Male Generative Organs.—The same physiological interest is not centered in the male organs of generation, as in those of the female, the principal interest being concentrated upon the organs which secrete the male fluid by which the ovule is impregnated. Our remarks will, therefore, be almost entirely confined to the organs concerned in the secretion of this fluid.

The male organs comprise the penis or organ of copulation, the prostate and Cowper's glands, the testicles, and vasa deferentia and vesiculæ seminales.

The prostate gland surrounds the neck of the bladder and commencement of the urethra (Fig. 253). It secretes a milky fluid, which is conveyed by the prostatic ducts to the floor of the urethra. Cowper's glands are two small glands which are situated between the layers of the deep perineal fascia at the anterior part of the membranous urethra. They secrete a viscid fluid, which is conveyed by ducts to the floor of the urethra.

The testes or testicles are two small flattened ovoidal glands, which are situated in a musculo-membranous pouch, called the

FIG. 252.
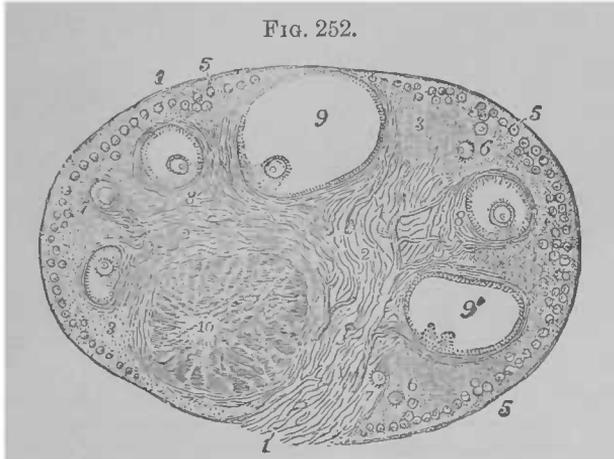
VIEW OF A SECTION OF THE PREPARED OVARY OF THE CAT. After SCHRON. 6·1.

1, outer covering and free border of the ovary; 1′, attached border; 2, the ovarian stroma, presenting a fibrous and vascular structure; 3, granular substance lying external to the fibrous stroma; 4, bloodvessels; 5, ovigerms in their earliest stages occupying a part of the granular layer near the surface; 6, ovigerms which have begun to enlarge and to pass more deeply into the ovary; 7, ovigerms round which the Graafian follicle and tunica granulosa are now formed, and which have passed somewhat deeper into the ovary and are surrounded by the fibrous stroma; 8, more advanced Graafian follicle with the ovum embedded in the layer of cells constituting the proligerous disk; 9, the most advanced follicle containing the ovum, etc.; 9′, a follicle from which the ovum has accidentally escaped; 10, corpus luteum.

scrotum, and suspended by the spermatic cords. Each testicle consists of two parts: the gland proper and the epididymis. The gland (Fig. 254) is composed of an outer fibrous coat, the *tunica albuginea*, this being covered by a serous membrane, the *tunica vaginalis*. The substance of the gland consists of a number of pyramidal lobular divisions, which are situated with their bases towards the surface. Each lobule is composed of several convoluted *tubuli seminiferi*, and are separated from adjoining lobules by prolongation of fibrous tissue from the tunica albuginea. The tubules are composed of a homogeneous basement membrane, which is lined by granular nucleated epithelium. In the apices

of the lobules they have a straight course, and form the *vasa recta*. They then enter the fibrous tissue of the mediastinum (Fig. 254), and form a plexus of tubes called the *rete testis*, which end in the upper part of the mediastinum as the *vasa efferentia*, and these becoming very much convoluted form the *globus major* or head of the epididymis. The tubules of the globus major
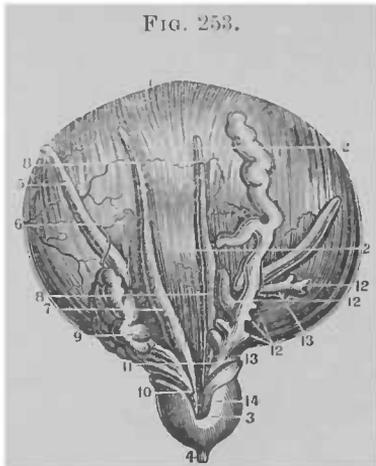
FIG. 253.—The Base of the Male Bladder, with the Vesiculæ Seminales and Prostate Gland. After HALLER   1, the urinary bladder ; 2, the longitudinal layer of muscular fibres ; 3, the prostate gland ; 4, membranous portion of the urethra ; 5, the ureters ; 6, bloodvessels ; 7, left ; 8, right vas deferens ; 9, left seminal vesicle in its natural position ; 10, ductus ejaculatorius of the left side traversing the prostate gland ; 11, right seminal vesicle injected and un- ravelled ; 12, 13, blind pouches of vesiculæ ; 14, right ductus ejaculatorius traversing the prostate.
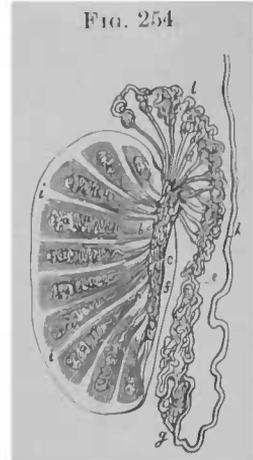
FIG 254.—*a*, lobules ; *b*, vasa recta ; *c*, mediastinum ; *d*, vasa efferentia ; *e*, body of epidid- ymis ; *f*, rete testes ; *g*, globus minor ; *h*, vas deferens ; *i*, tunica albuginea and its inter- lobular reflections ; *l*, globus major.

unite to form a single tube, which is very much convoluted, and constitutes the body and *globus minor* of the epididymis, and is then continued from the globus minor to the base of the bladder as the excretory duct or *vas deferens*.

The *vas deferens*, commencing at the globus minor, ascends in the posterior part of the spermatic cord through the spermatic canal into the pelvis, where it runs to the base of the bladder and becomes enlarged, sacculated, and narrowed, and joins with the duct of the vesicula seminalis to form a common ejaculatory duct. The walls of the vas deferens are composed of fibrous and muscular tissue, which is lined by a mucous membrane with columnar epithelium.

The *vesiculæ seminales* are two elongated sacculated bodies,

placed external to the vasa deferentia. The structure of the
seminal vesicles is similar to that of the vasa deferentia, con-
sisting of a fibro-muscular wall lined with a mucous membrane,
which is covered by granular, nucleated, polygonal epithelium
cells. These organs serve as receptacles for the seminal fluid
secreted by the testes, and at the same time produce a secretion
of their own which is added to it. The ejaculatory ducts, which
are formed by the union of the ducts of the vasa deferentia and
vesiculæ seminales, open into the prostatic portion of the urethra.
Their coats are thinner, but have essentially the same structure
as the vasa deferentia, with which they are continuous.

FIG. 255.
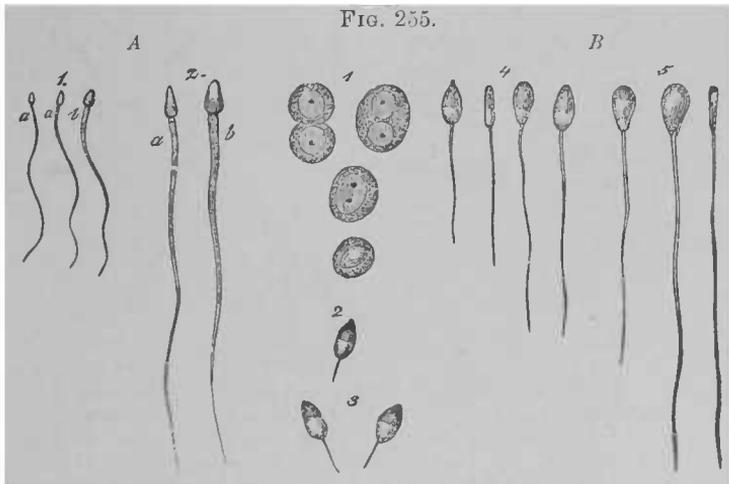
_A_, SPERMATOZOA FROM THE HUMAN VAS DEFERENS. After KOLLIKER.

1, magnified 350 diameters ; 2, magnified 800 diameters ; _a_, from the side ; _b_, from above.

_B_, SPERMATIC CELLS AND SPERMATOZOA OF THE BULL UNDERGOING DEVELOPMENT.
After KOLLIKER. 450–1.

1, spermatic cells, with one or two nuclei, one of them clear ; 2, 3, free nuclei, with sper-
matic filaments forming ; 4, the filaments elongated and the body widened ; 5, filaments
nearly fully developed.

The _seminal fluid_ is a complex secretion, being composed of
the anatomical elements of _spermatozoa_, which are formed in the
testes, and of the secretions of the vasa deferentia, vesiculæ
seminales, the prostate and Cowper's glands, and the mucous
glands of the urethra. The seminal fluid is of a thick, whitish,
striated appearance, and, if examined microscopically, is seen to
contain innumerable bodies which are in active motion. These
are the spermatozoids, and are the essential male elements con-
cerned in the fecundation of the ovule. Each of these bodies
(Fig. 255) consists of a flattened, ovoidal head, having at its base

a tapering caudate appendage in active vibratile motion. These anatomical elements were at first considered animalcula, but they are now looked upon as free masses of protoplasm with ciliary appendages, which endow them with the power of migration.

The spermatozoa are developed from the nuclei of vesicles which are formed in the tubules of the testes. The nuclei are metamorphosed into the heads of the spermatozoa, the ciliary appendages being afterwards developed as a sort of outgrowth. Different stages of the development and other interesting features are shown in the above figure.]

CHAPTER I.

MENSTRUATION.

FROM puberty, which occurs at from 13 to 17 years of age, to the climacteric, which arrives at from 45 to 50 years of age, the human female is subject to a monthly discharge of ova from the ovaries, accompanied by special changes, not only in those organs, but also in the Fallopian tubes and uterus, as well as by general changes in the body at large, the whole constituting "menstruation." The essential event in menstruation is the escape of an ovum from its Graaffian follicle (Fig. 256). The whole ovary at this time becomes congested, and the ripe follicle bulges from
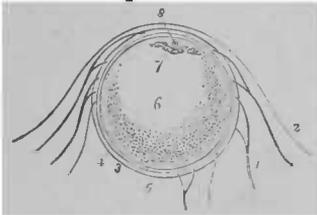
[FIG 256.   FIG. 257.
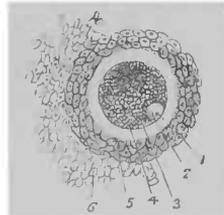
FIG. 256.—Section of Graafian Follicle of a Mammal. After VON BARR. 1, stroma of the ovary with bloodvessels ; 2, peritoneum ; 3 and 4, layers of the external coat of the Graafian follicle ; 5, membrana granulosa ; 6, fluid of the Graafian follicle ; 7, granular zone, or discus proligerus, containing the ovule (8).

FIG. 257.—Ovule of the Sow. After BARRY. 1, germinal spot ; 2, germinal vesicle ; 3, yolk ; 4, zona pellucida ; 5, discus proligerus ; 6, adherent granules or cells.]

its surface. The most projecting portion of the wall of the follicle, which has previously become excessively thin, is now ruptured, and the ovum, which having left its earlier position, is lying close under the projecting surface of the follicle, escapes, together with the cells of the *discus proligerus* (Fig. 257), into the Fallopian tube. How the entrance of the ovum into the Fallopian tube is secured is not exactly known. Some maintain that the ovary is grasped by the trumpet-shaped fimbriated mouth of the Fallopian tube, itself turgid and congested ; the movements necessary to bring this about being effected by the plain muscular fibres present in the mouth of the tube. Others, rejecting this view, and asserting that the turgescence of the tube does not occur until after the ovum has become safely lodged in the tube, suggest that the ovum is carried in the proper direction by currents in the peritoneal cavity set up by the action of the ciliated epithelium lining the tube, currents whose direction

and strength seem, as shown by experiment, to be adequate to carry into the uterus particles present in the peritoneal fluid. Arrived in the tube, the ovum travels downwards, very slowly, by the action probably of the cilia lining the tube, though possibly its progress may occasionally be assisted by the peristaltic contractions of the muscular walls. The stay of the ovum in the Fallopian tube may extend to several days. There is an effusion of blood into the ruptured follicle, which is subsequently followed by histological changes in the coats of the follicle resulting in a *corpus luteum*[1] (Fig. 258). The discharge of the ovum

[Fig. 258.
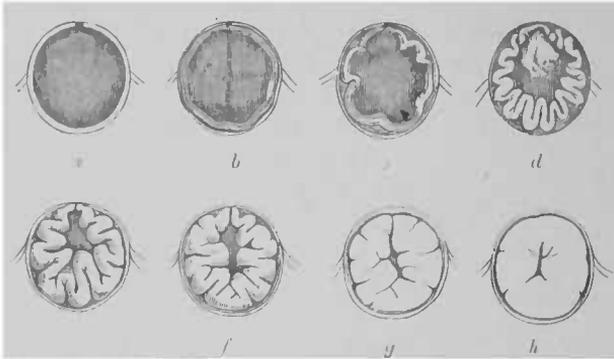
Successive Stages of the Formation of the Corpus Luteum in the Graafian Follicle of the Sow, as seen in vertical section; at *a* is shown the state of the follicle immediately after the expulsion of the ovule, its cavity being filled with blood, and no ostensible increase of its epithelial lining having yet taken place; at *b*, a thickening of this lining has become apparent; at *c* it begins to present folds which are deepened at *d*, and the clot of blood is absorbed *pari passu*, and at the same time decolorized; a continuance of the same process, as shown at *e, f, g, h,* forms the corpus luteum, with its delicate cicatrix.]

[1 The following tabular statement by Dalton expresses the principal differences between the corpus luteum of the non-pregnant and pregnant female:

	CORPUS LUTEUM OF MENSTRUATION.	CORPUS LUTEUM OF PREGNANCY.
At the end of three weeks.	Three-quarters of an inch in diameter; central clot reddish; convoluted wall pale.	
One month.	Smaller convoluted wall bright yellow; clot still reddish.	Larger; convoluted with bright yellow; clot still reddish.
Two months.	Reduced to the condition of an insignificant cicatrix.	Seven-eighths of an inch in diameter; convoluted wall bright yellow; clot perfectly decolorized.
Six months.	Absent.	Still as large as at end of second month; clot fibrinous; convoluted wall paler.
Nine months.	Absent.	One-half an inch in diameter; central clot converted into a radiating cicatrix; the external wall tolerably thick and convoluted, but without any bright yellow color.]

is accompanied, not only by a congestion or erection of the ovary and Fallopian tube, but also by marked changes in the uterus, especially in the uterine mucous membrane. While the whole organ becomes congested and enlarged, the mucous membrane, and especially the uterine glands, are distinctly hypertrophied. The swollen internal surface is thrown into folds which almost obliterate the cavity; and a hemorrhagic discharge, often considerable in extent, constituting the menstrual or catamenial flow, takes place from the greater part of its surface. The blood as it passes through the vagina becomes somewhat altered by the acid secretions of that passage, and when scanty coagulates but slightly; when the flow, however, is considerable, distinct clots may make their appearance. The swollen and hypertrophied mucous membrane then undergoes a rapid degeneration, and is shed, passing away sometimes in distinct masses, forming the latter part of the menstrual flow. The loss of the mucous membrane is so complete, that the bases only of the uterine glands are left, and from the epithelial cells lining these the regeneration of the new membrane is said to take place. It is not certain that menstruation, in the human subject at all events, is always accompanied by a discharge of an ovum; indeed, cases have been recorded in which menstruation continued after what appeared to be complete removal of both ovaries. And it seems probable also that under certain circumstances—*ex. gr.*, coitus—a discharge of an ovum may take place at other times than at the menstrual period. Since, however, the time during which both the ovum and the spermatozoon may remain in the female passages alive and functionally capable is considerable, probably extending to some days, coitus effected either some time after or some time before the menstrual escape of an ovum might lead to impregnation and subsequent development of an embryo; hence the fact that impregnation may follow upon coitus at some time after or before menstruation is no very cogent argument in favor of the view that such a coitus has caused an independent escape of an ovum. The escape of the ovum is said to precede, rather than coincide with or follow, the catamenial flow. If no spermatozoa come in contact with the ovum it dies, the uterine membrane returns to its normal condition, and no trace of the discharge of an ovum is left, except the corpus luteum in the ovary.

It is obvious that in these phenomena of menstruation we have to deal with complicated reflex actions affecting, not only the vascular supply, but, apparently in a direct manner, the nutritive changes of the organs concerned. Our studies on the nervous action of secretion render it easy for us to conceive in a general way how the several events are brought about. It is no more

difficult to suppose that the stimulus of the enlargement of a Graaffian follicle causes nutritive as well as vascular changes in the uterine mucous membrane, than it is to suppose that the stimulus of food in the alimentary canal causes those nutritive changes in the salivary glands or pancreas which constitute secretion.   In the latter case we can to some extent trace out the chain of events ; in the former case we hardly know more than that the maintenance of the lumbar cord is sufficient, as far as the central nervous system is concerned, for the carrying on of the work.   In the case of a dog in which the spinal cord had been completely divided in the dorsal region, while the animal was as yet a mere puppy, " heat " or menstruation took place as usual.

CHAPTER II.

IMPREGNATION.

In coitus the discharge of the semen containing the spermatozoa is most probably effected by means of the peristaltic contractions of the vesiculæ seminales and vasa deferentia, assisted by rhythmical contractions of the bulbo-cavernosus muscle, the whole being a reflex act, the centre of which appears to be in the lumbar spinal cord. In the dog, emission of semen can be brought about by stimulation of the glans penis after complete division of the spinal cord in the dorsal region. The emission of semen is preceded by an erection of the penis. This, we have already seen, p. 256, is in part at least due to an increased vascular supply brought about by means of the nervi erigentes; it is probable, however, that the condition is further secured by a compression of the efferent veins of the corpora cavernosa by means of smooth muscular fibres present in those bodies. The semen being received into the female organs, which are at the time in a state of turgescence resembling the erection of the penis, but less marked, the spermatozoa find their way into the Fallopian tubes, and here (probably in its upper part) come in contact with the ovum. In the case of some animals impregnation may take place at the ovary itself. The passage of the spermatozoa is most probably effected mainly by their own vibratile activity; but in some animals a retrograde peristaltic movement travelling from the uterus along the Fallopian tubes has been observed; this might assist in bringing the semen to the ovum, but inasmuch as these movements are probably parts of the act of coitus and impregnation may be deferred till some time after that event, no great stress can be laid upon them.

As the result of the action of the spermatozoa on the ovum, the latter, instead of dying as when impregnation fails, awakes to great nutritive activity accompanied by remarkable morphological changes; it enlarges and develops into an embryo.

[Preceding the time of the occurrence of the entrance of the spermatozoon into the egg, certain anatomical changes have been observed to occur, and in order thoroughly to understand these, as well as the changes which follow in the ovum, it will first be necessary to review the anatomy of the egg.

The ovule is a minute cell, the wall being formed by a struc-

tureless, transparent membrane, called the *zona pellucida*, or vitelline membrane. Within this is the yolk, or vitellus, which consists of a granular semi-fluid mass, having suspended in it a *nucleus* or *germinal vesicle*, containing a *nucleolus* or *germinal spot*. The germinal vesicle consists of a very delicate transparent homogeneous membrane, which encloses a fluid with granules, and suspended in it, an eccentric nucleolus of a granular and fibrillated structure.

Previous to the occurrence of the impregnation of the ovule a very interesting series of changes have been observed to take place. According to Balfour,[1] the first interesting point to be noticed is the migration of the germinal vesicle towards the cell wall. The vesicular wall then becomes wavy and gradully disappears, while at the same time the nucleolus or germinal spot has undergone metamorphosis, so that what remains of these structures is a spindle-shaped mass. One extremity of this mass gradually projects through the cell wall and is thrown off as a *polar vesicle*. From the other remaining portion a second polar vesicle is formed, the part of the mass then remaining in the ovule being permanent, and is called the *female pronucleus.* The next change observed is the appearance of a zone, of radial

FIG. 259.
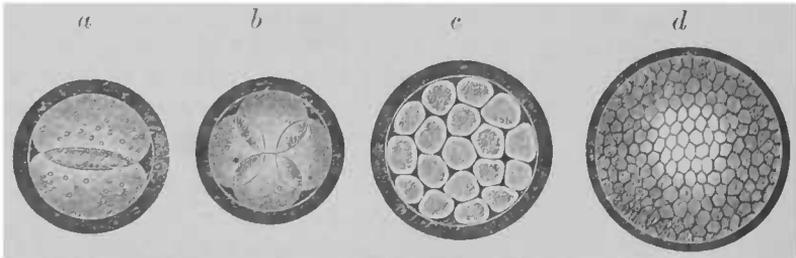
DIAGRAMS OF THE VARIOUS STAGES OF CLEAVAGE OF THE YOLK. After DALTON.

striæ around the pronucleus and its migration to the centre of the egg. The spermatozoon then penetrates the wall of the ovule, probably at the point of the formation of the polar vesicles. The tail of the spermatozoon becomes absorbed, and the head is metamorphosed into the *male pronucleus.* From the male pronucleus a number of radiating striæ are given off in all directions, and it then migrates towards the female pronucleus, and afterwards fuses with it, forming a single or *cleavage nucleus.*

Cleavage or segmentation of the vitellus then begins (Fig. 259), by which process the nucleus thus formed divides into two

[1] See Quarterly Journal of Microscopy, October, 1878.

parts, each taking with it half of the vitelline mass. These two divide into four, and these four into eight, and so on indefinitely until an agglomerate mass of nucleated cells results, each of which contains a part of the cleavage nucleus. This mass of cells is called the mulberry mass, and the cells constituting it arrange themselves about the interior of the *zona pellucida* and form the *blastodermic vesicle* or *membrane*. This membrane then splits up into two layers, the external and internal; a third or middle layer being afterwards formed between them.

Immediately after the formation of the two layers of blastoderm, an opaque rounded collection of small cells occurs, called the *area germinativa* or embryonic spot. (Fig. 260.) This

FIG. 260.
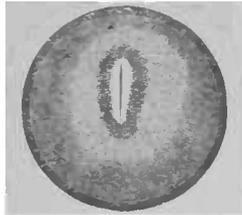
Impregnated Egg, with Commencement of Formation of Embryo; showing the area germinativa or embryonic spot, the area pellucida, and the primitive groove or trace. After DALTON

spot then becomes elongated, and in its longitudinal axis the first trace of the embryo appears as a faint line, termed the *primitive trace*, this being in the midst of a clear elongated mass of cells, the *area pellucida*, which is itself surrounded by a more opaque zone.

In front of the primitive trace two folds are formed from which a groove is prolonged backwards in a line with the primitive trace. These folds gradually extend along the entire length of the groove, and form the *laminæ dorsales*, which by growing, project more and more above the groove, and gradually approaching each other, coalesce and enclose the neural canal, which will afterwards contain the cerebro-spinal axis. At about the same period corresponding to the development of the dorsal laminæ similar laminæ are given off from the under surface of the blastoderm. These are the *laminæ ventrales*, which, by gradually enlarging and finally coalescing, enclose the abdominal cavity. Beneath the floor of the groove above described a delicate whitish collection of cells appears. This is the *chorda dorsalis* or notochord, around which are afterwards developed the bodies and processes of the vertebra.

During this period other changes have also taken place. The

cephalic and caudal extremities have become flexed and form the cephalic and caudal *flexures;* and the embryo also being curved upon itself laterally, the vitelline mass appears separated from it by a constriction. This constriction gradually increasing, finally separates the vitelline mass as a vesicular body, it being connected with the body of the embryo by the vitelline duct. (Fig. 261.) The vesicular body thus formed is called the *um-*

Fig. 261.
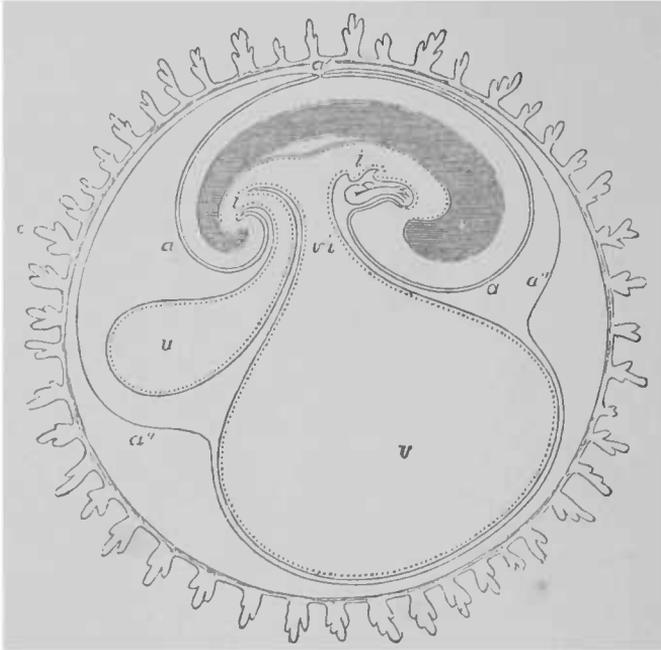
Diagrammatic Section showing the Relation in a Mammal and in a Man between the Primitive Alimentary Canal and the Membranes of the Ovum. The stage represented in this diagram corresponds to that of the fifteenth or seventeenth day in the human embryo, previous to the expansion of the allantois; *c,* the villous chorion; *a,* the amnion; *a',* the place of convergence of the amnion and reflection of the false amnion, *a'' a'',* or outer or corneus layer; *e,* the head and trunk of the embryo, comprising the primitive vertebræ and cerebrospinal axis; *i, i,* the simple alimentary canal in its upper and lower portions; *v,* the yolk-sac or umbilical vesicle; *vi,* the vitelline duct; *u,* the allantois connected by a pedicle with the anal portion of the alimentary canal.

bilical vesicle. This at first communicates with the intestinal cavity, but as development proceeds the duct of communication becomes closed, and the vesicle is merely attached by a pedicle, and finally disappears altogether. At the time of the development of the bloodvessels, vessels appear on the surface of the umbilical vesicle, constituting the *vascular area,* the chief vessels

being the omphalo-mesenteric arteries and veins. The vessels of the vascular area absorb the nutritive material contained within the vesicle and convey it to the embryo for its sustenance.

Shortly after the occurrence of the commencement of the formation of the umbilical vesicle, double folds, formed of the external layer of the blastoderm, are given off from the cephalic and caudal extremities and laterally, which curve around over the dorsal surface of the embryo, where they meet and coalesce, and their point of junction becoming absorbed, form the amniotic cavity. (Figs. 261, 262, 263, and 264.) The outer layer of the

FIG. 262.   FIG 263.

a, Chorion with Villi. The Villi are shown to be best developed in the part of the chorion to which the allantois is extending; this portion ultimately becomes the placenta; b, space between the two layers of the amnion; c, amniotic cavity; d, situation of the intestine, showing its connection with the umbilical vesicle; e, umbilical vesicle; f, situation of heart and vessels; g, allantois. After Todd and Bowman.

fold, or false amnion, gradually expands and covers the whole of the internal surface of the vitelline membrane, which it ultimately replaces; the inner layer, or true amnion, is continuous with the skin of the embryo at the umbilicus, and closely envelops it. The amniotic cavity or sac thus formed becomes filled with the liquor amnii, which gradually increases in quantity as pregnancy advances, up to about the fifth or sixth month, when the quantity gradually decreases up to the time of labor.

At about the time of the commencement of the development of the amnion a new organ, the *allantois*, appears as a pyriform mass of cells at a point immediately posterior to the vitelline duct and projecting through the same opening. (Fig. 264.) This mass of cells undergoes rapid growth, spreading itself between the true and false amniotic folds, finally completely enclosing the embryo and amnion (Fig. 265), becoming at the same time adjoined to the false amnion, when it is developed into the *true*

chorion. During the process of the development of the allantois, it has become very vascular; at first there are two arteries and two veins, afterwards one of the veins disappears. These vessels constitute the umbilical vessels, forming part of the umbilical cord which connects the allantois with the embryo. During the development of the allantois it presents three distinct anatomical

Fio 264.   Fio. 265.
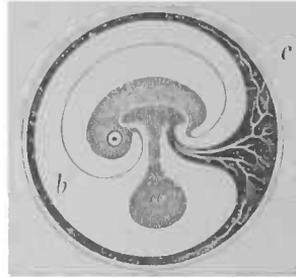
FIG. 264 —Diagram of Fecundated Egg. *a*, umbilical vesicle ; *b*, amniotic cavity ; *c*, allantois   After DALTON.

FIG. 265.—Fecundated Egg with Allantois nearly complete. *a*, inner layer of amniotic fold ; *b*, outer layer of ditto ; *c*, point where the amniotic folds come in contact. The allantois is seen penetrating between the outer and inner layers of the amniotic folds. This figure, which represents only the amniotic folds and the parts within them, should be compared with Figs. 262 and 263, in which will be found the structures external to these folds.

portions: a portion which becomes constricted off, as it were, from the rest and forms the urinary bladder; the outer portion forms the chorion, the intermediate portion forming the umbilical cord.

During the development of the embryo up to this time, the first chorion was formed by villosities formed on the vitelline membrane; and following that by villosities developed upon the false amnion. The allantois then becoming developed, completely covers the internal surface of the false amnion, which then gradually disappears as a distinct structure. The *true chorion* is then formed by the allantois, which becomes covered by a growth of a multitude of vascular shaggy tufts or *villi* (Fig. 266). These villi, at first, are distributed over the entire surface of the organ, but they soon commence disappearing, except at a small area corresponding to the attachment of the pedicle which connects the allantois with the embryo. At this point they become greatly increased in number, and also in size and vascularity. These villi are composed of a fibro-granular matrix, in which are numerous capillary loops, and are covered with a layer of epithelial cells (Fig. 267). This portion of the chorion forms the fœtal portion of the placenta.]

No sooner, however, have these changes begun in the ovum than correlative changes, brought about probably by reflex action, but at present most obscure in their causation, take place in the uterus. The mucous membrane of this organ, whether the coitus resulting in impregnation be coincident with a menstrual period or not, becomes congested, and a rapid growth takes place, characterized by a rapid proliferation of the epithelial and subepithelial tissues. Unlike the case of menstruation, however,

[FIG. 266.   FIG. 267.
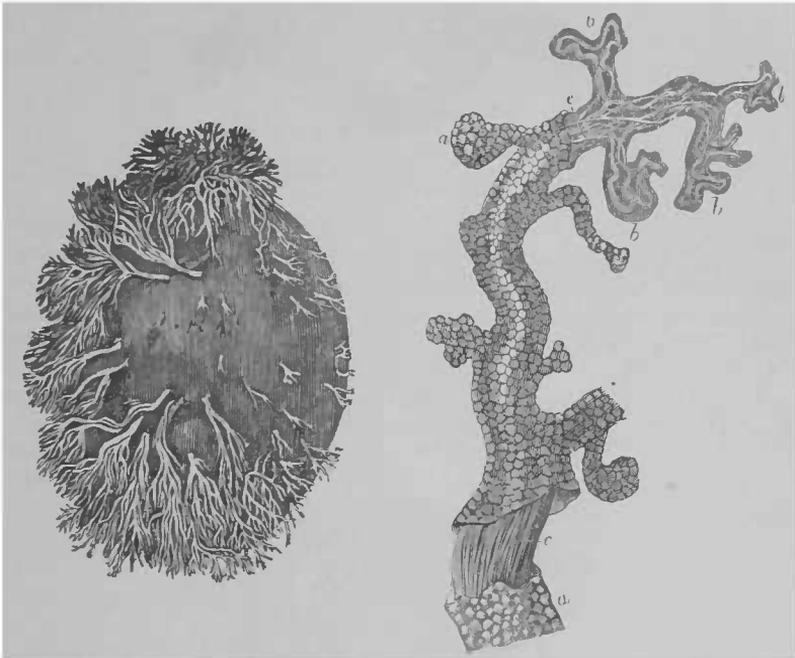
FIG. 266.—Entire Human Ovum of eighth week, sixteen lines in length (not reckoning the tufts); the surface of the chorion partly smooth and partly rendered shaggy by the growth of tufts.

FIG. 267.—Portion of one of the Fœtal Villi, about to form part of the Placenta, highly magnified, *a, a*, its cellular covering; *b, b, b*, its looped vessels; *c, c*, its basis of connective tissue.]

this new growth does not give way to immediate decay and hemorrhage, but remains, and may be distinguished as a new temporary lining to the uterus, the so-called decidua. Into this decidua the ovum, on its descent from the Fallopian tube, in which it has undergone developmental changes, extending most probably as far, at least, as the formation of the blastoderm, if not further, is received; and in this it becomes embedded, the new growth

closing in over it. (Figs. 268, 269.) Meanwhile the rest of the uterine structures, especially the muscular tissue, become also much enlarged; as pregnancy advances a large number of new muscular fibres are formed. As the ovum continues to increase in size, it bulges into the cavity of the uterus, carrying with it the portion of the decidua which has closed over it. Henceforward,

[Fig. 268.
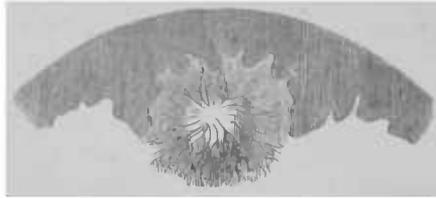
First Stage of the Formation of the Decidua Reflexa around the Ovum]

accordingly, a distinction is made in the now well-developed decidua between the *decidua reflexa*, or that part of the membrane which covers the projecting ovum, and the *decidua vera*, or the rest of the membrane lining the cavity of the uterus, the two being continuous round the base of the projecting ovum. That part of the decidua which intervenes between the ovum and the nearest uterine wall is frequently spoken of as the *decidua*

[Fig. 269.
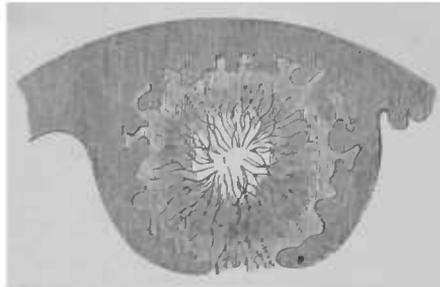
More Advanced Stage of Decidua Reflexa]

serotina. As the ovum develops into the foetus with its membranes, the decidua reflexa becomes pushed against the decidua vera; about the end of the third month, in the human subject, the two come into complete contact all over, and ultimately the distinction between them is lost. In the region of the decidua serotina, the allantoic vessels of the foetus develop a placenta.

[In the earliest stages of the development of the placenta, the

delicate villous processes of the chorion insinuate themselves into the hypertrophied follicles of the decidua serotina. The villi then undergo a rapid increase in size and vascularity, becoming branched into secondary and tertiary ramifications ; while, at the same time, corresponding changes are taking place in the follicles, by which they become greatly increased in size and vascularity, and at the same time forming diverticula in which are embedded the ramifications of the villi. The villi and follicles thus grow simultaneously, and finally become blended with each other and are no longer separate structures. The follicular bloodvessels first form capillary plexuses ; these vessels, however, become enlarged, forming frequent anastomoses, and finally coalescing to form *venous sinuses* (Fig. 270), in which are bathed

Fig. 270.
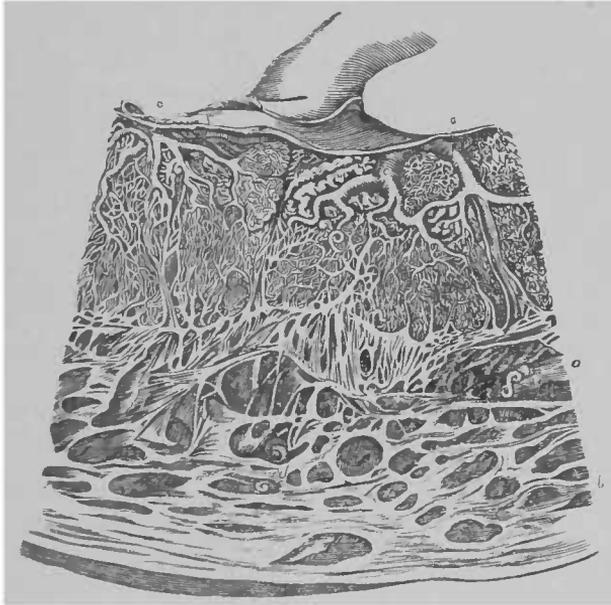
Section of a a portion of a fully formed Placenta, with the part of the Uterus to which it is attached. *a*, umbilical cord ; *b, b,* section of uterus, showing the venous sinuses ; *c, c, c,* branches of the umbilical vessels : *d, d,* curling arteries of the uterus.

the foetal villi There is no continuity established between the maternal and foetal blood ; the interchange of nutritive material necessary for the growth and development of the foetus takes place through the delicate walls of the villi.]

For further account of the various changes by which these events are brought about, as well as of the history of the embryo itself, we must refer the reader to anatomical treatises.

CHAPTER III.

THE NUTRITION OF THE EMBRYO.

DURING the development of the chick within the hen's egg the nutritive material needed for the growth first of the blastoderm, and subsequently of the embryo, is supplied by the yolk, while the oxygen of the air passing freely through the porous shell, gains access to all the tissues both of the embryo and yolk, either directly or by the intervention of the allantoic vessels. The mammalian embryo, during the period which precedes the extension of the allantoic vessels into the cavities of the uterine walls to form the placenta, must be nourished by direct diffusion, first from the contents of the Fallopian tube, and subsequently from the decidua; and its supply of oxygen must come from the same sources. All analogy would lead us to suppose that, from the very first, oxidation is going on in the blastodermic and embryonic structures; but the amount of oxygen actually withdrawn from without is probably exceedingly small in the early stages, seeing that nearly the whole energy of the metabolism going on is directed to the building up of structures, the expenditure of energy in the form of either heat or external work being extremely small. The marked increase of bulk which takes place during the conversion of the mulberry mass into the blastodermic vesicle, shows that at this epoch a relatively speaking large quantity of water at least, and probably of nutritive matter, must pass from without into the ovum; and subsequently, though the blastoderm and embryo may for some time draw the material for their continued construction at first hand from the yolk-sac or umbilical vesicle, both this and they continue probably until the allantois is formed to receive fresh material from the mother by direct diffusion.

As the thin-walled allantoic vessels come into closer and fuller connection with the maternal uterine sinuses, until at last in the fully formed placenta the former are freely bathed in the blood streaming through the latter, the nutrition of the embryo becomes more and more confined to this special channel. The blood of the fœtus flowing along the umbilical arteries effects exchanges with the venous blood of the mother, and leaves the placenta by the umbilical vein richer in oxygen and nutritive material and poorer in carbonic acid and excretory products than when it issued from the fœtus.

As far as the gain of oxygen and the loss of carbonic acid are concerned, these are the results of simple diffusion. Venous blood, as we have already seen, always contains a quantity of oxyhæmoglobin, and the quantity of this substance present in the blood of the uterine veins is sufficient to supply all the oxygen that the embryo needs ; the blood of the fœtus, containing less oxygen than even the venous blood of the mother, will take up a certain though small quantity. The fœtal blood travelling in the umbilical artery must, in proportion to the extent of the nutritive changes going on in the embryo, possess a higher carbonic tension than that in the umbilical vein or uterus sinus ; and by diffusion gets rid of this surplus during its stay in the placenta. The blood in the umbilical arteries and veins is therefore, relatively speaking, venous and arterial, respectively, though the small excess of oxyhæmoglobin in the blood of the umbilical vein is insufficient to give it a distinctly arterial color, or to distinguish it as sharply from the more venous blood of the umbilical artery, as is ordinary arterial from ordinary venous blood. Thus, the fœtus breathes by means of the maternal blood, in the same way that a fish breathes by means of the water in which it dwells.

The blood of the fœtus is very poor in hæmoglobin corresponding to its low oxygen consumption. When the mother is asphyxiated, the fœtus is asphyxiated too, the oxygen of the latter passing back again into the blood of the former ; and the asphyxia thus produced in the fœtus is much more rapid than that which results when the oxygen is used up by the tissues of the fœtus alone, as when the umbilicus is ligatured and the fœtus not allowed to breathe.

If oxygen and carbonic acid thus pass by diffusion to and from the mother and the fœtus, one might fairly expect that diffusible salts, proteids, and carbohydrates would be conveyed to the latter, and diffusible excretions carried away to the former, in the same way ; and if fats can pass directly into the portal blood during ordinary digestion, there can be no reason for doubting that this class of food-stuffs also would find its way to the fœtus through the placental structures. We do know from experiment that diffusible substances will pass both from the mother to the fœtus, and from the fœtus to the mother ; but we have no definite knowledge as to the exact form and manner in which, during normal intrauterine life, nutritive materials are conveyed to or excretions conveyed from the growing young. The placenta is remarkable for the great development of cellular structures, apparently of an epithelial nature, on the border-land between the maternal and fœtal elements ; and it has been suggested that these form a temporary digestive and secretory (excretory) organ.

But we have no exact knowledge of what actually does take place in these structures. From the cotyledons of ruminants may be obtained a white creamy-looking fluid, which from many features of its chemical composition might be almost spoken of as a " uterine milk."

Speaking broadly, the fœtus lives on the blood of its mother, very much in the same way as all the tissues of any animal live on the blood of the body of which they are the parts.

For a long time all the embryonic tissues are " protoplasmic " in character ; that is, the gradually differentiating elements of the several tissues remain still embedded, so to speak, in undifferentiated protoplasm ; and during this period there must be a general similarity in the metabolism going on in various parts of the body. As differentiation becomes more and more marked, it obviously would be an economical advantage for partially elaborated material to be stored up in various fœtal tissues, so as to be ready for immediate use when a demand arose for it, rather than for a special call to be made at each occasion upon the mother for comparatively raw material needing subsequent preparatory changes. Accordingly, we find the tissues of the fœtus at a very early period loaded with glycogen. The muscles are especially rich in this substance, but it occurs in other tissues as well. The abundance of it in the former may be explained partly by the fact that they form a very large proportion of the total mass of the fœtal body, and partly by the fact that, while during the presence of the glycogen they contain much undifferentiated protoplasm, they are exactly the organs which will ultimately undergo a large amount of differentiation, and, therefore, need a large amount of material for the metabolism which the differentiation entails. It is not until the later stages of intrauterine life, at about the fifth month, when it is largely disappearing from the muscles, that the glycogen begins to be deposited in the liver. By this time histological differentiation has advanced largely, and the use of the glycogen to the economy has become that to which it is put in the ordinary life of the animal ; hence we find it deposited in the usual place. Besides being present in the fœtal, glycogen is found also in the placental structures ; but here, probably, it is of use, not for the fœtus, but for the nutrition and growth of the placental structures themselves. We do not know how much carbohydrate material finds its way into the umbilical vein ; and we cannot, therefore, state what is the source of the fœtal glycogen ; but it is at least possible, not to say probable, that it arises, in part at all events, from a splitting up of proteid material.

Concerning the rise and development of the functional activities of the embryo, our knowledge is almost a blank. We know

scarcely anything about the various steps by which the primary fundamental qualities of the protoplasm of the ovum are differentiated into the complex phenomena which we have attempted in this book to expound. We can hardly state more than that while muscular contractility becomes early developed, and the heart probably, as in the chick, beats even before the blood-corpuscles are formed, movements of the fœtus do not, in the human subject, become pronounced until after the fifth month; from that time forward they increase and subsequently become very marked. They are often spoken of as reflex in character; but only a preconceived bias would prevent them from being regarded as largely automatic. The digestive functions are naturally, in the absence of all food from the alimentary canal, in abeyance. Though pepsin may be found in the gastric membrane at about the fourth month, it is doubtful whether a truly peptic gastric juice is secreted during intrauterine life; trypsin appears in the pancreas somewhat later, but an amylolytic ferment cannot be obtained from that organ till after birth. The date, however, at which these several ferments make their appearance in the embryo appears to differ in different animals. The excretory functions of the liver are developed early, and about the third month bile-pigment and bile-salts find their way into the intestine. The quantity of bile secreted during intrauterine life, accumulates in the intestine and especially in the rectum, forming, together with the smaller secretion of the rest of the canal, and some desquamated epithelium, the so-called meconium. Bile-salts, both unaltered and variously changed, the usual bile-pigments, and cholesterin, are all present in the meconium. The distinct formation of bile is an indication that the products of fœtal metabolism are no longer wholly carried off by the maternal circulation; and to the excretory function of the liver there are now added those of the skin and kidney. The substances escaping by these organs find their way into the allantois or into the amnion, according to the arrangement of the fœtal membranes in different classes of animals; in both these fluids urea or allied bodies have been found as well as the ordinary saline constituents; the latter may or may not have been actually secreted. From the allantoic fluid of ruminants the body allantoin has been obtained, and human and other amniotic fluids have been found to contain urea. It is maintained by some, however, that the fluid in the amnion is secreted by the mother, and that hence the substances present in it are of maternal origin.

About the middle of intrauterine life, when the fœtal circulation (Fig. 271) is in full development, the blood flowing along the umbilical vein is carried chiefly by the ductus venosus into

[FIG. 271.
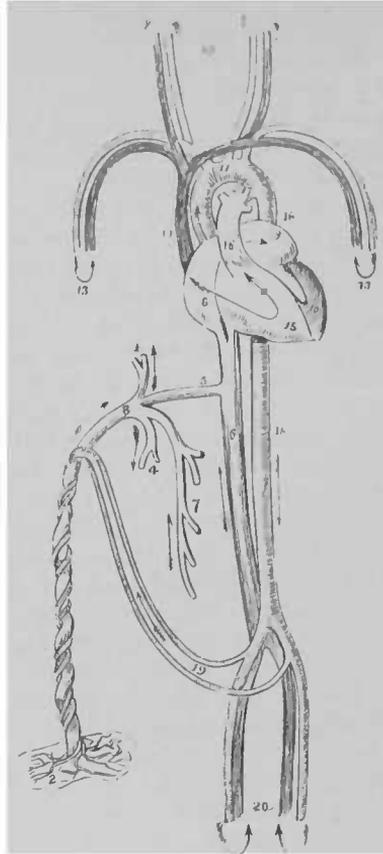
Diagram of the Fœtal Circulation. 1, the umbilical cord, consisting of the umbilical vein and two umbilical arteries, proceeding from the placenta (2) ; 3, the umbilical vein dividing into three branches, two (4, 4) to be distributed to the liver, and one (5 , the ductus venosus, which enters the inferior vena cava (6) ; 7, the portal vein, returning the blood from the intestines, and uniting with the right hepatic branch ; 8, the right auricle ; the course of the blood is denoted by the arrow proceeding from 8 to 9, the left auricle ; 10, the left ventricle ; the blood following the arrow to the arch of the aorta (11), to be distributed through the branches given off by the arch to the head and upper extremities ; the arrows 12 and 13 represent the return of the blood from the head and upper extremities through the jugular and subclavian veins to the superior vena cava (14), to the right auricle (8), and in the course of the arrow through the right ventricle (15), to the pulmonary artery (16) ; 17, the ductus arteriosus, which appears to be a proper continuation of the pulmonary artery ; the offsets at each side are the right and left pulmonary arteries cut off. The ductus arteriosus joins the descending aorta (18, 18), which divides into the common iliacs, and these into the internal iliacs, which become the umbilical arteries (19), and return the blood along the umbilical cord to the placenta, and the external iliacs (20), which are continued into the lower extremities. The arrows at the termination of these vessels mark the return of the venous blood by the to the inferior cava.]

the inferior vena cava, and so into the right auricle. Thence it is directed by the valve of Eustachius through the foramen ovale into the left auricle, passing from which into the left ventricle it is driven into the aorta. Part of the umbilical blood, however, instead of passing directly to the inferior cava, enters by the portal vein into the hepatic circulation, from which it returns to the inferior cava by the hepatic veins. The inferior cava also contains blood coming from the lower limbs and lower trunk. Hence, the blood which passing from the right auricle into the left auricle through the foramen ovale is distributed by the left ventricle through the aortic arch, though chiefly blood coming direct from the placenta, is also blood which on its way from the placenta has passed through the liver and blood derived from the tissues of the lower part of the body of the fœtus. The blood descending as fœtal venous blood from the head and limbs by the superior vena cava does not mingle with that of the inferior vena cava, but falls into the right ventricle, from which it is discharged through the ductus arteriosus (Botalli) into the aorta, below the arch, whence it flows partly to the lower trunk and limbs, but chiefly by the umbilical arteries to the placenta. A small quantity only of the contents of the right ventricle finds its way into the lungs. Now, the blood which comes from the placenta by the umbilical vein direct into the right auricle is, as far as the fœtus is concerned, arterial blood; and the portion of umbilical blood which traverses the liver probably loses at this epoch very little oxygen during its transit through that gland, the liver being at this period a simple excretory rather than an actively metabolic organ. Hence, the blood of the inferior vena cava, though mixed, is, on the whole, arterial blood; and it is this blood which is sent by the left ventricle through the arch of the aorta into the carotid and subclavian arteries. Thus, the head of the fœtus is provided with blood comparatively rich in oxygen. The blood descending from the head and upper limbs by the superior vena cava is distinctly venous; and this passing from the right ventricle by the ductus arteriosus is driven along the descending aorta, and together with some of the blood passing from the left ventricle round the aortic arch falls into the umbilical arteries and so reaches the placenta. The fœtal circulation then is so arranged, that while the most distinctly venous blood is driven by the right ventricle back to the placenta to be oxygenated, the most distinctly arterial (but still mixed) blood is driven by the left ventricle to the cerebral structures, which have more need of oxygen than have the other tissues. Contrary to what takes place afterwards, the work of the right ventricle is in the fœtus greater than that of the left; and, accordingly, that greater thickness of the left ventricular walls, so

characteristic of the adult, does not become marked until close upon birth.

In the later stages of pregnancy the mixture of the various kinds of blood in the right auricle increases preparatory to the changes taking place at birth. But during the whole time of intrauterine life the amount of oxygen in the blood passing from the aortic arch to the medulla oblongata is sufficient to prevent any inspiratory impulses being originated in the medullary respiratory centre. This during the whole period elapsing between the date of its structural establishment, or rather the consequent full development of its irritability, and the epoch of birth, remains dormant ; the oxygen supply to the protoplasm of its nerve-cells is never brought so low as to set going the respiratory molecular explosions. As soon however as the intercourse between the maternal and umbilical bood is interrupted by separation of the placenta or by ligature of the umbilical cord, or when, as by the death of the mother, the umbilical blood ceases to be replenished with oxygen by the maternal blood, or when in any other way blood of sufficiently arterial quality ceases to find its way by the left ventricle to the medulla oblongata, the supply of oxygen in the respiratory centre sinks, and when the fall has reached a certain point an impulse of inspiration is generated and the fœtus for the first time breathes. This action of the respiratory centre may be assisted by adjuvant impulses reaching the centre along various afferent nerves, such as those started by exposure of the body to the air, or to cold ; but these are subordinate, not essential. A retarded first breath may be hurried on by dashing water on the face of the new-born infant; but on the other hand, the fœtus, upon the cessation of the placental circulation, will make its first respiratory movements while it is still invested with the intact membranes and thus sheltered from the air and indeed from all external stimuli.

Before this first breath is taken the pulmonary alveoli contain no air, and the lungs when thrown into water sink at once ; they are then said to be "atelectatic." After the first breath, the alveoli contain air and the lungs float when thrown into water. A striking difference however exists between the lungs of a new-born infant and those of an older person. When the pleural cavity of the former is opened, the lungs do not collapse, no air is driven out by the trachea ; that partial distention of the lungs, and negative thoracic pressure, which we studied (p. 432) in treating of respiration, appears not to be established immediately upon birth. That portion of the residual air (p. 380) in the lungs of the adult, which, remaining after the most forcible expiration, is still driven from the lungs upon the pleural cavity being laid open, and which might be called "collapse air," is

wanting in the new-born infant. When the change from one condition to the other is effected is not at present known ; it may possibly arise from the growth of the chest outstripping that of the lungs.

When the first breath is taken, as under normal circumstances it is, with free access to the atmosphere, and the lungs become filled with air, the scanty supply of blood which at the moment was passing from the right ventricle along the pulmonary artery returns to the left auricle brighter and richer in oxygen than ever was the fœtal blood before. With the diminution of resistance in the pulmonary circulation caused by the expansion of the thorax, a larger supply of blood passes into the pulmonary artery instead of into the ductus arteriosus, and this derivation of the contents of the right ventricle increasing with the continued respiratory movements, the current through the latter canal at last ceases altogether, and its channel shortly after birth becomes obliterated. Corresponding to the greater flow into the pulmonary artery, a larger and larger quantity of blood returns from the pulmonary veins into the left auricle. At the same time the current through the ductus venosus from the umbilical vein having ceased, the flow from the inferior cava has diminished ; and the blood of the right auricle finding little resistance in the direction of the ventricle, which now readily discharges its contents into the pulmonary artery, but finding in the left auricle, which is continually being filled from the lungs, an obstacle to its passage through the foramen ovale, ceases to take that course. Any return of blood from the now vigorous and active left auricle into the right auricle is prevented by the valve which, during the latter stages of intrauterine life, has been growing up in the left auricle over the foramen ovale. At birth the edge of this valve is to a certain extent free, so that, in case of an emergency, as when the pulmonary circulation is obstructed, a direct escape of blood into the left auricle from the over-burdened right auricle can take place. Eventually, in the course of the first year, adhesion takes place, and the separation of the two auricles becomes complete. With its larger supply of blood and greater work the left ventricle acquires the greater thickness characteristic of it during life. Thus the fœtal circulation, in consequence of the respiratory movements to which its interruption gives rise, changes its course into that characteristic of the adult.

CHAPTER IV

PARTURITION.

In spite of the increasing distention of its cavity, the uterus remains quiescent, as far as any marked muscular contractions are concerned, until a certain time has been run. In the human subject the period of gestation generally lasts from 275 to 280 days—*i. e.*, about 40 weeks, the general custom being to expect parturition at about 280 days from the last menstruation. Seeing that, in many cases, it is uncertain whether the ovum which develops into the embryo left the ovary at the menstruation, preceding or succeeding coitus, or, as some have urged, independent of menstruation, by reason of the coitus itself, an exact determination of the duration of pregnancy is impossible.

In the cow the period of gestation is about 280 days, in the mare about 350, sheep about 150 days, dog about 60 days, rabbit about 30 days.

The extrusion of the fœtus is brought about, partly by rhythmical contractions of the uterus itself, and partly by a pressure exerted by the contraction of the abdominal muscles, similar to that described in defecation. The contractions of the uterus are the first to appear, and their first effect is to bring about a dilation of the os uteri; it is not till the later stages of labor, while the fœtus is passing into the vagina, that the abdominal muscles are brought into play.

The whole process of parturition may be broadly considered as a reflex act, the nervous centre being placed in the lumbar cord. In a dog, whose dorsal cord had been completely severed, parturition took place as usual; and the fact that, in the human subject, labor will progress quite naturally while the patient is unconscious from the administration of chloroform, shows that in woman also the whole matter is an involuntary action, however much it may be assisted by direct volitional efforts. That the uterus is capable of being thrown into contractions through reflex action, excited by stimuli applied to various afferent nerves, is well known. The contraction of the uterus, which is so necessary for the prevention of hemorrhage after delivery, may frequently be brought about by exerting pressure or by dashing cold water on the abdomen, by the introduction of foreign bodies into the vagina, and especially by putting the child to the nipple.

And we learn from experiments on animals that rhythmic contractions of the uterus, resembling at least those of parturition, may be brought about in a reflex manner by stimulating various afferent nerves. Similar movements may be induced by direct stimulation of the spinal cord along its whole length, as well as of various parts of the brain; but there are reasons for thinking that in these cases, the impulses started in the brain, and upper part of the spinal cord, produce their effects by working upon what may be called a "parturition" centre in the upper lumbar regions of the cord. And it would appear that the uterine contractions which are induced by such drugs as ergot, as well as those caused by asphyxia, are, at all events in part, brought about by the agency of the same lumbar centre. From this centre the paths for the efferent impulses appear (in the dog) to be twofold: one along sympathetic tracts, by nerves passing from the inferior mesenteric ganglion to the hypogastric plexus, and the other along spinal tracts by branches of the sacral nerves to the same plexus. It is stated that the characters of the movements induced by stimulating these two tracts are somewhat different, and, moreover, that the sympathetic tract is vaso-constrictor and the spinal tract vaso-dilator in nature; but the matter has not yet been fully worked out.

We are, however, hardly justified in considering the rhythmical contractions of the uterus during parturition as simple reflex acts excited by the presence of the fœtus. We are utterly in the dark as to why the uterus, after remaining apparently perfectly quiescent (or with contraction so slight as to be with difficulty appreciated) for months, is suddenly thrown into action, and within it may be a few hours or even less, gets rid of the burden it has borne with such tolerance for so long a time; none of the various hypotheses which have been put forward can be considered as satisfactory. And until we know what starts the active phase, we shall remain in ignorance of the exact manner in which the activity is brought about. The peculiar rhythmic character of the contractions, each "pain" beginning feebly, rising to a maximum, then declining, and finally dying away altogether, to be succeeded after a pause by a similar pain just like itself, pain following pain like the tardy long-drawn beats of a slowly beating heart, suggests that the cause of the rhythmic contraction is seated, like that of the rhythmic beat of the heart, in the organ itself. And this view is supported by the fact that contractions of the uterus, similar to those of parturition, have been observed in animals even after complete destruction of the spinal cord; and the movements induced by asphyxia seem in part, and those caused by some drugs such as ammonia, seem to be wholly due to an intrinsic action of the uterus itself.

Nevertheless general evidence supports the conclusion that, in a normal state of things at all events, the contractions of the uterus, like those of the lymph-hearts, are largely dependent on the spinal cord.

The occurrence of contractions in consequence of an asphyxiated condition of the blood, explains why when pregnant animals are asphyxiated, an extrusion of the fœtus frequently takes place. There is no evidence, however, that the onset of labor is caused by a gradual diminution of oxygen in the blood, reaching at last to a climax. Nor are there sufficient facts to connect parturition with any condition of the ovary resembling that of menstruation.

The action of the abdominal muscles in parturition is, on the other hand, obviously a reflex act carried out by means of the spinal cord, the necessary stimulus being supplied by the pressure of the fœtus in the vagina, or by the contractions of the uterus. Hence, the whole act of parturition may with reason be considered as a reflex one.

Whether it be wholly a reflex or partly an automatic one, the act can readily be inhibited by the action of the central nervous system. Thus, emotions are a very frequent cause of the progress of parturition being suddenly stopped; as is well known, the entrance into the bedroom of a stranger often causes for a time the sudden and absolute cessation of "labor" pains, which previously may have been even violent. Judging from the analogy of micturition, between which and parturition there are many points of resemblance, we may suppose that this inhibition of uterine contractions is brought about by an inhibition of the centre in the lumbar cord.

After the expulsion of the fœtus, the fœtal placenta separates from the uterine walls, and is, together with the remnants of the membranes, expelled after it. The uterus then falls into a firm tonic contraction, similar to that of the emptied bladder, by which means hemorrhage from the vessels torn by the separation of the placenta is avoided. The lining membrane of the uterus is gradually restored, the muscular elements are reduced by a rapid fatty degeneration, and in a short time the whole organ has returned to its normal condition.

CHAPTER V

THE PHASES OF LIFE.

THE child has at birth, on an average, rather less than one-third the maximum length, and about one-twentieth the maximum weight, to which in future years it will attain.

The composition of the body of the new-born babe, as compared with that of the adult, will be seen from the following table, in which the details are more full than those given on p. 522.

	Weight of organ in percentage of body-weight.		Weight of organ in adult, as compared with that of new-born babe taken as 1.
	New-born babe.	Adult.	
Eye	0.28	0.028	1.7
Brain	14 34	2.37	3.7
Kidneys	0.88	0 48	12
Skin	11.3	6.3	12
Liver	4 39	2.77	13.6
Heart	0.89	0.52	15
Stomach and Intestine	2.53	2.34	20
Lungs	2.16	2.01	20
Skeleton	16.7	15.35	26
Muscles, etc.	23.4	43.1	28
Testicle	0.037	0.8	60

It will be observed that the brain and eyes are, relatively to the whole body-weight, very much larger in the babe than in the adult, as is also, though to a less extent, the liver. This disproportion is a very marked embryonic feature, and as far as the brain and eye are concerned at least, has a morphological or phylogenic, as well as a physiological or teleological, significance. Inasmuch as the smaller body has relatively the larger surface, the skin is naturally proportionately greater in the babe. It is chiefly by the accumulation of muscle or flesh, properly so called, that the child acquires the bulk and weight of the man, the skeletal framework, in spite of its being specifically lighter in its earlier cartilaginous condition, maintaining throughout life about the same relative weight.

The increase in stature is very rapid in early infancy, proceeding, however, by decreasing increments. During or shortly before puberty, there is again a somewhat sudden rise, with a subsequent more steady but diminishing increase up to about the twenty-

fifth year. From thence to about fifty years of age the height remains stationary, after which there may be a decrease, especially in extreme old age.

The increase in weight is also very rapid at first, and proceeding, like the height, with diminishing increments, may continue till about the fortieth year. After the sixtieth year a decline of variable extent is generally witnessed. It is a remarkable fact, however, that in the first few days of life, so far from there being an increase, there is an actual decrease of weight, so that, even on the seventh day the weight still continues to be less than at birth.

The saliva of the babe is active on starch, and its gastric juice, unlike that of many new-born animals, has good peptic powers, from which we may infer that its digestive processes in general are identical with that of the adult; but the feces of the infant contain, besides considerable quantity of undigested food (fat, casein, etc.), unaltered bile-pigment, and undecomposed bile-salts.

The heart of the babe (see Table, p. 821) is, relatively to its body-weight, larger than the adult, and the frequency of the heart-beat much greater, viz., about 130 or 140 per minute, falling to about 110 in the second year, and about 90 in the tenth year. Corresponding to the smaller bulk of the body, the whole circuit of the blood system is traversed in a shorter time than in the adult (12 seconds as against 22); and consequently the renewal of the blood in the tissues is exceedingly rapid. The respiration of the babe is quicker than that of the adult, being at first about 35 per minute, falling to 28 in the second year, to 26 in the fifth year, and so onwards. The respiratory work, while it increases absolutely as the body grows, is, relatively to the body-weight, greatest in the earlier years. It is worthy of notice, that the absorption of oxygen is said to be relatively more active than the production of carbonic acid; that is to say, there is a continued accumulation of capital in the form of a store of oxygen-holding explosive compounds (see p. 415). This, indeed, is the striking feature of infant metabolism. It is a metabolism directed largely to constructive ends. The food taken represents, undoubtedly, so much potential energy; but before that energy can assume a vital mode, the food must be converted into tissue; and, in such a conversion, morphological and molecular, a large amount of energy must be expended. The metabolic activities of the infant are more pronounced than those of the adult, for the sake, not so much of energies which are spent on the world without, as of energies which are for a while buried in the rapidly increasing mass of flesh. Thus, the infant requires over and above the wants of the man, not only

an income of energy corresponding to the energy of the flesh actually laid on, but also an income corresponding to the energy used up in making that living sculptured flesh out of the dead amorphous proteids, fats, carbohydrates, and salts, which serve as food. Over and above this, the infant needs a more rapid metabolism to keep up the normal bodily temperature. This, which is no less—indeed, slightly (0.3°) higher—than that of the adult, requires a greater expenditure, inasmuch as the infant with its relatively far larger surface, and its extremely vascular skin, loses heat to a proportionately much greater degree than does the grown-up man. It is a matter of common experience that children are more affected by cold than are adults.

This rapid metabolism is, however, not manifest immediately upon birth. During the first few days, corresponding to the loss of weight mentioned above, the respiratory activities of the tissues are feeble; the embryonic habits seem as yet not to have been completely thrown off, and, as was stated on p. 442, new-born animals bear with impunity a deprivation of oxygen, which would be fatal to them later on in life.

The quantity of urine passed, though scanty in the first two days, rises rapidly at the end of the first week, and in youth the quantity of urine passed is, relatively to the body-weight, larger than in adult life. This may be, at least in quite early life, partly due to the more liquid nature of the food, but is also in part the result of the more active metabolism. For not only is the quantity of urine passed, but also the amount of urea and some other urinary constituents excreted, relatively to the body-weight, greater in the child than in the adult. The presence of uric, of oxalic, and, according to some, of hippuric acids in unusual quantities is a frequent characteristic of the urine of children. It is stated that calcic phosphates, and, indeed, the phosphates generally, are deficient, being retained in the body for the building up of the osseous skeleton.

Associated probably with these constructive labors of the growing frame is the prominence of the lymphatic system. Not only are the lymphatic glands largely developed and more active (as is probably shown by their tendency to disease in youth), but the quantity of lymph circulation is greater than in later years. Characteristic of youth is the size of the thymus body, which increases up to the second year, and may then remain for a while stationary, but generally before puberty, has suffered a retrogressive metamorphosis, and frequently hardly a vestige of it remains behind. The thyroid body is also relatively greater in the babe than in the adult; the spleen, on the other hand, which grows rapidly in early infancy, is not only absolutely but also relatively greater in the adult. It need hardly be said

that the recuperative power of infancy and early youth is very marked.

It would be beyond the scope of this work to enter into the psychical condition of the babe or the child, and our knowledge of the details of the working of the nervous system in infancy is too meagre to permit of any profitable discussion. It is hardly of use to say that in the young the whole nervous system is more irritable or more excitable than in later years; by which we probably to a great extent mean that it is less rigid, less marked out into what, in preceding portions of this work, we have spoken of as nervous mechanisms. It may be mentioned that stimulation of the various cerebral areas, in new-born animals, does not give rise to the usual localized movements. The sense of touch, both as regards pressure and temperature, appears well developed in the infant, as does also the sense of taste, and possibly, though this is disputed, that of smell. The pupil (larger in the infant than in the man) acts fully, and Donders observed normal binocular movements of the eyes in an infant less than an hour old. The eye is (in man) from the outset fully sensitive to light, though of course visual perceptions are imperfect. As regards hearing, on the other hand, very little reaction follows upon sounds—i. e., auditory sensations seem to be dull during the first few days of life; this may be partly, at least, due to absence of air from the tympanum and a tumid condition of the tympanic mucous membrane. As the child grows up his senses rapidly culminate, and in his early years he possesses a general acuteness of sight, hearing, and touch, which frequently becomes blunted as his psychical life becomes fuller. Children, however, are said to be less apt at distinguishing colors than in sighting objects; but it does not appear whether this arises from a want of perceptive discrimination or from their being actually less sensitive to variations in hue. A characteristic of the nervous system in childhood, the result probably of the more active metabolism of the body, is the necessity for long or frequent and deep slumber.

Dentition marks the first epoch of the new life. At about seven months the two central incisors of the lower jaw make their way through the gum, followed immediately by the corresponding teeth in the upper jaw. The lateral incisors, first of the lower and then of the upper jaw, appear at about the ninth month, the first molars at about the twelfth month, the canines at about a year and a half, and the temporary dentition is completed by the appearance of the second molars usually before the end of the second year.

About the sixth year the permanent dentition commences by the appearance of the first permanent molar beyond the second

temporary molar; in the seventh year the central permanent incisors replace their temporary representatives, followed in the next year by the lateral incisors. In the ninth year the temporary first molars are replaced by the first bicuspids, and in the tenth year the temporary second molars are similarly replaced by the second bicuspids. The canines are exchanged about the eleventh or twelfth year, and the second permanent molars are cut about the twelfth or thirteenth year. There is then a long pause, the third or wisdom tooth not making its appearance till the seventeenth or even twenty-fifth year, or, in some cases, not appearing at all.

Shortly after the conclusion of the permanent dentition (the wisdom teeth excepted) the occurrence of puberty marks the beginning of a new phase of life; and the difference between the sexes, hitherto merely potential, now becomes functional. In both sexes the maturation of the generative organs is accompanied by the well-known changes in the body at large; but the events are much more characteristic in the typical female than in the aberrant male. Though in the boy, the breaking of the voice and rapid growth of the beard which accompany the appearance of active spermatozoa, are striking features, yet they are, after all, superficial. The curves of his increasing weight and height, and of the other events of his economy, pursue for a while longer an unchanged course; the boy does not become a man till some years after puberty; and the decline of his functional manhood is so gradual that frequently it ceases only when disease puts an end to a ripe old age. With the occurrence of menstruation, on the other hand, at from thirteen to seventeen years of age, the girl almost at once becomes a woman, and her functional womanhood ceases suddenly at the climacteric in the fifth decennium. During the whole of the child-bearing period her organism is in a comparatively stationary condition. While before the age of puberty up to about the eleventh or twelfth year, the girl is lighter and shorter than the boy of the same age, in the next few years her rate of growth exceeds his; but she has then nearly reached her maximum, while he continues to grow. Her curve of weight from the nineteenth year onward to the climacteric, remains stationary, being followed subsequently by a late increase, so that while the man reaches his maximum of weight at about forty, the woman is at her greatest weight about fifty.

Of the statical differences of sex, some, such as the formation of the pelvis, and the costal mechanism of respiration, are directly connected with the act of child-bearing, while others have only an indirect relation to that duty; and indications at least of nearly all the characteristic differences are seen at birth. The baby boy

is heavier and taller than the baby girl, and the maiden of five breathes with her ribs in the same way as does the matron of forty. The woman is lighter and shorter than the man, the limits in the case of the former being from 1.444 to 1.740 metre of height and from 39.8 to 93.8 kilos of weight, in the latter from 1.467 to 1.890 of height, and from 49.1 to 98.5 kilos of weight. The muscular system and skeleton are both absolutely and relatively less in woman, and her brain is lighter and smaller than that of man, being about 1272 grammes to 1424. Her metabolism, as measured by the respiratory and urinary excreta, is also not only absolutely but relatively to the body-weight less, and her blood is not only less in quantity, but also of lighter specific gravity, and contains a smaller proportion of red corpuscles. Her strength is to that of man as about 5 to 9, and the relative length of her step as 1000 to 1157.

From birth onward (and, indeed, from early intrauterine life) the increment of growth progressively diminishes. At last a point is reached at which the curve cuts the abscissa line, and the increment becomes a decrement. After the culmination of manhood at forty and of womanhood at the climacteric, the prime of life declines into old age. The metabolic activity of the body, which at first was sufficient not only to cover the daily waste, but to add new material, later on is able only to meet the daily wants, and at last is too imperfect even to sustain in its entirety the existing frame. Neither as regards vigor and functional capacity, nor as regards weight and bulk, do the turning-points of the several tissues and organs coincide either with each other or with that of the body at large. We have already seen that the life of such an organ as the thymus is far shorter than that of its possessor. The eye is in its dioptric prime in childhood, when its media are clearest and its muscular mechanisms most mobile, and then it for the most part serves as a toy; in later years, when it could be of the greatest service to a still active brain, it has already fallen into a clouded and rigid old age. The skeleton reaches its limit very nearly at the same time as the whole frame reaches its maximum of height, the coalescence of the various epiphyses being pretty well completed by about the twenty-fifth year. Similarly the muscular system in its increase tallies with the weight of the whole body. The brain, in spite of the increasing complexity of structure and function to which it continues to attain even in middle life, early reaches its limit of bulk and weight. At about seven years of age it attains what may be considered as its first limit, for though it may increase somewhat up to twenty, thirty, or even later years, its progress is much more slow after than before seven. The vascular and digestive organs as a whole may continue to in-

crease even to a very late period. From these facts it is obvious that though the phenomena of old age are, at bottom, the result of the individual decline of the several tissues, they owe many of their features to the disarrangement of the whole organism produced by the premature decay or disappearance of one or other of the constituent bodily factors. Thus, for instance, it is clear that were there no natural intrinsic limit to the life of the muscular and nervous systems, they would nevertheless come to an end in consequence of the nutritive disturbances caused by the loss of the teeth. And what is true of the teeth is probably true of many other organs, with the addition that these cannot, like the teeth, be replaced by mechanical contrivances. Thus, the term of life which is allotted to a muscle by virtue of its molecular constitution, and which it could not exceed were it always placed under the most favorable nutritive conditions, is, in the organism, determined by the similar life-terms of other tissues; the future decline of the brain is probably involved in the early decay of the thymus.

Two changes characteristic of old age are the so-called calcareous and fatty degenerations. These are seen in a completely typical form in cartilage, as, for instance, in the ribs; here the protoplasm of the cartilage-corpuscle becomes hardly more than an envelope of fat globules, and the supple matrix is rendered rigid with amorphous deposits of calcic phosphates and carbonates, which are at the same time the signs of past and the cause of future nutritive decline. And what is obvious in the case of cartilage is more or less evident in other tissues. Everywhere we see a disposition on the part of protoplasm to fall back upon the easier task of forming fat rather than to carry on the more arduous duty of manufacturing new material like itself; everywhere almost we see a tendency to the replacement of a structured matrix by a deposit of amorphous material. In no part of the system is this more evident than in the arteries; one common feature of old age is the conversion by such a change of the supple elastic tubes into rigid channels, whereby the supply to the various tissues of nutritive material is rendered increasingly more difficult, and their intrinsic decay proportionately hurried.

Of the various tissues of the body the muscular and nervous are, however, those in which functional decline, if not structural decay, becomes soonest apparent. The dynamic coefficient of the skeletal muscles diminishes rapidly after thirty or forty years of life, and a similar want of power comes over the plain muscular fibres also; the heart, though it may not diminish, or even may still increase in weight, possesses less and less force, and the movements of the intestine, bladder, and other organs, diminish

in vigor. In the nervous system, the lines of resistance, which, as we have seen, help to map out the central organs into mechanisms, and so to produce its multifarious actions, become at last hindrances to the passage of nervous impulses in any direction, while at the same time the molecular energy of the impulses themselves becomes less. The eye becomes feeble, not only from cloudiness of the media and presbyopic muscular inability, but also from the very bluntness of the retina; the sensory or motor impulses pass with increasing slowness to and from the central nervous system, and the brain becomes a more and more rigid mass of protoplasm, the molecular lines of which rather mark the history of past actions than serve as indications of present potency. The epithelial glandular elements seem to be those whose powers are the longest preserved; and hence the man who in the prime of his manhood was a "martyr to dyspepsia" by reason of the sensitiveness of gastric nerves and the reflex inhibitory and other results of their irritation, in his later years, when his nerves are blunted, and when therefore his peptic cells are able to pursue their chemical work undisturbed by extrinsic nervous worries, eats and drinks with the courage and success of a boy.

Within the range of a lifetime are comprised many periods of a more or less frequent recurrence. In spite of the aids of a complex civilization, all tending to render the conditions of his life more and more equable, man still shows in his economy the effects of the seasons. Some of these are the direct results of varying temperature, but some probably, such as the gain of weight in winter and the loss in summer, are habits acquired by descent. Within the year, an approximately monthly period is manifested in the female by menstruation, though there is no exact evidence of even a latent similar cycle in the male. The phenomena of recurrent disease, and the marked critical days of many other maladies, may be regarded as pointing to cycles of smaller duration than that of the moon's revolution, unless we admit the view urged by some authors that in these cases the recurrence is to be attributed rather to periodical phases in the disease-producing germ itself, than to variations in the medium of the disease.

Prominent among all other cyclical events is the fact that most animals possessing a well-developed nervous system, must night after night, or day after day, or at least time after time, lay them down to sleep. The salient feature of sleep is the cessation of the automatic activity of the brain; it is the diastole of the cerebral beat. But the condition is not confined to the cerebral hemispheres; all parts of the body either directly or indirectly take share in it. The phenomena of sleep are per-

haps seen in their simplest form in the winter-sleep or hibernation to which especially cold-blooded animals, but also to some extent warm-blooded animals, are subject. In these cases the cold of winter slackens the vibrations and lessens the explosions of the protoplasm, not only of nervous but also of muscular and glandular structures; indeed the activity of the whole body is lowered, in some respects almost to actual arrest. At the same time that the labor of the cerebral molecules becomes insufficient to develop consciousness, the respiratory centre is either wholly quiescent or discharges feeble impulses at rare intervals, and the heart beats with a slow infrequent stroke, not by reason of any inhibitory restraint, but because its very substance in its slow molecular travail can gather head for explosions only after long pauses of rest. And such few and distant beats as do occur are amply sufficient to meet the needs of the feeble metabolism of the several tissues. The sleep of every day differs from the sleep of winter-cold chiefly because the slackening of molecular activities is due in the former not to extrinsic but to intrinsic causes, not to changes in the medium, but to exhaustion of the subject, and because the phenomena are largely confined to the cerebral hemispheres. It is true that the whole body shares in the condition. The pulse and breathing are slower, the intestine and other internal muscular mechanisms are more or less at rest, the secreting organs are less active, some apparently being wholly quiescent, and the sleeper on waking rubs his eyes to bring back to his conjunctiva its needed moisture. Indeed the whole metabolism and the dependent temperature of the body are lowered; but we cannot say at present how far these are the indirect results of the conditions of the nervous system, or how far they indicate a partial slumbering of the several tissues.

Thoracic respiration is said to become more prominent than diaphragmatic respiration during sleep, and the Cheyne-Stokes rhythm of respiration (see p. 429) is frequently observed. During sleep the pupil is contracted, during deep sleep exceedingly so; and dilation often unaccompanied by any visible movements of the limbs or body, takes place when any sensitive surface is stimulated; on awaking also the pupils dilate. The eyeballs have been generally described as being during sleep directed upwards and converging, or, according to some authors, diverging; but others maintain that in true sleep the visual axes are parallel and directed to the far distance. The eyes of children have been described as continually executing during sleep movements, often irregular and unsymmetrical and unaccompanied by changes in the pupils.

We are not at present in a position to trace out the events which culminate in this inactivity of the cerebral structures. It

has been urged that during sleep the brain is anæmic; but even if this anæmia is a constant accompaniment of sleep, it must, like the vascular condition of a gland or any other active organ, be regarded as an effect, or at least as a subsidiary event, rather than as a primary cause.   Nor can the view which regards sleep as the result of a shifting of the mechanical arrangements of the cranial circulation be considered as satisfactory.   The explanation of the condition is rather to be sought in purely molecular changes; and the analogy between the systole and diastole of the heart, and the waking and sleeping of the brain, may be profitably pushed to a very considerable extent.   The sleeping brain in many respects closely resembles a quiescent but still living ventricle.   Both are as far as outward manifestations are concerned at rest, but both may be awakened to activity by an adequately powerful stimulus.   Both, though quiescent, are irritable, in both the quiescence will ultimately give place to activity, and in both an appropriate stimulus applied at the right time will determine the change from rest to action.   Just as a single prick will under certain circumstances awake a ventricle, which for some seconds has been motionless, into a rhythmic activity of many beats, so a loud noise will start a man from sleep into a long day's wakefulness.   And just as in the heart the cardiac irritability is lowest at the beginning of the diastole and increases onwards till a beat bursts out, so is sleep deepest at its commencement after the day's labor; thence onward slighter and slighter stimuli are needed to wake the sleeper.   For, judging of the depth of ordinary nocturnal sleep by the intensity of the noise required to wake the sleeper, it may be concluded that, increasing very rapidly at first, it reaches its maximum within the first hour; thence it diminishes, at first rapidly, but afterwards more slowly.

We cannot, however, at present make any definite statements concerning the nature of the molecular changes which determine this rhythmic rise and fall of cerebral irritability.   The fact that the products of protoplasmic activity when they accumulate within the protoplasm appear to become in the end an obstruction to that activity, has suggested the idea that the presence in the cerebral tissue of an excess of the products of nervous metabolism is the cause of sleep.   Indeed, lactic acid, the increase of which was supposed to be the cause of the acid reaction of muscular and nervous tissues after exercise, has been especially pointed to in this connection; but, as we have seen, the acid reaction in question appears not to be due to any increased production of lactic acid.   Besides, if the accumulation of metabolic products of any kind were the cause of sleep, it is not clear why we should ever have any hope of waking.   More may be said in

favor of the conception that during the waking hours the expenditure of oxygen exceeds the income, and that the quiescence, which we call sleep, comes from the exhaustion of the body's store of oxygen, more especially of that "intramolecular" oxygen of which we spoke, in dealing with the respiration of the tissues. But to this view must be added some hypothesis, such as the byplay of some inhibitory mechanism, whereby the respiratory centre is not roused to increased activity by this lack of oxygen, for, as we have seen, the breathing shares in the slumber of the body, though continuing to play with an amount of energy, which permits a gradual restoration of the lost store of oxygen, and so finally brings on the awakening which ends the sleep. And the necessity for such a complication indicates that the explanation is, at present at least, inadequate.

The phenomena of sleep show very clearly to how large an extent an apparent automatism is the ultimate outcome of the effects of antecedent stimulation. When we wish to go to sleep we withdraw our automatic brain as much as possible from the influence of all extrinsic stimuli; and an interesting case is recorded of a lad whose connection with the external world was, from a complicated anæsthesia, limited to that afforded by a single eye and a single ear, and who could be sent to sleep at will, by closing the eye and stopping the ear.

The cycle of the day is, however, manifested in many other ways than by the alternation of sleeping and waking, with all the indirect effects of these two conditions. There is a diurnal curve of temperature (see p. 547), apparently independent of all immediate circumstances, the hereditary impress of a long and ancient sequence of days and nights. Even the pulse, so sensitive to all bodily changes, shows, running through all the immediate effects of the changes of the minute and the hour, the working of a diurnal influence which cannot be accounted for by waking and sleeping, by working and resting, by meals and abstinence between meals. And the same may be said concerning the rhythm of respiration, and the products of pulmonary, cutaneous, and urinary excretion. There seems to be a daily curve of bodily metabolism, which is not the product of the day's events. Within the day we have the narrower rhythm of the respiratory centre with the accompanying rise and fall of activity in the vaso-motor centres. And lastly, there stands out the fundamental fact of all bodily periodicity, that alternation of the heart's systole and diastole which ceases only at death. Though, as we have seen, the intermittent flow in the arteries is toned down in the capillaries to an apparently continuous flow, still the constantly repeated cycle of the cardiac shuttle must leave its mark throughout the whole web of the body's life. Our means of in-

vestigation are, however, still too gross to permit us to track out its influence. Still less are we at present in a position to say how far the fundamental rhythm of the heart itself, that rhythm which is influenced, but not created, by the changes of the body of which it is the centre, is the result of cosmical changes, the reflection as it were in little of the cycles of the universe, or how far it is the outcome of the inherent vibrations of the molecules which make up its substance.

CHAPTER VI.

DEATH.

WHEN the animal kingdom is surveyed from a broad standpoint, it becomes obvious that the ovum, or its correlative, the spermatozoon, is the goal of an individual existence: that life is a cycle beginning in an ovum and coming round to an ovum again. The greater part of the actions which, looking from a near point of view at the higher animals alone, we are apt to consider as eminently the purposes for which animals come into existence, when viewed from the distant outlook whence the whole living world is surveyed, fade away into the likeness of the mere byplay of ovum-bearing organisms. The animal body is in reality a vehicle for ova; and after the life of the parent has become potentially renewed in the offspring, the body remains as a cast-off envelope whose future is but to die.

Were the animal frame not the complicated machine we have seen it to be, death might come as a simple and gradual dissolution, the "sans everything" being the last stage of the successive loss of fundamental powers. As it is, however, death is always more or less violent; the machine comes to an end by reason of the disorder caused by the breaking down of one of its parts. Life ceases not because the molecular powers of the whole body slacken and are lost, but because a weakness in one or other part of the machinery throws its whole working out of gear.

We have seen that the central factor of life is the circulation of the blood, but we have also seen that blood is not only useless, but injurious, unless it be duly oxygenated; and we have further seen that in the higher animals the oxygenation of the blood can only be duly effected by means of the respiratory muscular mechanism, presided over by the medulla oblongata. Thus, the life of a complex animal is, when reduced to a simple form, composed of three factors: the maintenance of the circulation, the access of air to the hæmoglobin of the blood, and the functional activity of the respiratory centre; and death may come from the arrest of either of these. As Bichat put it, death takes place by the heart or by the lungs, or by the brain. In reality, however, when we push the analysis further, the central fact of death is the stoppage of the heart, and the consequent arrest of the circulation; the tissues then all die, because they lose their internal

medium.   The failure of the heart may arise in itself, on account of some failure in its nervous or muscular elements, or by reason of some mischief affecting its mechanical working.   Or its stoppage may be due to some fault in its internal medium, such, for instance, as a want of oxygenation of the blood, which in turn may be caused by either a change in the blood itself, as in carbonic oxide poisoning, or by a failure in the mechanical conditions of respiration, or by a cessation of the action of the respiratory centre.   The failure of this centre, and, indeed, that of the heart itself, may be caused by nervous influences proceeding from the brain, or brought into operation by means of the central nervous system ; it may, on the other hand, be due to an imperfect state of blood, and this in turn may arise from the imperfect or perverse action of various secretory or other tissues.   The modes of death are in reality as numerous as are the possible modifications of the various factors of life; but they all end in a stoppage of the circulation, and the withdrawal from the tissues of their internal medium.   Hence, we come to consider the death of the body as marked by the cessation of the heart's beat, a cessation from which no recovery is possible ; and by this we are enabled to fix an exact time at which we say the body is dead.   We can, however, fix no such exact time to the death of the individual tissues.   They are not mechanisms, and their death is a gradual loss of power.   In the case of the contractile tissues, we have apparently in rigor mortis a fixed term, by which we can mark the exact time of their death.   If we admit that after the onset of rigor mortis recovery of irritability is impossible, then a rigid muscle is one permanently dead.   In the case of the other tissues, we have no such objective sign, since the rigor mortis of simple protoplasm manifests itself chiefly by obscure chemical signs.   And in all cases it is obvious that the possibility of recovery, depending as it does on the skill and knowledge of the experimenter, is a wholly artificial sign of death.   Yet we can draw no other sharp line between the seemingly dead tissue, whose life has flickered down into a smouldering ember, which can still be fanned back again into flame, and the handful of dust, the aggregate of chemical substances into which the decomposing tissue finally crumbles.

Moreover, the failure of the heart itself is at bottom loss of irritability, and the possibility of recovery here also rests, as far as is known at present, on the skill and knowledge of those who attempt to recover.   So that after all, the signs of the death of the whole body are as artificial as those of the death of the constituent tissues.

APPENDIX.

ON THE CHEMICAL BASIS OF THE ANIMAL BODY.

THE animal body, from a chemical point of view, may be regarded as a mixture of various representatives of three large classes of chemical substances, viz., proteids, carbohydrates, and fats, in association with smaller quantities of various saline and other crystalline bodies. By proteids are meant bodies containing carbon, oxygen, hydrogen, and nitrogen in a certain proportion, varying within narrow limits, and having certain general features; they are frequently spoken of as albuminoids. By carbohydrates are meant starches and sugars and their allies. We have also seen that the animal body may be considered as an assemblage of protoplasm under various modifications and of numerous products of protoplasmic activity. We do not at present know anything definite about the molecular composition of active living protoplasm; but when we submit protoplasm to chemical analysis, in which act it is killed, we always obtain from it a considerable quantity of the material spoken of as proteid. And many authors go so far as to speak of protoplasm as being purely proteid in nature: they regard the living protoplasm as proteid material, which, in passing from death to life, has assumed certain characters and presumably has been changed in construction, but still is proteid matter; they sometimes speak of protoplasm as "living proteid" or "living albumin." It is worthy of notice, however, that even simple forms of protoplasm, like that constituting the body of a white corpuscle, forms of protoplasm which we may fairly consider as native protoplasm, when they can be obtained in sufficient quantity for chemical analysis, are found to contain some representatives of carbohydrates and fats as well as of proteids. We might perhaps even go so far as to say, that in all forms of living protoplasm, the proteid basis is found upon analysis to have some carbohydrate and some kind of fat associated with it. Further, not only does the normal food which is eventually built up into protoplasm consist of all three classes; but, as we have seen in the sections on nutrition, protoplasm gives rise by metabolism to members of the same three classes; and, as far as we know at present, carbohydrates and fats, when formed in the body out of proteid food, are so formed by the agency of living protoplasm, by some living tissue. Hence there is at least some reason for thinking it probable that the molecule of protoplasm, if we may use such a phrase, is far more complex than a molecule of proteid matter, that it contains in itself residues, so to speak, not only of proteid, but also of carbohydrate and fatty material.

Be this as it may—for no dogmatic statement can at present be made—

when we examine the various tissues and fluids of the animal body from a chemical point of view, we find present in different places, or at different times, several varieties and derivatives of the three chief classes; we find many forms of proteids, and bodies closely allied to proteids, in the forms of mucin, gelatine, etc.; many varieties of fats; and several kinds of carbohydrates.

We find, moreover, many other bodies which we may regard as stages in the constructive or destructive metabolism of both native and differentiated protoplasm, and which are important, not so much from the quantity in which they occur in the animal body at any one time, as from their throwing light on the nature of animal metabolism; these are such bodies as urea, other organic crystalline bodies, and the extractives in general.

In the following pages the chemical features of the more important of these various substances which are known to occur in the animal body will be briefly considered, such characters only being described as possess or promise to possess physiological interest. The physiological function of any substance must depend ultimately on its molecular (including its chemical) nature; and, though at present our chemical knowledge of the constituents of an animal body gives us but little insight into their physiological properties, it cannot be doubted that such chemical information as is attainable is a necessary preliminary to all physiological study.

PROTEIDS.

These form the principal solids of the muscular, nervous, and glandular tissues, of the serum of blood, of serous fluids, and of lymph. In a healthy condition, sweat, tears, bile, and urine contain more traces, if any, of proteids. Their general percentage composition may be taken as

	O.		H.		N.		C.		S.
From	20.9		6.9		15.2		51.5		0.3
to	23.5	to	7.3	to	17.0	to	54.5	to	2.0

(Hoppe-Seyler.[1])

These figures are obtained from a consideration of numerous analyses, slight differences in the various results being immaterial, where the purity of the substance operated upon cannot be definitely determined.

In addition to the above constituents, proteids leave on ignition a variable quantity of ash. In the case of egg-albumin the principal constituents of the ash are chlorides of sodium and potassium, the latter greatly exceeding the former in amount. The remainder consists of sodium and potassium, in combination with phosphoric, sulphuric, and carbonic acids, and very small quantities of calcium, magnesium, and iron in union with the same acids. There is also a trace of silica.[2] The ash of serum-albumin contains an excess of sodium chloride, but the ash of the proteids of muscle contains an excess of potash salts and phosphates. The nature of the connection of the ash with the proteid is still a matter of obscurity. Globin from hæmoblobin is said to leave no ash on ignition.

Proteids as met with in the animal body are all amorphous; some are soluble, some insoluble in water, and all are for the most part insoluble in alcohol and ether; they are all soluble in strong acids and alkalies,

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[1] Hdb. Phys. Path. Chem. Anal.. Ed. iv. (1875) S. 223.
[2] See Gmelin, Hdb. Org. Chem., Bd. viii. S. 285.

but in becoming dissolved mostly undergo decomposition. Their solutions possess a left-handed rotatory action on the plane of polarization, the amount depending on various circumstances, and being, with one exception—viz., peptones—changed by heating.

Crystals into whose composition certain proteid (especially globulin)[1] elements enter were long since observed in the seeds of many plants; as yet they have not been obtained sufficiently isolated or in quantities large enough to permit any accurate analysis to be made. A method of isolating in quantity and re-crystallizing these substances has, however,[2] been indicated, and it seems probable that analysis of these may lead to interesting information on the subject of the constitution and combination of proteids.

The presence of proteids may be determined by the following tests :

1. Heated with strong nitric acid, they or their solutions turn yellow, and this color is, on the addition of ammonia, or caustic soda or potash, changed to a deep orange hue. (Xanthoproteic reaction.)

2. With Millon's reagent they give, when present in sufficient quantity, a precipitate, which turns red on heating. If they are only present in traces, no precipitate is obtained, but merely a red coloration of the solution.

3. If mixed with some concentrated solution of sodic hydrate, and one or two drops of a solution of cupric sulphate, a violet color is obtained, which deepens in tint on boiling.

The above serve to detect the smallest traces of all proteids. The two following tests may be used when there is more than a trace present, but do not hold for every kind of proteid.

4. Render the fluid strongly acid with acetic or other acid, and add a few drops of a solution of ferrocyanide of potassium ; a precipitate shows the presence of proteids.

5. Render the fluid, as before, strongly acid with acetic acid, add an equal volume of a concentrated solution of sodic sulphate, and boil. A precipitate is formed if proteids are present.

This last reaction is useful, not only on account of its exactness, but also because the reagents used produce no decomposition of other bodies which may be present; and hence after filtration the same fluid may be further analyzed for other substances. Additional methods of freeing a solution from proteids are, acidulating with acetic acid and boiling, avoiding any excess of the acid ; precipitation by excess of alcohol; in the latter case the solution must be neutral or faintly acid. Hoppe-Seyler[3] recommends the employment of a saturated solution of freshly precipitated ferric hydrate, in acetic acid; this is added to the solution, and on boiling the whole of the proteids are precipitated as well as the ferric salt, the latter as basic acetate. Brücke's method of removing the last traces of proteids from glycogen solutions is also of use (see glycogen). Precipitation of the last traces of proteids by means of hydrated oxide of lead at a boiling temperature[4] may be also employed.

Proteids may be conveniently divided into classes.

CLASS I.—*Native Albumins.*

Members of this class, as their name implies, occur in a natural condition in animal tissues and fluids. They are soluble in water, are not

1 Vines, Jl. of Physiol. vol. iii. (1880) p 93.
2 Dreschsel, Journ. f. prakt. Chem., N. F. Bd. xix. (1879) S. 331.
3 Op. cit. S. 227.
4 Hofmeister, Zeitsch. f. physiol. Chem., Bd. ii. (1878) S. 288.

precipitated by very dilute acids, by carbonates of the alkalies, or by sodium chloride. They are coagulated by heating in solution to a temperature of about 70° C. If dried at 40° C., the resulting mass is of a pale yellow color, easily friable, tasteless, inodorous, and soluble.

1. Egg-albumin.

Forms in aqueous solution a neutral, transparent, yellowish fluid. From this it is precipitated by excess of strong alcohol. If the alcohol be rapidly removed, the precipitate may be readily redissolved in water; if subjected to lengthier action a coagulation occurs, and the albumin is then no longer thus soluble. Strong acids, especially nitric acid, cause a coagulation similar to that produced by heat or by the prolonged action of alcohol; the albumin becomes profoundly changed by the action of the acid and does not dissolve upon removal of the acid. Mercuric chloride, argentic nitrate, and lead acetate, precipitate the albumin, forming insoluble compounds of variable composition with it; the precipitant may be removed by means of sulphuretted hydrogen and the albumin again obtained, apparently unaltered, in solution.

Strong acetic acid in excess gives no precipitate, but when the solution is concentrated the albumin is transformed into a transparent jelly. A similar jelly is produced when strong caustic potash is added to a concentrated solution of egg-albumin. In both these cases the substance is profoundly altered, becoming in the one case acid, in the other alkali-albumin.

The specific rotatory power of egg-albumin in aqueous solution is, for yellow light, —35.5°. Hydrochloric acid, added until the reaction is strongly acid, increases this rotation to —37.7°. The formation of the gelatinous compound with caustic potash is at first accompanied with an increase, but this is followed by a decrease of rotation.

Preparation.—White of hen's egg is broken up with scissors into small pieces, diluted with an equal bulk of water, and the mixture shaken strongly in a flask till quite frothy; on standing, the foam rises to the top, and carries all the fibres in whose meshwork the albumin was contained The fluid, from which the foam has been removed, is strained, and treated carefully with dilute acetic acid as long as any precipitate is formed: the precipitate is then filtered off, and the filtrate after neutralization concentrated at 40° to its original bulk. [The white of the hen's egg contains a considerable portion of globulin, and the dilute acetic acid is added to precipitate this principle. Instead of the acid, about an equal bulk of carbonic acid water, or the common soda water of commerce, can be used for the same purpose. The quantity of carbonic acid water necessary will, of course, depend upon the degree of alkalinity of the white of egg solution. The carbonic acid gas forms carbonates with the free alkali, which are natural constituents of the white of egg, and we avoid the contamination of so foreign a constituent as acetic acid.]

2. Serum-albumin.

This form of albumin resembles, to a great extent, the one previously described. The following may suffice as distinguishing features.

1. The specific rotation of serum-albumin is —56°; that of egg-albumin is —35.5°; both measured for yellow light.

2. Serum-albumin is not coagulated by being shaken up with ether, egg-albumin is.

3. Serum-albumin is not very readily precipitated by strong hydro-

chloric acid, and such precipitate as does occur is readily redissolved on further addition of the acid; the exact reverse of these two features holds good for egg-albumin.

4. Precipitated or coagulated serum-albumin is readily soluble, egg-albumin is with difficulty soluble, in strong nitric acid.

5. Egg-albumin, if injected subcutaneously or into a vein, reappears unaltered in the urine;[1] serum-albumin similarly injected does not thus normally pass out by the kidney.

Serum-albumin is found not only in blood-serum, but also in lymph, both that contained in the proper lymphatic channels and that diffused in the tissues; in chyle, milk, transudations, and many pathological fluids.

It is this form in which albumin generally appears in the urine.

In addition to the above, Scherer[2] has described two closely related bodies, to which he gives the names Paralbumin and Metalbumin. The first he obtained from ovarian cysts; its alkaline solutions are remarkable for being very ropy. It seems doubtful whether this body is a proteid; it differs sensibly in composition from these. Haerlin[3] gives as its composition, O 26.8, H 6.9, N 12.8, C 51.8, S 1.7 per cent. It seems to be associated with some body like glycogen, capable of being converted into a substance giving the reactions of dextrose. Metalbumin, found in a dropsical fluid, resembles the preceding, but is not precipitated by hydrochloric acid, or by acetic acid and ferrocyanide of potassium; it is precipitated, but not coagulated, by alcohol; its solution is scarcely coagulated on boiling.

Albumins are generally found associated with small but definite amounts of saline matter. A Schmidt[4] says that they may be freed from these by dialysis, and that they are then not coagulated on boiling. From this it might be inferred that the albumin and the saline matters were peculiarly related, and that the latter played some special part during the coagulation of the former by heat. Schmidt's observations, however, have not been conclusively corroborated by subsequent observers.

CLASS II.—*Derived Albumins (Albuminates)*.

1. Acid-albumin.

When a native albumin in solution, such as serum-albumin, is treated for some little time with a dilute acid, such as hydrochloric, its properties become entirely changed. The most marked changes are (1) that the solution is no longer coagulated by heat; (2) that when the solution is carefully neutralized the whole of the proteid is thrown down as a precipitate; in other words, the serum-albumin which was soluble in water, or at least in a neutral fluid containing only a small quantity of neutral salts, has become converted into a substance insoluble in water or in similar neutral fluids. The body into which serum-albumin thus becomes converted by the action of an acid is spoken of as *acid-albumin*. Its characteristic features are that it is insoluble in distilled water, and in neutral saline solutions, such as those of sodic chloride, that it is readily soluble in dilute acids or dilute alkalies, and that its solutions in acids or alkalies are not coagulated by boiling. When suspended, in the undis-

[1] Stokvis, Rech. exp. sur les condit. pathol. de l'albuminurie, Bruxelles, 1867; also Lehmann, Arch. f. path. Anat., Bd. xxx. (1864) S. 593.

[2] Ann. der Chem. und Pharm., Bd. 82, S. 135.

[3] Chem. Centralblatt, 1862, No. 56.

[4] Pflüger's Archiv, xi. (1875) S. 1.

solved state, in water, and heated to 70° C., it becomes coagulated, and is then undistinguishable from coagulated serum-albumin, or indeed from any other form of coagulated proteid. It is evident that the substance when in solution in a dilute acid is in a different condition from that in which it is when precipitated by neutralization. If a quantity of serum- or egg-albumin be treated with dilute hydrochloric acid, it will be found that the conversion of the native albumin into acid-albumin is gradual; a specimen heated to 70° C. immediately after the addition of the dilute acid, will coagulate almost as usual; and another specimen taken at the same time will give hardly any precipitate on neutralization. Some time later, the interval depending on the proportion of the acid to the albumin, on temperature, and on other circumstances, the coagulation will be less, and the neutralization precipitate will be considerable. Still later the coagulation will be absent, and the whole of the proteid will be thrown down on neutralization.

If finely chopped muscle, from which the soluble albumins have been removed by repeated washing, be treated for some time with dilute (0.2 per cent.) hydrochloric acid, the greater part of the muscle is dissolved. The transparent acid filtrate contains a large quantity of proteid material in a form which, in its general characters at least, agrees with acid-albumin. The acid solution of the proteid is not coagulated by boiling, but the whole of the proteid is precipitated on neutralization; and the precipitate, insoluble in neutral sodic chloride solutions, is readily dissolved by even dilute acids or alkalies. The proteid thus obtained from muscle has been called *syntonin*, but we have at present no satisfactory test to distinguish the acid-albumin (or syntonin) prepared from muscle from that prepared from egg- or serum-albumin. When coagulated albumin or other coagulated proteid or fibrin is dissolved in strong acids, acid-albumin is formed; and when fibrin or any other proteid is acted upon by gastric juice, acid-albumin is one of the first products; and these acid-albumins cannot be distinguished from acid-albumin prepared from muscle or native albumin. Though hydrochloric acid is perhaps the most convenient acid for forming acid-albumin, other acids may also be used for the purpose of preparing it. Acid-albumin is soluble not only in dilute alkalies, but also in dilute solutions of alkaline carbonates; its solutions in these are not coagulated by boiling.

If sodic chloride in excess is added to an acid solution of acid-albumin, the acid-albumin is precipitated: this also occurs on adding sodic acetate or phosphate.

As special tests of acid-albumin may be given: 1. Partial coagulation of its solution in lime-water on boiling. 2. Further precipitation of the same solution after boiling, on the addition of calcic chloride, magnesic sulphate, or sodic chloride.

Dissolved in very dilute hydrochloric acid, acid-albumin (syntonin) prepared from muscle possesses a specific lævo-rotatory power of —72° for yellow light, this being independent of the concentration.[1] On heating the solution in a closed vessel in a water-bath, the rotatory power rises to —84.8°.

The body known as parapeptone, which makes its appearance during the peptic digestion of proteids, is closely allied to the substances just described. (See p. 294.)

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[1] Hoppe-Seyler, Hdb. Phys. Path. Chem. Anal., Ed. iv. (1875) S. 246.

2. Alkali-albumin.

If serum- or egg-albumin or washed muscle be treated with dilute alkali instead of with dilute acid, the proteid undergoes a change quite similar to that which was brought about by the acid. The alkaline solution, when the change has become complete, is no longer coagulated by heat, the proteid is wholly precipitated on neutralization, and the precipitate, insoluble in water and in neutral sodic chloride solutions, is readily soluble in dilute acids or alkalies. Indeed, in a general way, it may be said that acid-albumin and alkali-albumin are nothing more than solutions of the same substance in dilute acids and alkalies, respectively. When the precipitate obtained by the neutralization of a solution of acid-albumin in dilute acid is dissolved in a dilute alkali, it may be considered to become alkali-albumin; and, conversely, when the precipitate obtained from an alkali-albumin solution is dissolved in dilute acid, it may be regarded as acid-albumin.

It is stated[1] as a characteristic reaction of this modified or derived albumin, that it is not precipitated when its alkaline solutions are neutralized in the presence of alkaline phosphates; solutions of acid-albumin, on the contrary, are said to be precipitated on neutralization in the presence of alkaline phosphates, and this difference is considered to be a distinguishing feature of the two proteids. But doubt has been cast on this statement.[2]

Alkali-albumin may be prepared by the action not only of dilute alkalies, but also of strong caustic alkalies on native albumins, as well as on coagulated albumin and other proteids. The jelly produced by the action of caustic potash on white of egg, spoken of in Class I., 1, is alkali-albumin; the similar jelly produced by strong acetic acid is acid-albumin. One of the most productive methods of obtaining alkali-albumin is that introduced by Lieberkühn,[3] and consists in adding a strong solution of caustic potash to purified white of egg until the above-mentioned jelly is obtained. This is then cut into small pieces, and dialyzed until quite white. The lumps are then dissolved by heating on the water-bath, and the alkali-albumin precipitated by the careful addition of acetic acid.

Both alkali- and acid-albumin are with difficulty precipitated by alcohol from their alkaline or acid solutions. The neutralization precipitate, however, becomes coagulated under the prolonged action of alcohol.

The body "protein" described by Mulder appears, if it exists at all, to be closely connected with this body. All subsequent observers have, however, failed to confirm his views.

The rotatory power of alkali-albumin varies according to its source; thus, when prepared by strong caustic potash from serum-albumin, the rotation rises from —56° (that of serum-albumin) to —86°, for yellow light. Similarly prepared from egg-albumin, it rises from —38.5° to —47°, and if from coagulated white of egg, it rises to —58.8° Hence, the existence of various forms of alkali-albumin is probable.

In addition to the methods given above, alkali-albumin may be also readily obtained by shaking milk with strong caustic soda solution and ether, removing

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[1] Hoppe-Seyler, loc. cit., S. 245.
[2] Soyka. Pflüger's Arch., Bd. xii. (1876) S. 347.
[3] Poggendorff's Annalen, Bd. lxxxvi. S. 118.

the ethereal solution, precipitating the remaining fluid with acetic acid and washing the precipitate with water, cold alcohol, and ether.

The most satisfactory method of regarding acid- and alkali-albumin is to consider them as respectively acid and alkali compounds of the neutralization precipitate. We have reason to think that when the precipitate is dissolved in either an acid or an alkali, it does enter into combination with them. The neutralization precipitate is in itself neither acid- nor alkali-albumin, but may become either, upon solution in the respective reagent.

It is probable that several derived albumins exist,[1] differing according to the proteid from which they are formed or possibly according to the mode of their preparation, and that each of these may exist in its correlative forms of acid- and alkali-albumin; but the whole subject requires further investigation.

Acid-albumin, prepared by the direct action of dilute acids on native albumins or on muscle-substance, contains sulphur, as shown by the brown coloration which appears when the precipitate is heated with caustic potash in the presence of basic lead acetate. Alkali-albumin, at all events as prepared by the action of strong caustic potash or soda, does not contain any sulphur; and the acid-albumin, prepared by the solution in an acid of the neutralization precipitate from such an alkali-albumin solution, is similarly free from sulphur.

3. Casein.

This is the well-known proteid existing in milk. When freed from fat, and in the moist condition, it is a white, friable, opaque body. In most of its reactions it corresponds closely with alkali-albumin; thus, it is readily soluble in dilute acids and alkalies, and is reprecipitated on neutralization; if, however, potassic phosphate is present, as is the case in milk, the solution must be strongly acid before any precipitate is obtained.

Various reactions have at different times been assigned to casein as distinguishing it from the closely allied body alkali-albumin. Later researches have, however, in most cases cast so much doubt on these differences that the identity or non-identity of casein and alkali-albumin must be left an open question, the discussion of which would be out of place here.

Casein, as occurring in milk, has had several reactions ascribed to it, as characteristic, but these lose their importance on considering that milk contains, in addition to casein, other substances, such as potassic phosphate, and a number of bodies which yield acids by fermentation. The presence of potassic phosphate has an especial influence on the reactions of casein. In the entire absence of this salt, acetic acid in the smallest quantities, as also carbonic anhydride, gives a precipitate; but if this salt is present, carbonic anhydride gives no precipitate, and acetic acid one only when the solution is acid from the presence of free acid, and not from that of acid potassic phosphate.[2]

When prepared from milk by magnesic sulphate (see below), freed by ether from fats, and dissolved in water, casein possesses a specific rotatory power of $-80°$ for yellow light; in dilute alkaline solutions, of $-76°$; in strong alkaline solutions, of $-91°$; in dilute hydrochloric acid of $-87°$.

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[1] Mörner. Pflüger's Arch., Bd. xvii. (1878) S. 468
See Kühne, Lehrb. d. Physiol. Chem., 1868, S. 565.

Casein has been asserted to occur in muscle, in serous fluids, and in blood-serum (serum-casein). In many cases it has probably been confounded with globulins (see Class III.); but blood-serum and muscle-plasma undoubtedly contain an alkali-albumin in addition to whatever globulin may be present, but the usual doubt exists as to the identity of this with true casein. Its presence may be shown by adding dilute acetic acid to blood-serum which has been freed from globulin by a current of carbonic anhydride; a distinct precipitate is thrown down. A substance similar to casein has also been described as existing in unstriated muscle and in the protoplasm of nerve-cells.

Preparation.—Dilute milk with several (ten to fifteen) times its bulk of water, add dilute acetic acid till a precipitate begins to appear, then pass a current of carbonic anhydride, filter, and wash the precipitate with water, alcohol, and ether; the complete removal of the fat carried down with the casein presents some difficulties. Magnesic sulphate added to saturation also precipitates casein from milk; the precipitate as thus formed is readily soluble on the addition of water.

CLASS III.—*Globulins.*

Besides the native albumins there are a number of native proteids which differ from the albumins in not being soluble in distilled water; they need for their solution the presence of an appreciable, though it may be a small, quantity of a neutral saline body such as sodic chloride. Thus, they resemble the albuminates in not being soluble in distilled water, but differ from them in being soluble in dilute sodic chloride or other neutral saline solutions. Their general characters may be stated as follows :

They are insoluble in water, soluble in dilute (1 per cent.) solutions of sodic chloride; they are also soluble in dilute acids and alkalies, being changed on solution into acid- and alkali-albumin, respectively, unless the acids and alkalies are exceedingly dilute. The saturation with solid sodic chloride of their solutions in dilute sodic chloride, precipitates most members of this class.

1. Globulin (*Crystallin*).

If the crystalline lens be rubbed up with fine sand, extracted with water and filtered, the filtrate will be found to contain at least three proteids. On passing a current of carbonic anhydride, a copious precipitate occurs; this is globulin.

The addition of dilute acetic acid to the filtrate from the globulin, gives a precipitate of alkali-albumin,[1] and the filtrate from this if heated gives a further precipitate, due to serum-albumin.

In its general reactions, globulin corresponds almost exactly with the next members of this class (paraglobulin and fibrinogen), but has no power to form or promote the formation of fibrin in fluids containing the above-mentioned bodies, and possesses the following special features. 1. According to Lehmann, its oxygenated, neutral solutions become cloudy on heating to 73° C., and are coagulated at 93° C. 2. It is readily precipitated on the addition of alcohol. According to Hoppe-Seyler, it is not precipitated on saturation with sodic chloride, resembling vitellin in this respect.

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[1] But see also Pflüger's Arch., Bd. xiii. (1876) S. 631.

According to Kühne[1] and Eichwald[2] a globulin with properties identical with those just given may be precipitated from dilute serum by the cautious addition of acetic acid. This body is stated by Weyl[3] to be the same as paraglobulin (fibrinoplastin), the latter differing from it only by a small admixture of fibrin-ferment.

2. Paraglobulin (*Fibrinoplastin*).

Preparation.—Blood-serum is diluted ten-fold with water, and a brisk current of carbonic anhydride is passed through it. The first-formed cloudiness soon becomes a flocculent precipitate, which is finally quite granular, and may easily be separated by decantation and filtration; it should be washed on the filter with water containing carbonic acid.

It has usually been stated that paraglobulin may be separated from serum by saturation with sodic chloride. But Hammarsten[4] has shown that this is only in part true, a considerable portion of the globulin remaining unprecipitated. The separation may, however, be completely effected by saturation with magnesic sulphate. When determined by this method, the amount of paraglobulin in serum is very considerable, amounting, in some cases according to Hammarsten, to as much as 4.565 per cent. (reckoned on 100 cc. of serum). The quantity seems to vary in different animals, the precipitation being much more complete in serum from ox-blood than in that from the blood of horses.

From its solution in dilute sodic chloride, paraglobulin may be precipitated by a current of carbonic anhydride or the addition of *exceedingly dilute* (less than 1 pro mille) acetic acid. If the acid is strong, the precipitated proteid becomes immediately changed into acid-albumin (Class II., 1). In pure water, free from oxygen, paraglobulin is insoluble, but on shaking with air or passing a current of oxygen, solution readily takes place; from this it may be reprecipitated by a current of carbonic anhydride. *Very dilute* alkalies dissolve this body without change; if, however, the strength of the alkali be raised even to 1 per cent., the paraglobulin is changed into alkali-albumin (Class II., 2).

According to Kühne and A. Schmidt, the solutions of this body in water containing oxygen or in very dilute alkalies are not coagulated on heating. The sodic chloride solutions do, however, coagulate when heated to 68°–70° C.,[5] and if the substance itself be suspended in water and heated to 70° C. it is coagulated. Although insoluble in alcohol, its solutions are with difficulty precipitated by this reagent.

Paraglobulin occurs not only in blood-serum, but it is also found in white corpuscles, in the stroma of red corpuscles (to some extent at least), in connective tissue, the cornea, aqueous humor, lymph, chyle, and serous fluids.

For the occurrence of globulin in urine see Edlefsen[6] and Senator.[7]

3. Fibrinogen.

The general reactions of this body are identical with those of paraglobulin. The most marked difference between the two is the point at

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[1] Lehrb. d. Physiol. Chem., 1868, S. 175.

[2] Beiträge zur Chem., d. gewebebild. Subst. Berlin, 1873. Hf. i.

[3] Zeitschr. f. Physiol. Chem., Bd. i. (1878) S. 79.

[4] Pflüger's Archiv, Bd. xvii. (1878) S. 416. Bd. xviii. (1878) S. 38.

[5] Hammarsten, op. cit.

[6] Centralblatt f. d. med. Wiss. Jahrg., 1870, S. 367. Also Arch. f. klin. Med., Bd. vii. S. 69.

[7] Virchow's Archiv, Bd. lx. S. 476.

which coagulation of their solutions takes place. Hammarsten[1] has shown that fibrinogen in a 1–5 per cent. solution of sodic chloride coagulates at from 52°–55° C., whereas, as stated above, paraglobulin (fibrinoplastin) coagulates first at from 68°–70° C. This, however, is disputed by A. Schmidt, who holds that the substance coagulating at 52°–55° C. is not fibrinogen, but a sort of nascent fibrin. There is also a marked difference in the precipitability of the two bodies by sodic chloride. (See below.) Other differences between the two may be thus enumerated: In precipitating fibrinogen by a current of carbonic anhydride, the containing fluid must be much more strongly diluted, and the gas must pass for a much longer time. The precipitate thus obtained differs from that of paraglobulin in that it forms a viscous deposit, adhering more closely to the sides and bottom of the containing vessel; there is also no flocculent stage previous to the viscous precipitate.

Fibrinogen occurs in blood, chyle, serous fluids, and in various transudations. The relations of fibrinogen and paraglobulin to the formation of fibrin have been discussed in the text, p. 43.

Preparation.[2]—Salted plasma, obtained by centrifugalizing blood whose coagulation is prevented by the addition of a certain proportion of magnesic sulphate, is mixed with an equal volume of a saturated (35.87 per cent. at 14° C.)[3] solution of sodic chloride; the fibrinogen is thus precipitated while the paraglobulin remains in solution. The adhering plasma may be removed by washing with a solution of sodic chloride, and the fibrinogen finally purified by being several times dissolved in and reprecipitated by sodic chloride.

There is no proof that the *whole* of the substance thrown down by carbonic anhydride from diluted blood-serum is fibrinoplastic; indeed, we know that a true globulin devoid of fibrinoplastic properties may be prepared from serum.[4] Weyle[5] considers that there is only one globulin in serum, which he characterizes by the name of "serum-globulin," and regards fibrinoplastin as a mixture of this body with a portion of fibrinferment. We know for certain (see p. 40) that the whole of the fibrinoplastic precipitate, used to cause the coagulation of a fibrinogenous fluid, does not enter into the composition of the fibrin produced; we also know that such a precipitate may lose its fibrinoplastic powers without any marked change in its general reactions. It would seem advisable, therefore, to speak of the deposit produced by carbonic anhydride in dilute serum, or by saturation with sodic chloride in undiluted serum, as globulin, and to distinguish it as fibrinoplastic globulin when it is able to give rise to fibrin. Fibrinogen similarly might be spoken of as fibrinogenous globulin. The name crystallin rather than globulin might then be given to the substance obtained from the crystalline lens.

4. Myosin.

This is the substance which forms the chief proteid constituent of dead, rigid muscle; its general properties and mode of preparation have been already described at p. 94. In the moist condition, it forms a gelatinous, elastic, clotted mass; dried, it is very brittle, slightly transparent, and elastic. From its solution in sodic chloride it is precipitated, either by

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[1] Upsala Läkareförenings förhandlingar. Bd. xi., 1876.
[2] See Hammarsten, Nov. Act. Reg. Soc. Sci. Upsala, Ser. iii. Vol. x. (1875) p. 32. Also Pflüger's Archiv. Bd. xix. (1879) S. 563, Bd. xxii. (1880) S. 431.
[3] Poggiale, Ann. Chim. Phys., (3) Vol. viii. p. 469.
[4] Kühne and Eichwald, loc. cit. [5] Loc. cit.

extreme dilution, or by saturation with the solid salt. When precipitated by dilution and submitted to the prolonged action of water, myosin loses its property of being soluble in solutions of sodic chloride.[1] The sodic chloride solution, if exposed to a rising temperature, becomes milky at 55° C., and gives a flocculent precipitate at 60° C. This precipitate is, however, no longer myosin, for it is insoluble in a 10 per cent. sodic chloride solution, and does not, until after many days' digestion, yield syntonin on treatment with hydrochloric acid (0.1 per cent.). It is, in fact, coagulated proteid (see Class V.).

Myosin is excessively soluble in dilute acids and alkalies. Advantage may be taken of its solubility in the former to extract it from muscles.[2] But if the reagents are at all concentrated, myosin undergoes in the act of solution a radical change, becoming in the one case acid-albumin or syntonin, in the other alkali-albumin (Class II.).

Like fibrin, it can in some cases decompose hydrogen dioxide, and oxidize guaiacum with formation of a blue color.

5. Vitellin.

As obtained from yolk of egg, of which it is the chief proteid constituent, vitellin is a white granular body, insoluble in water, but very soluble in dilute sodic chloride solutions; it surpasses myosin in this respect, for the solution may be easily filtered. Its coagulation temperature is higher than that of myosin, lying, according to Weyl,[3] between 70° C. and 80° C. Saturation with solid sodic chloride gives no precipitate; in this respect it differs from most other members of this class. In yolk of egg vitellin is always associated with, and probably exists in combination with, the peculiar complex body, lecithin.

Denis, and after him Hoppe-Seyler, have shown that vitellin before the treatment requisite to free it from lecithin, possesses properties quite different from other proteids.

A theory has been advanced that vitellin is really a complex body like hæmoglobin, and on treatment with alcohol splits up into coagulated proteid and lecithin. When well purified it contains 0.75 per cent. sulphur, but no phosphorus. Dilute acids or alkalies readily convert it in its uncoagulated form into a member of Class II.

Fremy and Valenciennes[4] have described a series of proteids, viz., ichthin, ichthidin, etc., derived from fish and amphibia. They appear to be either identical with, or closely related to, vitellin.

Preparation.—Yolk of egg is treated with successive quantities of ether, as long as this extracts any yellow coloring matter; the residue is dissolved in moderately strong (10 per cent.) sodic chloride solution, and filtered. The filtrate on falling into a large excess of water is precipitated. In this state it is mixed with lecithin and nuclein, and in order to free it from these it was usually treated with alcohol. This, as above stated, entirely changes the vitellin into a coagulated form. It seems probable that the separation of vitellin from the other bodies with which it is mixed in the yolk of egg may be effected by precipitating the sodic chloride solution by the addition of excess of water; the precipitate is

[1] Weyl, Zeitschr. f. physiol. Chem., Bd. i. (1878) S. 77.
[2] Danilewsky, Zeitsch. f. physiol. Chem., Bd. v. (1881) S. 158.
[3] Op. cit.   [4] Compt. Rend., T. xxxviii. pp. 469 and 525.

then redissolved in 10 per cent. solution of sodic chloride, and the process repeated as rapidly as possible.[1]

6. Globin.

Globin, stated by Preyer[2] to be the proteid residue of the complex body hæmoglobin (see p. 408), ought probably to be considered as an outlying member of this class. It is, however, not readily soluble either in dilute acids or sodic chloride solutions. It is said to be absolutely free from asb.

CLASS IV.—*Fibrin.*

Insoluble in water and dilute sodic chloride solutions; soluble with difficulty in dilute acids and alkalies, and more concentrated neutral saline solutions.

Fibrin, as ordinarily obtained, exhibits a filamentous structure, the component threads possessing an elasticity much greater than that of any other known solid proteid.

If allowed to form gradually in large masses, the filamentous structure is not so noticeable, and it resembles in this form pure India-rubber. Such lumps of fibrin are capable of being split in any direction, and no definite arrangement of parallel bundles of fibres can be made out.

At ordinary temperatures fibrin is insoluble in water, being dissolved only at very high temperatures, and then undergoing a complete change in its characters. In hydrochloric acid solutions of 1–5 per cent., fibrin swells up and becomes transparent, but is not dissolved.[3] In this condition the mere removal of the acid by an excess of water, neutralization, or the addition of some salt, causes a return to the original state. If, however, the acid be allowed to act for many days at ordinary temperatures, or for a few hours at 40°–60° C., solution takes place, and the resulting proteid is syntonin. In dilute alkalies and ammonia, fibrin is much more readily soluble, though in this case, also, the solution is greatly aided by warming; the resulting fluid contains no longer fibrin, but alkali-albumin. This property is not distinctly characteristic of fibrin, although it dissolves, perhaps, more readily in both dilute acids and alkalies than do coagulated proteids. None of these solutions can be coagulated on heating, which is intelligible when it is remembered that they no longer contain fibrin, but either acid or alkali-albumin. In addition to the above, fibrin is soluble, though with difficulty and only after a considerable time, in 10 per cent. solutions of sodic chloride, potassic nitrate, or sodic sulphate, the solution being often accompanied by putrefactive changes. These solutions may be coagulated by a temperature of 60° C., and are precipitated by dilution with water or saturation with solid sodic chloride; in fact, by the action of the neutral saline solutions, the fibrin has become converted into a body exceedingly like myosin or globulin.[4]

On ignition of fibrin, a residue of inorganic matter is always obtained; it is, however, considered that sulphur is the only one of these elements which enters essentially into its composition. In other respects, fibrin corresponds entirely in general composition with other proteids.

Suspended in water and heated to 70° C., it loses its elasticity, and

[1] Weyl, op. cit. S. 64.   [2] Die Blutkrystalle (1871), S. 166.

[3] Complete solution may, however, take place if the fibrin, as is frequently the case, contains any adherent pepsin.

[4] Gautier, Compt. Rend., T. lxxix. (1874) p. 227.

becomes opaque; it is then indistinguishable from other coagulated proteids.

A peculiar property of this body remains yet to be mentioned, viz., its power of decomposing hydrogen dioxide. Pieces of fibrin placed in this fluid, though themselves undergoing no change, soon become covered with bubbles of oxygen; and guaiacum is turned blue by fibrin in presence of hydrogen dioxide or ozonized turpentine.

Preparation.—By vigorously stirring blood with a bundle of twigs and then washing with water until it is quite white. If required perfectly pure and colorless, it should be prepared from plasma free from corpuscles. If the blood, before stirring, be diluted with an equal bulk of water, the subsequent washing of the fibrin is much facilitated, and it may readily be obtained quite white. Any adherent fats may be removed by ether.

When globulin, myosin, and fibrin are compared each with the other, it will be seen that they form a series in which myosin is intermediate between globulin and fibrin. Globulin is excessively soluble in even the most dilute acids and alkalies; fibrin is almost insoluble in these; while myosin, though more soluble than fibrin, is less soluble than globulin. Globulin, again, dissolves with the greatest ease in a very dilute solution of sodic chloride. Myosin, on the other hand, dissolves with difficulty; it is much more soluble in a 10 per cent. than in a 1 per cent. solution of sodic chloride; and even in a 10 per cent. solution the myosin can hardly be said to be dissolved, so viscid is the resulting fluid and with such difficulty does it filter. Fibrin, again, dissolves with great difficulty and very slowly in even a ten per cent. solution of sodic chloride, and in a one per cent. solution it is practically insoluble. When it is remembered that fibrin and myosin are, both of them, the results of coagulation, their similarity is intelligible. Myosin is, in fact, a somewhat more soluble form of fibrin, deposited not in threads or filaments, but in clumps and masses.

Class V.—*Coagulated Proteids.*

These are insoluble in water, dilute acids and alkalies, and neutral saline solutions of all strengths. In fact, they are really soluble only in strong acids and strong alkalies, though prolonged action of even dilute acids and alkalies will effect some solution, especially at high temperatures. During solution in strong acids and alkalies, a destructive decomposition takes place, but some amount of acid- or alkali-albumin is always produced.

Very little is known of the chemical characteristics of this class. They are produced by heating to 70° C., solutions of egg- or serum-albumin, globulins suspended in water or dissolved in saline solutions; by boiling for a short time fibrin suspended in water or dissolved in saline solutions, or precipitated acid- and alkali-albumin suspended in water. They are readily converted at the temperature of the body into peptones, by the action of gastric juice in an acid, or of pancreatic juice in an alkaline medium.

All proteids in solutions are precipitated by an excess of strong alcohol. If the precipitant be rapidly removed they are again soluble in water, but if the precipitated proteids are subjected for some time to the action of the alcohol they are, with the exception of peptones, coagulated and lose their solubility. It appears, however, that the proteids contained

in the aleurone-grains of plants are exceedingly resistant to this coagulating action of alcohol.[1]

It seems scarcely necessary to point out the distinction in the use of the word "coagulation" as applied to blood or muscle-plasma on the one hand and to the action of heat and alcohol upon proteids on the other. The difference is obvious when it is remembered that in the first case the coagulation leads to the formation of fibrin (Class IV.), or myosin (Class III.), and that these bodies may then further be coagulated by heat or alcohol as described above.

Class VI.—*Peptones.*

Very soluble in water, and not precipitated from their aqueous solutions by the addition of acids or alkalies, or by boiling. Insoluble in alcohol, they are precipitated with difficulty by this reagent, and are unchanged in the process; they differ from all other proteids in not being coagulated by prolonged exposure to alcohol. They are not precipitated by cupric sulphate, ferric chloride, or, except in the instances to be mentioned presently, by potassic ferrocyanide, and acetic acid. In these points they differ from most other proteids. On the other hand, precipitation is caused by chlorine, iodine, tannin, mercuric chloride, nitrates of mercury and silver, and both acetates of lead; also by bile-acids in an acid solution. In common with all proteids, these bodies possess a specific lævo-rotatory power over polarized light; but they differ from all other proteids in the fact that boiling produces no change in the amount of rotation.

A solution of peptones, mixed with a strong solution of caustic potash, gives, on the addition of a *mere trace* of cupric sulphate, a *pink* color. An excess of the cupric salt gives a violet color, which deepens in tint on boiling—in fact, the ordinary proteid reaction. Other proteids simply give the violet color. But the most characteristic feature of peptones is their relatively great diffusibility, a property which they alone, of all the proteids, may be said to possess, since all other forms of proteids pass through membranes with the greatest difficulty, if at all.

The diffusibility of peptones is, however, absolutely small as compared with that of crystalline bodies such as sodic chloride; in fact, solutions of peptones may be freed from salts by dialysis, a process employed in their preparation.

Notwithstanding their probable formation in large quantities in the stomach and intestine, to judge from the results of artificial digestion, a very small quantity only can be found in the contents of these organs. They are probably absorbed as soon as formed. Another point of interest is their reconversion into other forms of proteids, since this must occur to a great extent in the body. We are, however, as yet ignorant of the manner in which this reverse change is effected.

Production.—All proteids, with the exception of lardacein (see p. 852), yield peptones (and other products) on treatment with acid gastric or alkaline pancreatic juice, most readily at the temperature of the human body. Peptones are likewise produced, in the absence of pepsin and trypsin, by the action of dilute and moderately strong acids at medium temperatures, also by the action of distilled water at high temperatures under pressure. For various methods of preparing peptones, see Maly,[2] Adamkiewicz,[3] Henninger,[4] and Pekelharing.[5]

1 See Vines, Jl. of Physiol., Vol. iii. p. 108.
2 Pflüger's Arch., Bd. ix. (1874) S. 585.
3 Die Natur u. Nährwerth d. Peptons (1877), S. 33.
4 De la Nature et du Rôle physiologique des Peptones, Paris, 1878.
5 Pflüger's Arch., Bd. xxii. (1882) S. 185.

It appears possible to reobtain ordinary coagulable proteids from peptones by the action of either prolonged heating to 140°-170° C. or of dehydrating agents.[1]

No difference in percentage composition between peptones and the proteid from which they are formed has, at present, been definitely established.

We have used the phrase "peptones" in the plural number because we have reason to think that more than one kind of peptone exists. Meissner[2] described three peptones, naming them respectively A-, B-, and C-peptone. He distinguished them as follows: A-peptone is precipitated from its aqueous solutions by concentrated nitric acid, and also by potassic ferrocyanide in the presence of even weak acetic acid. B-peptone is not precipitated by concentrated nitric acid, nor will potassic ferrocyanide give a precipitate unless a considerable quantity of strong acetic acid be added at the same time. C-peptone is precipitated neither by nitric acid nor by potassic ferrocyanide and acetic acid, whatever be the strength of the acetic acid. In place, however, of speaking of all these as peptones, it is better to consider C-peptone as the only real peptone, and the A- and B- peptones as not peptones at all. Nevertheless we have reason, from the researches of Kühne, to speak of more than one peptone, viz., of a hemipeptone which is capable under the action of trypsin of being converted into leucin and tyrosin, and of an antipeptone which resists such a decomposition. The name antipeptone is given to the latter on account of this resistance which it offers toward trypsin; the name hemipeptone, given to the former, signifies that this peptone is the twin or correlative half of antipeptone.

We have seen (p. 294) that when any proteid is digested with pepsin, what we may preliminarily call a by-product makes its appearance. This by-product, which has many resemblances to acid-albumin or syntonin, appearing as a neutralization precipitate soluble in dilute acids and alkalies, but insoluble in distilled water, is generally spoken of as parapeptone. According to Finkler[3] this neutralization precipitate is especially abundant if the pepsin be previously modified by exposure to a temperature of 40° to 60° C. The pepsin thus modified is spoken of by Finkler as "isopepsin." Many authors regard parapeptone, syntonin, and acid-albumin as being the same thing. Meissner, however, gave the name parapeptone to a body, which need not and probably does not make its appearance during normal natural digestion or during artificial digestion with a thoroughly active pepsin, but which is formed when proteids are subjected to the action of weak hydrochloric acid, either alone or in company with an imperfectly acting pepsin, and which in certain characters is quite distinct from ordinary syntonin or acid-albumin. Its distinguishing feature is that it cannot be changed into peptone by the action of even the most energetic pepsin, though it is readily so converted under the influence of trypsin; otherwise it very closely resembles syntonin. We have here an indication that the simple characters by which we have described acid-albumin may be borne by bodies having marked differences from each other. The researches of Kühne[4] have thrown an im-

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[1] Henninger, loc. cit., Hofmeister, Zeitsch. f. physiol. Chem., Bd. ii. (1878), S. 206. Pekelharing, loc. cit.

[2] Zeitschr. f. rat. Med., Bde. vii., viii., x., xii., und xiv.

[3] Pflüger's Archiv, xiv. (1877) S. 128.

[4] Only a short account of these has as yet been published. Verhand. d. Naturhist-Med. Ver-Heidelbg, Bd. i. Hf. 4, 1876.

portant light on these differences. The fundamental notion of Kühne's view is that an ordinary native albumin or fibrin contains within itself two residues, which he calls respectively an anti-residue and a hemi-residue. The result of either peptic or tryptic digestion is to split up the albumin or fibrin, and to produce on the part of the anti-residue anti-peptone, and on the part of the hemi-residue hemipeptone, the latter being distinguished from the former by its being susceptible of further change by tryptic digestion into leucin, tyrosin, etc. Antipeptone remains as antipeptone even when placed under the action of the most powerful trypsin, provided putrefactive changes do not intervene.

Before the stage of peptone (whether anti- or hemi-) is reached, there is an intermediate stage corresponding to the formation of syntonin. In both normal peptic and tryptic digestion antipeptone is preceded by an anti-albumose, and hemipeptone by a hemi-albumose. Of these the anti-albumose is closely related to syntonin, and has hitherto been regarded as syntonin. The hemi-albumose has not been so frequently observed; it was, however, isolated by Meissner; it is apparently the body called by him A-peptone. It possesses several peculiar features. If its solutions are heated, they partially coagulate at about 60°–65° C.; the precipitate is soluble at about 70° C., and is reprecipitated as the temperature again falls. It also yields a precipitate with nitric acid and potassic ferrocyanide, and this also is soluble at the higher temperature reprecipitating on cooling. In these respects it closely resembles a proteid body observed by Bence-Jones in the urine of osteomalacia. It approaches myosin in being readily soluble in a 10 per cent. solution of sodic chloride.

If, however, albumin be digested with insufficient or with imperfectly active pepsin, or simply with dilute hydrochloric acid at 40° C., anti-albumose is not formed, but in its place a body makes its appearance which Kühne calls anti-albumate.[1] Its characteristic property is that it cannot be converted by peptic digestion into peptone, though it can be so changed by tryptic digestion. It is, in fact, the parapeptone of Meissner.

It may, perhaps, be advisable, now that Meissner's parapeptone is cleared up, to reserve the name parapeptone for the initial products of both peptic and tryptic digestion, and to speak of anti-albumose and hemi-albumose as being both parapeptones. But in this sense parapeptone will be an intermediate and not a collateral product of digestion.

Meissner also described a particularly insoluble form of his parapeptone as dyspeptone, and another intermediate product as metapeptone; but further investigation of both these bodies, as well as of his B-peptone, is necessary. Under the influence of dilute hydrochloric acid, anti-albumate becomes changed into a body which Kühne calls anti-albumid, and which seems identical with the very insoluble proteid described by Schützenberger as "hemiprotein," and probably with Meissner's dyspeptone. The same body is produced at once in company with products belonging to the hemi-group by the action of 3 to 5 per cent. sulphuric acid on native albumin or fibrin. The following tables show the relations and genesis of the bodies we have just described. The several products (antipeptone, etc.) are given in duplicate, on the hypothesis (which, though not proved, is probable) that the changes of digestion are essentially hydrolytic changes,[2] accompanied by a deduplication; that just as a molecule of starch splits up into at least two molecules of dextrose, or as a molecule of cane-sugar splits up into a molecule of dextrose

[1] An albumate must not be confounded with an *albuminate*.

[2] Henninger, loc. cit. p. 49.

and a molecule of levulose, so a molecule of **antialbumose**, for instance, splits up into two molecules of antipeptone, and so on. But the whole scheme is, of course, only provisional.

DECOMPOSITION OF PROTEIDS BY DIGESTION.

Albumin.

Action of Pepsin.   *Special action of Trypsin.*

Antialbumose.   Hemialbumose.

Antipeptone.   Antipeptone.   Hemipeptone.   Hemipeptone.

Leucin. Tyrosin. etc.   Leucin. Tyrosin. etc.
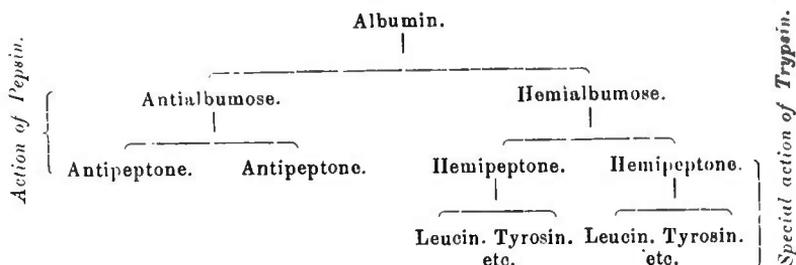
DECOMPOSITION BY ACIDS.

1.

By 0.25 per cent. HCl at 40° C.
Albumin.

Antialbumate.   Hemialbumose.

Antialbumid.   Hemipeptone.   Hemipeptone.
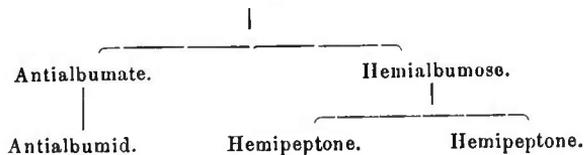
2.

By 3–5 per cent. H_2SO_4 at 100° C.
Albumin.

Antialbumid.   Hemialbumose.

Hemipeptone.   Hemipeptone.

Leucin. Tyrosin. etc.   Leucin. Tyrosin, etc
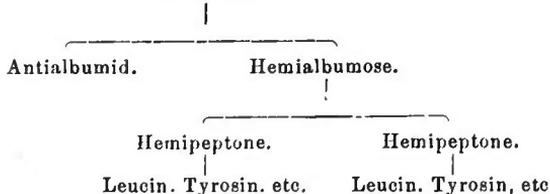
CLASS VII.—*Lardacein, or the so-called amyloid substance.*

The substance to which the above name is applied, is found as a pathological deposit in the spleen and liver, also in numerous other organs, such as the bloodvessels, kidneys, lungs, etc.

It is insoluble in water, dilute acids, and alkalies, and neutral saline solutions.

In centesimal composition, it is almost identical with other proteids,[1] viz:

O. and S.	H.	N.	C.
24.4	7.0	15.0	53.6

[1] C. Schmidt, Ann. d. Chem. u. Pharm., Bd. ex. S. 250, and Friedreich and Kekulé, Virchow's Archiv, Bd. xvi. S. 50.

The sulphur in this body exists in the oxidized state, for boiling with caustic potash gives no sulphide of the alkali. The above results of analysis would lead at once to the ranking of lardacein as a proteid, and this is strongly supported by other facts. Strong hydrochloric acid converts it into acid-albumin, and caustic alkalies into alkali-albumin. On the other hand, it exhibits the following marked differences from other proteids: It wholly resists the action of ordinary digestive fluids; it is colored red, not yellow, by iodine, and violet or pure blue by the joint action of iodine and sulphuric acid. From these last reactions it has derived one of its names, "amyloid," though this is evidently badly chosen; for not only does it differ from the starch group in composition, but by no means can it be converted into sugar; this latter is one of the crucial tests for a true member of the carbohydrate group. According to Heschl[1] and Cornil,[2] anilin-violet (methyl-anilin) colors lardaceous tissue rosy red, but sound tissue blue.

The colors mentioned above, as being produced by iodine and sulphuric acid, are much clearer and brighter when the reagents are applied to the purified lardacein. When the reagents are applied to the crude substance in its normal position in the tissues, the colors obtained are always dark and dirty looking.

Purified lardacein is readily soluble in moderately dilute ammonia, and can, by evaporation, be obtained from this solution in the form of tough, gelatinous flakes and lumps; in this form it gives feeble reactions only with iodine. If the excess of ammonia is expelled, the solution becomes neutral, and is precipitated by dilute acids.

Preparation.—The gland or other tissue containing this body is cut up into small pieces, and as much as possible of the surrounding tissue removed. The pieces are then extracted several times with water and dilute alcohol, and if not thus rendered colorless, are repeatedly boiled with alcohol containing hydrochloric acid. The residue after this operation is digested at 40° C., with good artificial gastric juice in excess. Everything except lardacein, and small quantities of mucin, nuclein, keratin, together with some portion of the elastic tissue, will thus be dissolved and removed.[3] From the latter impurities it may be separated by decantation of the finely powdered substance.

The chief products of the decomposition of proteids are ammonia, carbonic anhydride, leucin, and tyrosin. Several other bodies, for the most part, like leucin, amidated acids, such as aspartic acid, glutamic acid, etc., have also been obtained; also by tryptic digestion, hypoxanthin, and perhaps xanthin. But urea has never yet been derived by direct decomposition from proteid material, the statements to this effect having been based on errors. In spite of numerous researches, we cannot at present state definitely what is the real constitution of a proteid, or in what manner these several residues are contained in the undecomposed substance. It is unnecessary to give here any of the formulæ, nearly all empirical, which have been made to represent a proteid; they all give with equal exactitude the percentage composition, but beyond this they are untrustworthy. Of the various attempts which have been made to assign to proteids some definite molecular structure, none appear, at the present stage of information, sufficiently reliable for general acceptance.

1 Wien. med. Wochenschr., No. 32, S. 714.
2 Compt Rend., T. lxxx. (1875) p. 1288.
3 Kühne und Rudneff, Vircbow's Areh., Bd. xxxiii. (1865) S. 66.

Among the most elaborate labors in this direction may be mentioned those of Hlasiwetz and Haberman. In their first publication,[1] starting from the general similarity of the products of decomposition of the proteids and carbohydrates, they tried to establish a definite relation between the two classes of bodies. In this they were not successful, and in their second research[2] they come to the conclusion that the carbohydrates take no part in the formation of the proteids.

Other experiments in the same direction have been made by Schützenberger.[3] He shows that albumin can be decomposed into carbonic anhydride and ammonia, and that the ratio of these two is the same as though urea had been the body on which he operated. From this he concludes that "the molecule of albumin contains the grouping of urea and represents a complex ureide." In his second publication[4] he confirms his previous results, stating that the ammonia, carbonic anhydride, and oxalic acid, produced by the decomposition of proteids, are so connected quantitatively as to be capable of derivation from varying proportions of urea and oxamide. He also obtained from the decomposition of proteids a nitrogenous residue which could be formulated as giving rise to all the amidated acids and other bodies spoken of above. Thus according to him, albumin, built up as a complex ureide, decomposes into ammonia, carbonic, oxalic, and acetic acids, and this nitrogenous body; this last then gives rise to the other products of decomposition.[5]

It will be noticed that in the general description of the various proteids, distinctive reactions for each could not be given, but that varying solubilities were the chief means at our disposal for distinguishing them. They may be arranged according to their solubilities in the following tabular form:

Soluble in distilled water :

Aqueous solution not coagulated on boiling	*Peptones.*
Aqueous solution coagulated on boiling .	*Albumins.*

Insoluble in distilled water :

Soluble in NaCl solution 1 per cent	*Globulins.*
Insoluble in NaCl solution 1 per cent.	
Soluble in HCl 0.1 per cent. in the cold.	{ *Acid- and Alkali-albumin.*
Insoluble in HCl 0.1 per cent. in the cold, but soluble at 60° . . .	} *Fibrin.*
Insoluble in HCl 0.1 per cent. at 60°; soluble in strong acids.	
Soluble in gastric juice	*Coagulated albumin.*
Insoluble in gastric juice	*Lardacein.*

Such a classification is, however, obviously a wholly artificial one, useful for temporary purposes, but in no way illustrating the natural relations of the several members. Nor is a division into "native" and "derived" proteids much more satisfactory. It is true that we may thus put together serum- and egg-albumin, with vitellin, myosin, and fibrin, on the one hand, and peptones, coagulated proteids, and acid- with alkali-albumin, on the other. But in what light are we to consider casein, seeing that, though a natural product, it has so many resemblances to alkali-albumin? Moreover, the system of classification must be useless

[1] Ann. d. Chem. u. Pharm., Bd. 159, S. 304.

[2] Ibid. Bd. 169, S. 150.

[3] Comptes Rendus, T. 80 (1875), p. 232. Bull. de la Soc. chim., xxiii. 161, 193, 216, 242, 385, 433, xxiv. 2 et 145.

[4] Compt. Rend., T. 81, p. 1108. Bull. de la Soc. chim., xxv. 147.

[5] See also Schützenberger, Ann. de Chem., et de phys., T. xvi. (1879) p. 280.

which would place fibrinoplastic globulin and fibrinogen in the same class as fibrin, and yet we can hardly speak of either of the two former bodies as derived proteids. If the view be true that when fibrin is converted into peptone the large molecule of the former is split up, with assumption of water, into two smaller molecules of the latter, one belonging to the "anti" and the other to the "hemi" group, we might speculate on a possible classification of all proteids into hemi-proteids, anti-proteids, and holo-proteids. Thus serum- and egg-albumin, myosin, and fibrin would be undoubtedly holo-proteids, peptones either anti- or hemi-proteids, and we should have to distinguish probably in the heterogeneous group of derived albumins both anti-, hemi, and holo-proteid members. It is possible, moreover, that fibrinoplastic and fibrinogenous globulin and casein may be natural hemi- or anti-proteids and not holo-proteids. But we have at present no positive knowledge on these points.

NITROGENOUS NON-CRYSTALLINE BODIES ALLIED TO PROTEIDS.

These resemble the proteids in many general points, but exhibit among themselves much greater differences than do the proteids. As regards their molecular structure nothing satisfactory is known. Their percentage composition approaches that of the proteids, and like these they yield, under hydrolytic treatment, large quantities of leucin and in some cases tyrosin. They are all amorphous.

Mucin. (O, 35.75. H, 6.81. N, 8.50. C, 48.94.)[1]

The characteristic component of mucus. Its exact composition is not yet known, the figures given above being merely an approximation.

As occurring in the normal condition it gives to the fluids which contain it the well-known ropy consistency, and can be precipitated from these by acetic acid, alcohol, alum, and mineral acids; the latter, if in excess, redissolve the precipitate, but this is not the case with acetic acid. In its precipitated form it is insoluble in water, but swells up strongly in it, and this effect is increased by the presence of many alkali salts. Alkalies and alkaline earths dissolve it readily. Its solutions do not dialyze; they give the proteid reactions with Millon's reagent and nitric acid, but not that with sulphate of copper, and are precipitated by basic lead acetate only when neutral or faintly alkaline. According to Eichwald,[2] when heated with dilute mineral acids, mucin yields acid-albumin, and another body which in many of its properties closely resembles a sugar, inasmuch as it reduces solutions of cupric sulphate. Prolonged boiling with sulphuric acid gives leucin and about 7 per cent. of tyrosin.

Preparation.[3] Ox-gall or an aqueous extract of finely chopped submaxillary gland is acidulated with acetic acid; the precipitated mucin is then washed with water, dissolved in dilute sodic carbonate, and finally precipitated with acetic acid. It may also be obtained from snails.[4]

Chondrin. (O, 31.04. H, 6.76. N, 13.87. C, 47.74. S, 0.60 per cent.)[5]

[1] Eichwald, Ann. d. Chem. u. Pharm., Bd. 134, S. 193. Op. cit
[3] Eichwald, op. cit., and Chem. Centralb., 1866, No. 14. Staedeler, Ann. de Chem. u. Pharm., Bd. 111, S. 14. Landwehr, Zeitsch. f. physiol. Chem., Bd. v. (1881) S. 371.
[4] Landwehr, Zeitsch. f. physiol. Chem., Bd. vi. (1882) S. 75.
[5] I. v. Mering, Beitrag zur Chemie des Knorpels, 1873.

This is usually regarded as forming the essential part of the matrix of hyaline cartilage, and is contained in the interstices of the fibres in elastic cartilage. A similar substance can be prepared from the cornea. Boiled with water, it dissolves slowly, forming an opalescent solution, which is precipitated by acetic acid, lead acetate, dilute mineral acids, alum, and salts of silver and copper; an excess of the last four reagents redissolves the precipitate. Solutions of this body gelatinize on standing, even if very dilute; the solid mass is insoluble in cold water, readily soluble in hot water, alkalies, and ammonia.

The aqueous and alkaline solutions of chondrin possess a left-handed rotatory power on polarized light of —213.5°: in presence of excess of alkali this becomes —552.0°, both measured for yellow light.[1]

It seems, according to the observations of many, that chondrin can, by heating with hydrochloric acid, be converted into a body whose reactions resemble those of syntonin, and another substance, which like the similar product from mucin, so far resembles grape-sugar that it reduces cupric salts in alkaline solution;[2] it appears, however, to contain nitrogen. The existence of chondrin as a distinct substance has, however, been denied[3] on the supposition that it is in all cases a mere mixture of other bodies. It is stated that a substance having all the reactions of the so-called chondrin, may, at any time, be produced by a mixture of mucin, glutin, inorganic salts. The extreme similarity in the reactions of chondrin and mucin point to a close relationship between the two. The whole subject, however, requires more complete investigation. With alkalies or dilute sulphuric acid chondrin gives leucin, but no tyrosin or glycin. Whether chondrin exists as such in cartilage is uncertain; it seems probable that it does not, since its extraction from cartilage requires an amount of boiling with water much greater than that requisite to dissolve dried chondrin.

Preparation.—From cartilage by extracting with water, and precipitating with acetic acid.

Gelatin or Glutin.[4] (O, 23.21. H, 7.15. N, 18.32, C, 50.76. S, 0.56 per cent.)

This is the substance which is yielded when connective tissue fibres are heated for several days with very dilute acetic acid, at a temperature of about 15° C., or by the prolonged action of water in a Papin's digester. The elastic elements of connective tissue are unaffected by the above treatment.

As obtained in this way glutin is when heated a thin fluid, solidifying on cooling to the well-known gelatinous form. When dried it is a colorless, transparent, brittle body, swelling up, but remaining undissolved in cold water; heating, or the addition of traces of acids or alkalies, readily effects its solution. When dissolved in water it possesses a lævo-rotatory power of —130°, at 30° C.; the addition of strong alkali or acetic acid reduces this to —112° or —114°, both measured for yellow light.[5] Its solution will not dialyze.

Mercuric chloride and tannic acid are the only two reagents which yield insoluble precipitates with this body. Its presence prevents the

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[1] Hoppe-Seyler, Hdb. phys. path. chem. Anal., 4 Aufl. 1875, S. 262.
[2] De Bary, Hoppe-Seyler's Untersuch., Hft. i. S. 71.]
[3] Morochowetz, Verhand. naturhist. med. Ver. Heidelberg., Bd. i. (1876) Hft. 5.
[4] Not to be confounded with the vegetable proteid "gluten."
[5] Hoppe-Seyler, Hbd. d. phys. path. chem. Anal., 4 Aufl. 1875, S. 222.

action of Trommer's sugar test, since it readily dissolves up the precipitated cuprous oxide. The proteid reactions of glutin are so feeble that they are probably due merely to impurities. Heated with sulphuric acid it yields ammonia, leucin, and glycin, but no tyrosin.

It appears improbable that glutin exists ready formed in connective tissue fibres, since these do not swell up in water, and only yield glutin after prolonged treatment with boiling water; to which it may be added that while glutin is acted upon by trypsin, the connective tissue fibres in their natural condition resist its action (see p. 309). When glutin is submitted for some time to the action of dilute hydrochloric acid, at 38° C., and the change is brought about even more readily by the action of pepsin, it loses its power of gelatinizing, and is now diffusible through porous membranes; the name of gelatin-peptone has been given to the product thus obtained.[1]

Elastin. (O, 20.5. H, 7.4. N, 16.7. C, 55.5 per cent.)

This characteristic component of elastic fibres is left on the removal of all the glutin, mucin, etc., from such tissues as "ligamentum nuchæ," advantage being taken of its not being altered when it is heated with water, even under pressure, with strong acetic acid, or with dilute alkalies. When moist it is yellow and elastic, but on drying becomes brittle. It is soluble in strong alkalies at boiling temperatures, and concentrated sulphuric and nitric acids dissolve it even in the cold; it is also dissolved by the action of papaya juice. It is precipitated from solutions by tannic acid, but not by the addition of ordinary acids. Notwithstanding that it closely approaches the proteids in its percentage composition, and gives distinct although feeble proteid reactions, any very close relationship between the two appears improbable, since elastin when treated with sulphuric acid, yields leucin (30–40 per cent.) only and no tyrosin.

Hilger[2] has obtained a similar body from the shell membrane of snakes' eggs.

Keratin.[3] (O, 20.7–25. H, 6.4–7. N, 16.2–17.7. C, 50.3–52.5. S, 0.7–5 per cent.)

This body, though somewhat resembling the proteids in general composition, differs from them and also from the preceding bodies so widely in other properties, that its description is placed here for convenience rather than anything else. Hair, nails, feathers, horn, and epidermic scales consist for the most part of keratin. Heated with water in a digester at 150° C., keratin is partially dissolved with evolution of sulphuretted hydrogen; the solution then gives with acetic acid and ferrocyanide of potassium, a precipitate soluble in excess of the acid. Prolonged boiling with alkalies and acids, even acetic, dissolves keratin; the alkaline solutions evolve sulphuretted hydrogen on treatment with acids. The sulphur in keratin is evidently very loosely united to the substance, and in all its reactions there appears to be a want of similarity between keratin and either proteids, mucin, or gelatin. The most common of its products of decomposition are leucin (10 per cent.), and tyrosin (3.6 per cent.), and some aspartic acid; no glycin is formed. What is gener-

[1] Hofmeister, Zeitsch. f. physiol. Chem., Bd. ii. (1878) S. 299.
[2] Ber. d. deutsch. chem. Gesellsch., 1873, S. 166. But see also next reference.
[3] Lindwall, Nagra hidrag till kann. om. Ker. Upsala Läkarefs. förh. xvi. (1881) p. 446.

ally known as keratin is probably a compound body, which has not yet been resolved into its components.

Ewald and Kühne[1] have described a new body to which, since it occurs as a constituent of nervous tissue (both of nerves and of the central nervous system), and is yet closely identical with ordinary horny tissue, they give the name of neuro-keratin. It is prepared in quantity from the brain by extracting this tissue with alcobol and ether, and subjecting the residue to the action of pepsin and trypsin. The final residue is neuro-keratin, and amounts to 15-20 per cent. of the original tissue.

Nuclein. $C_{29}H_{49}N_9P_3O_{22}$.

Discovered by Miescher[2] in the nuclei of pus corpuscles and in the yellow corpuscles of yolk of egg. Other observers have subsequently obtained it from yeast, from semen, from the nuclei of the red blood-corpuscles of birds and amphibia, from hepatic cells, and it is probably present in all nuclei.

When newly prepared it is a colorless amorphous body, soluble to a slight extent in water, readily soluble in many alkaline solutions; but its solubilities alter on keeping. If added gradually in sufficient quantity to a solution of caustic alkali it first neutralizes the solution and then renders it acid. It seems to possess an indistinct xanthoproteic reaction, but gives no reaction with Millon's fluid. It yields precipitates with several salts, e. g., zinc chloride, argentic nitrate, and cupric sulphate.

Preparation.[3]—Since nuclein is very resistant to the action of pepsin, it may be obtained from the granular residue consisting chiefly of nuclei, which occurs after digesting pus with pepsin. The most remarkable feature of this body is its large percentage of phosphorus, 9.59 per cent. This phosphorus is readily separated by boiling with strong hydrochloric acid or caustic alkalies; the same occurs when solutions of nuclein are acidulated and allowed to stand.

Chitin. $C_{15}H_{26}N_2O_{10}$.[4]

Although not found as a constituent of any mammalian tissue, this substance composes the chief part of the exoskeleton of many invertebrates. It may probably be regarded as the animal analogue of the cellulose of plants, and from this point of view it possesses considerable morphological interest. Both cellulose and chitin appear to yield some form of sugar when treated with strong acids.

When purified, chitin is a white amorphous body, often retaining the shape of the tissue from which it has been prepared. It is insoluble in all reagents except strong mineral acids, the best solvents being sulphuric or hydrochloric acids. The immediate addition of water to these solutions reprecipitates the chitin in an unaltered form; but the prolonged action of sulphuric acid causes a decomposition resulting, according to some observers, in the formation of an amorphous fermentible carbohydrate; and when hydrochloric acid is used an amidated carbohydrate is obtained to which the name of glycosamin[5] has been given.

[1] Verband. naturhist. med. Ver Heidelberg., Bd. i. (1876) Heft 5.
[2] Med. Chem. Untersuch. Hoppe-Seyler, Heft 4, 1872, S. 441 und 502.
[3] See Kossel, Zeitsch. f. physiol. Chem., Bd. iii. (1879) S. 284, iv (1880) S. 290, vii. (1883) S. 7. "Untersuch. über d. Nuclein u. ihre Spaltungsprod," Strassb., 1881.
[4] Ledderbose, Zeitsch. f. physiol. Chem., Bd. ii. (1878) S. 213.
[5] Ledderbose, loc. cit. Bd. iv. (1880) S. 139.

Preparation.[1]—The cleaned exoskeleton of a lobster is thoroughly extracted with dilute hydrochloric acid and then with caustic soda. To purify it finally it is submitted to prolonged boiling with a solution of potassic permanganate.

CARBOHYDRATES.

Certain members only of this class occur in the human body; of these, the most important and widespread are those known as glycogen and the two sugars, grape-sugar or dextrose (glucose), with which diabetic sugar seems to be identical,[2] and maltose. Next to these comes milk-sugar. Inosit is another body of this class, although it differs in many important points from the preceding two.

Sugars are often considered to be polytomic alcohols. Several of them stand in peculiar relation to mannit, and may be converted into that substance by the action of sodium amalgam.[3]

1. **Dextrose** (Grape-sugar). $C_6H_{12}O_6 + H_2O$.

Occurs in the contents of the alimentary canal to a variable extent dependent on the nature of the food taken. It is also a normal constituent of blood, chyle, and lymph. Concerning its presence in the liver, see p. 495. The amniotic fluid also contains this body. Bile in the *normal* condition is free from sugar, so also is urine, though this point has given rise to great dispute.[4] The disease diabetes is characterized by an excess of dextrose in the fluids and tissues of the body (see p. 501).

When pure, dextrose is colorless and crystallizes from its aqueous solution in six-sided tables or prisms, often agglomerated into warty lumps. The crystals will dissolve in their own weight of cold water, requiring, however, some time for the process; they are very readily soluble in hot water. Dextrose is somewhat sparingly soluble in alcohol, and crystallizes from anhydrous alcohol in prisms free from water of crystallization; it is, moreover, insoluble in ether.

The freshly prepared cold aqueous solution of the crystals possesses a dextrorotatory power of $+ 104°$ for yellow light. This, quickly on heating, more slowly on standing, falls to $+ 56°$, at which point it remains constant.

Dextrose readily forms compounds with acids and many salts; the latter are very unstable, decomposition rapidly ensuing on heating them. When its metallic compounds are decomposed the decomposition is in many cases accompanied by the precipitation of the metals, *e. g.*, silver, gold, bismuth. Caustic alkalies readily decompose them, as also does ammonia.

Dextrose is readily and completely precipitated by lead acetate and ammonia.

An important property of this body is its power of undergoing fermentations. Of these the two principal are: (1) *Alcoholic.* This is produced in aqueous solutions of dextrose, under the influence of yeast. The decomposition is the following: $C_6H_{12}O_6 = 2C_2H_6O + 2CO_2$, yielding (ethyl) alcohol and carbonic anhydride. Other alcohols of the acetic series are

[1] Bütschli, Arch. f. Anat. u. Physiol. Jahrg. 1874, S. 362.
[2] The question, however, whether several varieties of sugar occurring in the animal body have not been confounded together under the common name of dextrose or glucose may be considered at present an open one.
[3] Linnemann, Ann. d. Chem. u. Pharm., Bd. 123, S, 136.
[4] See Seegen, Der Diabetes Mellitus, 2 Ed. S. 196.

found in traces, as also are glycerine, succinic acid, and probably many other bodies. The fermentation is most active at about 25° C. Below 5° C. or above 45° C. it almost entirely ceases. If the saccharine solution contains more than 15 per cent. of sugar it will not all be decomposed, as excess of alcohol stops the reaction. (2) *Lactic.* This occurs in the presence of decomposing nitrogenous matter, especially of casein, and is probably the result of the action of a specific ferment.[1] The first stage is the production of lactic acid, $C_6H_{12}O_6 = 2C_3H_6O_3$. In the second butyric acid is formed with evolution of hydrogen and carbonic anhydride: $2C_3H_6O_3 = C_4H_8O_2 + 2CO_2 + 2H_2$. The above changes, the first of which is probably undergone by sugar to a considerable extent in the intestine, are most active at 35° C.: the presence of alkaline carbonates is also favorable. It is, moreover, essential that the lactic acid should be neutralized as fast as it is formed, otherwise the presence of the free acid stops the process.

The preparation, detection, and estimation of dextrose are so fully given in various books that they need not be detailed here.

2. Maltose.　$C_{12}H_{22}O_{11} + H_2O$.

This form of sugar was first described by Dubrunfaut[2] as a product of the action of malt extract on starch. Its existence was for a long time doubted until O'Sullivan[3] repeated and confirmed the previous experiments. According to him it crystallizes in fine acicular crystals, possesses a specific rotatory power of $+150°$ and a reducing power which is only one-third as great as that of dextrose. It seems probable that this is the chief sugar obtained by the action not only of diastase but of ptyalin and pancreatic ferment upon starch and perhaps also upon glycogen;[4] although some dextrose may at the same time be formed. Musculus and Gruber[5] have shown that maltose may also be formed by the action of dilute sulphuric acid on starch, and that it is capable of undergoing alcoholic fermentation.

Preparation.—See Musculus and Gruber (*loc. cit.*).

3. Milk-sugar.　$C_{12}H_{22}O_{11} + H_2O$.

Also known as *Lactose.* It is found in milk, and is characteristic of this secretion. It is said, however, to occur abnormally in the urine of lying-in women.[6]

It yields, when pure, hard colorless crystals, belonging to the rhombic system (four-sided prisms). It is less soluble in water than dextrose, requiring for solution six times its weight of cold, but only two parts of boiling, water; it is entirely insoluble in alcohol and ether. It is fully precipitated from its solutions by the addition of lead acetate and ammonia.

When freshly dissolved, its aqueous solution possesses a specific dextrorotatory power of $+93.1°$ for sodium light; this diminishes, slowly on standing, rapidly on boiling, until it finally remains constant at $+52.5°$. The amount of rotation is independent of the concentration of the solution.

Lactose unites readily with bases, forming unstable compounds; from its metallic compounds the metal is precipitated in the reduced state on boiling; it

[1] Lister, Path. Soc. Trans., Vol. for 1873, p. 425, also Quart. Jl. of Micros. Science, Vol. xviii. (1878) p. 177.

[2] Ann. Chim. Phys., (3) xxi. (1847) p. 178.

- Jl. Chem. Soc., Ser. 2, vol. x. (1872) p. 579.

[4] Musculus u. v. Mering, Zeitsch. f. physiol. Chem., Bd. ii. (1878) S. 403.

[5] Zeitschr. f. physiol. Chem., Bd. ii. (1878) S. 177.

[6] Hofmeister, Ibid. Bd. i. (1877) S. 101.

reduces copper salts as readily as dextrose but to a less extent, viz., in the ratio of 70 : 100.

Lactose is generally stated to admit of no direct alcoholic fermentation; this may, however, sometimes be induced by the prolonged action of yeast. By boiling with dilute mineral acids lactose is converted into galactose, which readily undergo alcoholic fermentation and possess a greater rotatory power than lactose.

It may be remarked here that though *isolated* lactose is incapable of direct alcoholic fermentation, milk itself may be fermented; Berthelot was unable in this direct alcoholic fermentation to detect any intermediate change of the lactose into any other fermentable sugar.

Lactose is, however, *directly* capable of undergoing the lactic and butyric fermentations; the circumstances and products are the same as in the case of dextrose (see above). The action is generally productive of a collateral small quantity of alcohol.

Lactose is thus distinguished from dextrose by its smaller solubility in water, insolubility in alcohol, crystalline form, lower cupric oxide reducing power, and its incapability of undergoing direct alcoholic fermentation.

Preparation.—After the removal of the casein and other proteids of the milk, the mother liquor is evaporated to the crystallizing point; the crystals are purified by repeated crystallization from warm water.

4. Inosit. $C_6H_{12}O_6 + 2H_2O$.

This substance occurs but sparingly in the human body; it was found originally by Scherer[1] in the muscles of the heart. Cloetta showed its presence in the lungs, kidneys, spleen, and liver,[2] and Müller in the brain.[3] It occurs, also, in diabetic urine, and in that of "Bright's disease," and is found in abundance in the vegetable kingdom.

Pure inosit forms large efflorescent crystals (rhombic tables); in microscopic preparations it is usually obtained in tufted lumps of fine crystals. Easily soluble in water, it is insoluble in alcohol and ether. It possesses no action on polarized light, and does not reduce solutions of metallic salts.

It admits of no direct alcoholic, but is capable of undergoing the lactic fermentation; according to Hilger,[4] the acid formed is sarcolactic. It is unaltered by heating with dilute mineral acids.

Preparation.—It may be precipitated from its solutions by the action of *basic* lead acetate and ammonia; the lead is then removed by sulphuretted hydrogen and the inosit precipitated with excess of alcohol.

As a special test (Scherer's), may be mentioned the production of a bright violet color by careful evaporation to dryness on platinum foil, with a little ammonia and calcium chloride.

5. Dextrin. $C_6H_{10}O_5$.

By boiling starch-paste with dilute acids, or by the action of ferments, the starch is converted into an isomeric body, to which, from its action on polarized light, the name dextrin has been given. It is soluble in water, but is precipitated by alcohol. It does not undergo alcoholic fermentation until after it has been changed into dextrose, nor can it reduce

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[1] Ann. d. Chem. u. Pharm., Bd. 73, S. 322.   [2] Ibid. Bd. 99, S. 289.
[3] Ibid. Bd. 103, S. 140.   [4] Ibid. Bd. 160, S. 333.

metallic salts. It yields a reddish port-wine color with iodine, which disappears on warming and does not return on cooling. Further action of acids or of ferments converts dextrin into dextrose. Dextrin is present in the contents of the alimentary canal after a meal containing starch, and has also been found in the blood.

There is not the least doubt that several modifications of dextrin exist and may be obtained by the action of acids and ferments on starch Of these, two of the best known are those described by Brücke[1] under the name of erythrodextrin and achroodextrin, the former giving a red color with iodine, the latter not yielding any color at all. Erythrodextrin may be readily converted into a sugar by the action of ferments, and thus is not found as a product of the complete action of ptyalin on starch. Achroodextrin, on the other hand, is not thus converted by ferments, and therefore remains in solution, together with the sugar formed by the action of ptyalin on starch. Achroodextrin may be converted into dextrose by boiling with dilute hydrochloric acid.

6. Glycogen. $C_6H_{10}O_5$.

Belongs to the starch division of carbohydrates. Discovered by Bernard in the liver and other organs (see p. 492).

Glycogen is, when pure, an amorphous powder, colorless, and tasteless, readily soluble in water, insoluble in alcohol and ether. Its aqueous solution is generally though not always strongly opalescent, but contains no particles visible microscopically; the opalescence is much reduced by the presence of free alkalies. The same solution possesses, according to Hoppe-Seyler, a very strong dextro-rotatory power, about three times as great as that of dextrose;[2] it dissolves hydrated cupric oxide; but this is not reduced on boiling.

By the action of dilute mineral acids (except nitric) it is partially converted into a form of sugar very closely resembling, though probably differing somewhat from true dextrose, and the same conversion is also readily effected by the action of amylolytic ferments. The sugar into which the glycogen of the liver is naturally converted after death (see p. 501) appears to be true dextrose;[3] so, also, the sugar of diabetes. The result of the action of diastase, or salivary or pancreatic ferment, upon glycogen is, however, according to Musculus and v. Mering,[4] a mixture of achroodextrin and maltose; the quantity of dextrose making its appearance at the same time being very small.

Opalescent solutions of glycogen usually become clear on the addition of caustic alkali; Vintschgau and Dietl[5] have shown that this is accompanied on boiling by a change which converts a portion of the glycogen into a substance to which they give the name of β.-glycogen-dextrine. (Kühne[6] had previously described a body to which he gave the name glycogen-dextrin. That described by Vintschgau and Dietl differs slightly from Kühne's body, hence the name.) According to these authors, one-fifth of the glycogen is at the same time changed into some

[1] Sitzber. d. Wien. Akad., 1872, iii. Abth. Also Vorlesungen 2. Aufl. 1875, Bd. i. S. 224.
[2] See Külz, Pflüger's Arch., Bd. xxiv. (1881) S. 85.
[3] Pflüger's Arch., Bd. xix. (1879) S. 106, and xxii. (1880) S. 206. Also Külz, Ibid. Bd. xxiv. (1881) S. 52.
[4] Zeitschr. f. physiol. Chem., Bd. ii. (1878) S. 403.
[5] Pflüger's Arch., Id. xvii. (1878) S. 154.
[6] Lehrb. d. physiol. Chem. (1868), S. 63.

other, at present undetermined, substance. Normal lead acetate gives a cloudiness, the basic salt a precipitate, in solutions of glycogen.

As tests for this body may be used the formation of a port-wine color with iodine; this disappears on warming, but returns on cooling. The same color is produced by the action of iodine on dextrin, but this does not reappear on cooling after its disappearance by warming.

Preparation of Glycogen.—The following is Brücke's[1] method. The filtered or simply strained decoction of perfectly fresh liver or other glycogenic tissue is, when cold, treated alternately with dilute hydrochloric acid, and a solution of the double iodide of potassium and mercury,[2] as long as any precipitate occurs. In the presence of free hydrochloric acid, the double iodide precipitates proteid matters so completely as to render their separation by filtration easy.. The proteids being thus got rid of, the glycogen is precipitated from the filtrate by adding alcohol to the extent of between 60 and 70 per cent. Too much alcohol is to be avoided, since other substances as well as glycogen are thereby precipitated. The glycogen is now washed with alcohol first of 60 and then of 95 per cent., afterwards with ether, and finally with absolute alcohol. It is then dried over sulphuric acid.

Tunicin. $(C_6H_{10}O_5)n.$

This body is regarded by many observers as identical with the true cellulose of plants, while others have ascribed to it properties differing from those of cellulose sufficiently to justify its receiving a distinct name. It appears to be more resistant to the action of chemical reagents than plant-cellulose.

It constitutes the chief part of the integument of the Ascidia or Tunicata. As prepared from this source, it is when pure quite white and usually retains the shape of the tissue. It is unacted upon by any reagent except strong acids and alkalies, and by the action of the former it yields some form of sugar.

FATS, THEIR DERIVATIVES AND ALLIES.

THE ACETIC ACID SERIES.

General formula, $C_n H_{2n} O_2$ (monobasic).

This, which is one of the most complete homologous series of organic chemistry, runs parallel to the series of monatomic alcohols. Thus formic acid corresponds to methyl alcohol, acetic acid to ethyl (ordinary) alcohol, and so on. The several acids may be regarded as being derived from their respective alcohols by simple oxidation: thus, ethyl alcohol yields by oxidation acetic acid: $C_2H_6O + O_2 = C_2H_4O_2 + H_2O.$ The various members differ in composition by CH_2, and the boiling points rise successively by about 19° C. Similar relations hold good with regard to their melting points and specific gravities. The acid properties are strongest in those where n has the least value. The lowest members of the series are volatile liquids, acting as powerful acids; these succes-

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[1] Sitzungsber. d. Wiener Akad., Bd. 63 (1871) ii. Abth.

This may be prepared by precipitating potassic iodide with mercuric chloride and dissolving the washed precipitate in a hot solution of potassic iodide as long as it continues to be taken up. On cooling, some amount of precipitate occurs, which must be filtered off; the filtrate is then ready for use.

sively become less and less fluid, and the highest members are colorless solids, closely resembling the neutral fats in outward appearance. Consecutive acids of the series present but very small differences of chemical and physical properties, hence the difficulty of separating them; this is further increased in the animal body by the fact that exactly those acids which present the greatest similarities usually occur together.

The free acids are found only in small and very variable quantities in various parts of the body; their derivatives, on the other hand, form most important constituents of the human frame, and will be considered further on.

Formic acid. CHO.OH.

When pure is a strongly corrosive, fuming fluid, with powerful irritating odor, solidifying at $0°$ C., boiling at $100°$ C., and capable of being mixed in all proportions with water and alcohol. It has been obtained from various parts of the body, such as the spleen, thymus, pancreas, muscles, brain, and bood; in the latter its presence may be due to the action of acids on the hæmoglobin. According to some authors,[1] it occurs also in urine.

Heated with sulphuric acid it yields carbonic oxide and water; with caustic potash it gives hydrogen and oxalic acid.

Acetic acid. $C_2H_3O.OH$.

It is distinguished by its characteristic odor; its boiling point is $117°$ C.; it solidifies at $5°$ and is fluid at all temperatures above $15°$ C. It is soluble in all proportions in alcohol and water.

It occurs in the stomach as the result of fermentative changes in the food, and is frequently present in diabetic urine. In other organs and fluids it exists only in minute traces.

With ferric chloride it yields a blood-red solution, decolorized by hydrochloric acid. (It differs in this last reaction from sulphocyanide of iron.) Heated with alcohol and sulphuric acid, the characteristic odor of acetic ether is obtained. It does not reduce silver nitrate.

Propionic acid. $C_3H_5O.OH$.

This acid closely resembles the preceding one. It possesses a very sour taste and pungent odor; is soluble in water, boils at $141°$ C., and may be separated from its aqueous solution by excess of calcic chloride.

It occurs in small quantities in sweat, in the contents of the stomach, and in diabetic urine when undergoing fermentation. It is similarly produced, mixed however with other products, during alcoholic fermentation, or by the decomposition of glycerine. It partially reduces silver nitrate solution on boiling.

Butyric acid. $C_4H_7O.OH$.

An oily colorless liquid, with an odor of rancid butter, soluble in water, alcohol, and ether, boiling at $162°$ C. Calcic chloride separates it from its aqueous solution.

Found in sweat, the contents of the large intestine, feces, and in urine. It occurs in traces in many other fluids, and is plentifully

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[1] Buliginsky, Hoppe-Seyler's Med. chem. Mittheilung., Heft. 2, S. 240. Thudichum, Journ. of the Chem. Soc., vol. 8, p. 400.

obtained when diabetic urine is mixed with powdered chalk and kept at a temperature of 35° C. It exists, as a neutral fat, in small quantities in milk.

This is the principal product of the second stage of lactic fermentation. (See Dextrose.)

Valerianic acid. $C_5H_9O.OH$.

An oily liquid, of penetrating odor and burning taste; soluble in 30 parts of water at 12° C., readily soluble in alcohol and ether. Boils at 175° C. Possesses, in free and combined form, a feeble right-handed rotation of the plane of polarization.

It is found in the solid excrements, and is formed readily by the decomposition, through putrefaction, of impure leucin, ammonia being at the same time evolved; hence its occurrence in urine when that fluid contains leucin, as in cases of acute atrophy of the liver.

Caproic acid.	$C_6H_{11}O.OH$.
Caprylic acid.	$C_8H_{15}O.OH$.
Capric (Rutic) **acid.**	$C_{10}H_{19}O.OH$.

These three occur together (as fats) in butter, and are contained in varying proportions in the feces from a meat diet. The first is an oily fluid, slightly soluble in water, the others are solids and scarcely soluble in water; they are soluble in all proportions in alcohol and ether. They may be prepared from butter, and separated by the varying solubilities of their barium salts.

Laurostearic acid.	$C_{12}H_{23}O.OH$.
Myristic acid.	$C_{14}H_{27}O.OH$.

These occur as neutral fats in spermaceti, in butter and other fats. They present no points of interest.

Palmitic acid.	$C_{16}H_{31}O.OH$.
Stearic acid.	$C_{18}H_{35}O.OH$.

These are solid, colorless when pure, tasteless, odorless, crystalline bodies, the former melting at 62° C., the latter at 69.2° C. In water they are quite insoluble; palmitic acid is more readily soluble in cold alcohol than stearic: both are readily dissolved by hot alcohol, ether, or chloroform. Glacial acetic acid dissolves them in large quantity, the solution being assisted by warming. They readily form soaps with the alkalies, also with many other metals. The varying solubilities of their barium salts afford the means of separating them when mixed:[1] this may also be applied to many others of the higher members of this series.

These acids in combination with glycerine (see below), together with the analogous compound of oleic acid, form the principal constituents of human fat. As salts of calcium they occur in the feces and in "adipocire," and probably in chyle, blood and serous fluids, as salts of sodium. They are found in the *free* state in decomposing pus, and in the caseous deposits of tuberculosis.

The existence of margaric acid, intermediate to the above two, is not now admitted, since Heintz[2] has shown that it is really a mixture of palmitic and stearic acids. Margaric acid possesses the anomalous melting point of 59.9° C. A mixture of 60 parts stearic and 40 of palmitic acids, melts at 60.3°.

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[1] Heintz, Annal. d. Phys. u. Chem., Bd. 92, S. 588.   [2] Op. cit.

ACIDS OF THE OLEIC (ACRYLIC) SERIES. $H(C_nH_{2n-3})O_2$ (monobasic).

Many acids of this series occur as glycerine compounds in various fats. They are very unstable, and readily absorb oxygen when exposed to the air. The higher members are decomposed on attempting to distil them. Their most peculiar property is that of being converted by traces of NO_2 into solid, stable, metameric acids, capable of being distilled. They bear an interesting relation to the acids of the acetic series, breaking up when heated with caustic potash into acetic acid and some other member of the same series, thus:

Oleic acid.   Potassic acetate. Potassic palmitate.

$$HC_{18}H_{33}O_2 \quad 2KHO = KC_2H_3O_2 + KC_{16}H_{31}O_2 + H_2.$$
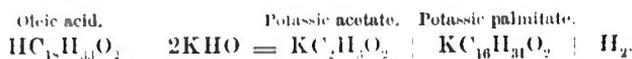
Oleic Acid. $C_{18}H_{33}O.OH.$

This is the only acid of the series which is physiologically important. It is found united with glycerin in all the fats of the human body.

When pure it is, at ordinary temperatures, a colorless, odorless, tasteless, oily liquid, solidifying at $4°C$ to a crystalline mass. Insoluble in water, it is soluble in alcohol and ether. It cannot be distilled without decomposition. It readily forms with potassium and sodium soaps, which are soluble in water; its compounds with most other bases are insoluble. It may be distinguished from the acids of the acetic series by its reaction with NO_3, and by the changes it undergoes when exposed to the air.

THE NEUTRAL FATS.

These may be considered as ethers formed by replacing the exchangeable atoms of hydrogen in the triatomic alcohol glycerin (see below), by the acid radicles of the acetic and oleic series. Since there are three such exchangeable atoms of hydrogen in glycerin, it is possible to form three classes of these ethers; only those, however, which belong to the third class occur as natural constituents of the human body; those of the first and second are of theoretical importance only.

They possess certain general characteristics. Insoluble in water and cold alcohol, they are readily soluble in hot alcohol, ether, chloroform, etc.; they also dissolve one another. They are neutral bodies, colorless, and tasteless, when pure; are not capable of being distilled without undergoing decomposition, and yield as a result of this decomposition, solid and liquid hydrocarbons, water, fatty acids, and a peculiar body, acrolein. (Glycerin contains the elements of one molecule of acrolein, and two molecules of water.)

They possess no action on polarized light.

They may readily be decomposed into glycerin and their respective fatty acids by the action of caustic alkalies, or of superheated steam.

Palmitin (Tri-palmitin). $\left.\begin{matrix}(C_3H_5)\\(C_{16}H_{36}O)_3\end{matrix}\right\}O_3.$

The following reaction for the formation of this fat is typical for all the others:

Glycerin.   Palmitic acid.   Palmitin.

$$\left.\begin{matrix}C_3H_5\\H_3\end{matrix}\right\}O_3+3\begin{matrix}C_{16}H_{31}O\\H\end{matrix}\right\}O=\left.\begin{matrix}C_3H_5\\(C_{16}H_{31}O)_3\end{matrix}\right\}O_2+3\begin{matrix}H\\H\end{matrix}\right\}O.$$
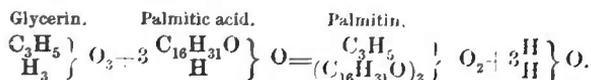
Palmitin is slightly soluble in cold alcohol, readily so in hot alcohol, or in ether; when pure, it crystallizes in fine needles; if mixed with

stearin, it generally forms shapeless lumps, although the mixture may at times assume a crystalline form, and was then regarded as a distinct body, namely, margarin. It possesses three different melting points, according to the previous temperatures to which it has been subjected. It solidifies in all cases at 45° C.

Preparation.—From palm oil, by removing the free palmitic acid with alcohol, and crystallizing repeatedly from ether.

Stearin (Tri-stearin). $\left. \begin{array}{c} C_3H_5 \\ (C_{18}H_{35}O)_3 \end{array} \right\} O_3.$
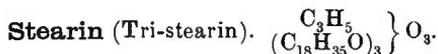
This is the hardest and least fusible of the ordinary fats of the body; is also the least soluble, and hence is the first to crystallize out from solutions of the mixed fats. It crystallizes usually in square tables. It presents peculiarities in its fusing points similar to those of palmitin.

Preparation.—From mutton suet, its separation from palmitin and olein being effected by repeated crystallization from ether, stearin being the least soluble.

Olein (Tri-olein). $\left. \begin{array}{c} (C_{18}H_{33}O)_3 \\ C_3H_5 \end{array} \right\} O_3.$
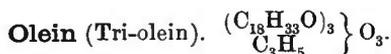
Is obtained with difficulty in the pure state, and is then fluid at ordinary temperatures. It is more soluble than the two preceding ones. It readily undergoes oxidation when exposed to the air, and is converted by mere traces of NO_2 into a solid isomeric fat. Olein yields, on dry distillation, a characteristic acid, the sebacic, and is saponified with much greater difficulty than are palmitin and stearin.

Preparation.—From olive oil, either by cooling to 0° C. and pressing out the olein that remains fluid; or by dissolving in alcohol and cooling, when the olein remains in solution while the other fats crystallize out.

Glycerin. $\left. \begin{array}{c} C_3H_5 \\ H_3 \end{array} \right\} O_3.$
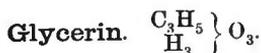
This principal constituent of the neutral fats may, as above stated, be looked upon as a triatomic alcohol.

When pure, glycerin is a viscid, colorless liquid, of a well-known sweet taste. It is soluble in water and alcohol in all proportions, insoluble in ether. Exposed to very low temperatures it becomes almost solid; it may be distilled in close vessels without decomposition, between 275°—280° C.

It dissolves the alkalies and alkaline earths, also many oxides, such as those of lead and copper; many of the fatty acids are also soluble in glycerin.

It possesses no rotatory power on polarized light.

It is easily recognized by its ready solubility in water and alcohol, its insolubility in ether, its sweet taste, and its reaction with bases. The production of acrolein is also characteristic of glycerin.

$$C_3H_8O_3 - 2H_2O = C_3H_4O \text{ (Acrolein)}.$$
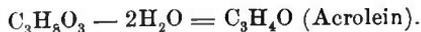
Preparation.—By saponification of the various oils and fats. It is also formed in small quantities during the alcoholic fermentation of sugar.[1]

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[1] Pasteur, Ann. d. Chem. u. Pharm., Bd. 106, S. 338.

Soaps. These may be formed by the action of caustic alkalies on fats. The process consists in a substitution of the alkali for the radicle of glycerin, the latter combining with the elements of water to form glycerin. Thus,

$$
\left.\begin{matrix}(C_{18}H_{35}O_2)_3\\ C_3H_5\end{matrix}\right\}O_3 + 3\left.\begin{matrix}K\\ H\end{matrix}\right\}O = 3\left.\begin{matrix}C_{18}H_{35}O\\ K\end{matrix}\right\}O + \left.\begin{matrix}C_3H_5\\ H_3\end{matrix}\right\}O_3.
$$

<div align="center">Tristearin.   Potassic stearate   Glycerin.</div>
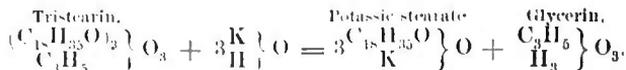
Pancreatic juice can split up fats into glycerin and free fatty acids (see p. 310), and the bile is known to be capable of saponifying those fatty acids. The amount of soaps formed in the alimentary canal is, however, small and unimportant.

ACIDS OF THE GLYCOLIC SERIES.

Running parallel to the monatomic alcohols ($C_n H_{2n} + _2O$) is the series of diatomic alcohols or glycols ($C_n H_{n} + _2O_2$). Thus corresponding to ethyl alcohol is the diatomic alcohol, ethyl-glycol. As from the monatomic alcohols, so from the glycols, acids may be derived by oxidation; from the latter (glycols), however, two series of acids can be obtained, known respectively as the glycolic and oxalic series. The first stage of oxidation of the glycol gives a member of the glycolic series, thus:

<div align="center">Ethyl-glycol.   Glycolic acid.</div>

$$C_2H_6O_2 + O_2 = C_2H_4O_3 + H_2O,\text{ or more generally}$$
$$C_n H_{2n} + _2O_2 + O_2 = C_n H_{2n} O_3 + H_2O.$$
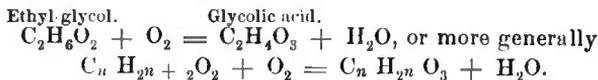
By further oxidation a member of the glycolic series can be converted into a member of the oxalic series, thus:

<div align="center">Glycolic acid.   Oxalic acid.</div>

$$C_2H_4O_3 + O_2 = C_2H_2O_4 + H_2O,\text{ or more generally}$$
$$C_n H_{2n} O_3 + O_2 = C_n H_{2n} - _2O_4 + H_2O.$$
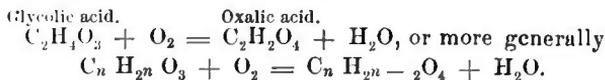
The acids of the glycolic series are diatomic but monobasic; those of the oxalic series are diatomic and diabasic.

The following table may be given to show the general relationships of alcohols and acids:

Radicle.	Alcohol.	Acid.	Glycols.	Acid I.	Acid II.
Methyl (CH_3)	$CH_3(OH)$	Formic. $HCHO_2$	"	Carbonic. H_2CO_3	"
Ethyl (C_2H_5)	$C_2H_5(OH)$	Acetic. $HC_2H_3O_2$	Ethyl-glycol $C_2H_4(OH)_2$	Glycolic. $HC_2H_2O_3$	Oxalic. $H_2C_2O_4$
Propyl (C_3H_7)	$C_3H_7(OH)$	Propionic. $HC_3H_5O_2$	Propyl-glycol $C_3H_6(OH)_2$	Lactic. $HC_3H_5O_3$	Malonic. $H_2C_3H_2O_4$
Butyl (C_4H_9)	$C_4H_9(OH)$	Butyric. $HC_4H_7O_2$	Butyl-glycol $C_4H_8(OH)_2$	Oxybutyric $HC_4H_7O_3$	Succinic. $H_2C_4H_4O_4$

GLYCOLIC ACID SERIES.

Lactic acid. $C_3H_6O_3$.

Next to carbonic acid, the most important member of this series, as far as physiology is concerned, is lactic acid.

Lactic acid exists in four isomeric modifications, but of these only

three have been found in the human body. These three all form sirupy, colorless fluids, soluble in all proportions in water, alcohol, and ether. They possess an intensely sour taste, and a strong acid reaction. When heated in solution they are partially distilled over in the escaping vapor. They form salts with metals, of which those with the alkalies are very soluble and crystallize with difficulty. The calcium and zinc salts are of the greatest importance, as will be seen later on.

1. **Ethylidene-lactic acid.** This is the ordinary form of the acid, obtained as the characteristic product of the well-known "lactic fermentation." It occurs in the contents of the stomach and intestines. According to Heintz[1] it is found also in muscles, and according to Gscheidlen[2] in the ganglionic cells of the gray substance of the brain. In many diseases it is found in urine, and exists to a large amount in this excretion after poisoning by phosphorus.[3]

It may he prepared hy the general methods of slowly oxidizing the corresponding glycol or hy acting or monochlorinated proprionic acid with moist silver oxide. In obtaining it from the products of lactic fermentation, the crusts of zinc lactate are purified hy several crystallizations, and the acid liberated from the compound hy the action of sulphuretted hydrogen.

2. **Ethylene-lactic acid.**—This acid is found accompanying the next to be described, in the watery extract of muscles. From this it is separated by taking advantage of the different solubilities in alcohol of the zinc salts of the two acids. It seems probable, however, that it has not yet been prepared in the pure state by this method.

Wislicenus first ohtained this acid hy heating hydroxycyanide of ethylene with aqueous solutions of the alkalies.[4]
The same observer found it in many pathological fluids.

3. **Sarcolactic acid.**—This acid has not yet been procured synthetically As its name implies, it is that form of the acid which chiefly occurs in muscles, and hence exists in large quantities in Liebig's "extract of meat." It is often found also in pathological fluids. This is the only acid of the series which possesses any power of rotating the plane of polarized light; it is otherwise indistinguishable from the preceding ethylidene-lactic acid, and is generally represented by the same formula. The free acid has dextro-, the anhydride lævo-rotatory action. The specific rotation for the zinc salt in solution is —7.65° for yellow light.
The zinc and calcium salts of sarcolactic acid are more soluble hoth in water and alcohol, than those of ethylidene-lactic acid, hut less so than those of ethylene-lactic acid, and the same salts of ethylene-lactic acid contain more water of crystallization than those of the other two.

Heintz[5] has compared the ahove acids to the modifications capahle of existing in tartaric acid.[6]

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[1] Ann. d. Chem. u. Pharm., Bd. 157, S. 320.
[2] Pflüger's Archiv, Bd. viii. (1873–74) S. 171.
[3] Schultzen and Riess, Ueher acute Phosphorvergiftung. Chem. Centralb., 1869, S. 681.
[4] Ann. d. Chem. u. Pharm., Bd. 128, S. 6.
[5] Op. cit.
[6] See further, Wislicenus, op. cit. Also Ann. d. Chem. u. Pharm., Bd. 166, S. 3, Bd. 167, S. 302, and Zeitschr. f. Chem., Bd. xiii. S. 159.

Hydracrylic acid, the fourth in this series of lactic acids, is distinguished by the nature of its decomposition on heating. It is never found as a constituent of animal bodies.

<center>OXALIC ACID SERIES.</center>

Oxalic acid. $H_2C_2O_4$.

In the free state this acid does not occur in the human body.[1]   Calcic oxalate, however, is a not unfrequent constituent of urine, and enters into the composition of many urinary calculi, the so-called mulberry calculus consisting almost entirely of it.   It may occur in feces, and in the gall-bladder, though this is rarely observed.

As ordinarily precipitated from solutions of calcic salts by ammonic oxalate, calcic oxalate is quite amorphous, but in urinary deposits it assumes a strong characteristic crystalline form, viz., that of rectangular octahedra.   In some cases it presents the anomalous forms of rounded lumps, dumb-bells, or square columns with pyramidal ends.   It is insoluble in water, alcohol, and ether, also in ammonia and acetic acid.   Mineral acids dissolve this salt readily, as also to a smaller extent do solutions of sodic phosphate or urate.   All the above characteristics serve to detect this salt; its microscopical appearance, however, is generally of most use for this purpose.

The pure acid is prepared either by oxidizing sugar with nitric acid, or decomposing ligneous tissue with caustic alkalies.

Succinic acid. $H_2C_4H_4O_4$.

This is the third acid of the oxalic series, being separated from oxalic acid by the intermediate malonic acid, $H_2C_3H_2O_4$.   It occurs in the spleen, the thymus, and thyroid bodies, hydrocephalic and hydrocele fluids.

According to Meissner and Shepard[1] it is found as a normal constituent of urine.   This is contested by Salkowski,[2] and also by von Speyer.   It seems probable, however, that since wines and fermented liquors contain succinic acid, and this latter passes unchanged into the urine, that it may thus be occasionally present in this excretion.

Succinic acid crystallizes in large rhombic tables, also at times in the form of large prisms; they are soluble in 5 parts of cold water, and 2.2 of boiling, slightly soluble in alcohol, and almost insoluble in ether. The crystals melt at 180° C., and boil at 235° C., being at the same time decomposed into the anhydride and water.   The alkali salts of this acid are soluble in water, insoluble in alcohol and ether.

Preparation.—Apart from the synthetic methods, it may readily be obtained by the fermentation of calcic malate, acetic acid being produced simultaneously.

Its presence is recognized by the microscopic examination of its crystals, and its characteristic reaction with normal lead acetate.   With this it gives a precipitate, easily soluble in excess of the precipitant, but coming down again on warming and shaking.[3]

---

[1] Untersuch. über d. Entsteh. d. Hippursäure.   Hannover, 1866.
[2] Pflüger's Archiv, Bd. ii. (1869) S. 367, and Bd. iv. (1871) S. 95.
[3] For further particulars see Meissner, op. cit., and Meissner and Soily, Zeitschr. f. rat. Med. (3) Bd. xxiv. S. 97.

CHOLESTERIN. $(C_{26}H_{44}O.)$

This is the only alcohol which occurs in the human body in the free state. (The triatomic alcohol glycerin is almost always found combined as in the fats; and cetyl-alcohol, or ethal, is obtained only from spermaceti.) It is a white crystalline body, crystallizing in fine needles from its solution in ether, chloroform, or benzol; from its hot alcoholic solutions it is deposited on cooling in rhombic tables. When dried it melts at 145°, and distils in closed vessels at 360° C. It is quite insoluble in water and cold alcohol; soluble in solutions of bile salts.

Solutions of cholesterin possess a left-handed rotatory action on polarized light, of —32° from yellow light, this being independent of concentration and of the nature of the solvent.

Heated with strong sulphuric acid it yields a hydrocarbon; with concentrated nitric it gives cholesteric acid and other products. It is capable of uniting with acids and forming compound ethers.

Cholesterin occurs in small quantities in the blood and many tissues, and is present in abundance in the white matter of the cerebro-spinal axis and in nerves. It is a constant constituent of bile, forming frequently nearly the whole mass of some gall-stones. It is found in many pathological fluids, hydrocele, the fluid of ovarial cysts, etc.

Preparation.—From gall-stones by simple extraction with boiling alcohol, and treatment with alcoholic potash to free from extraneous matter.

As tests for this substance may be given: With concentrated sulphuric acid and a little iodine a violet color is obtained, changing through green to red or blue. This is applicable to the microscopic crystals. After dissolving in chloroform a blood-red solution is formed on the addition of an equal volume of concentrated sulphuric acid; this solution if exposed to the air in an open dish turns blue, green, and finally yellow; the sulphuric acid under the chloroform has a green fluorescence. After evaporation to dryness with nitric acid, the residue turns red on treating with ammonia.

This body is described here rather for the sake of convenience than from its possessing any close relationship to the substances immediately preceding.

COMPLEX NITROGENOUS FATS.

Lecithin. $C_{44}H_{90}NPO_9$.

Occurs widely spread throughout the body. Blood, bile, and serous fluids contain it in small quantities, while it is a conspicuous component of the brain, nerves, yolk of egg, semen, pus, white blood-corpuscles, and the electrical organs of the ray.

When pure, it is a colorless, slightly crystalline substance, which can be kneaded, but often crumbles during the process. It is readily soluble in cold, exceedingly so in hot alcohol; ether dissolves it freely though in less quantities, as also do chloroform, fats, benzol, carbon disulphide, etc. It is often obtained from its alcoholic solution, by evaporation, in the form of oily drops. It swells up in water and in this state yields a flocculent precipitate with sodium chloride.

Lecithin is easily decomposed: not only does this decomposition set in at 70° C., but the solutions, if merely allowed to stand at the ordinary temperature, acquire an acid reaction, and the substance is decomposed. Acids and alkalies, of course, effect this much more rapidly. If heated

with baryta water it is completely decomposed, the products being neurin, glycerinphosphoric acid, and baric stearate. This may be thus represented :

Lecithin.		Stearic acid.	Glycerinphosphoric acid	Neurin.

$$C_{44}H_{90}NPO_9 + 3H_2O = 2C_{15}H_{36}O_2 + C_3H_9PO_6 + C_5H_{15}NO_2.$$
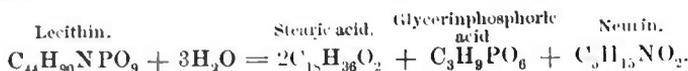
When treated in an ethereal solution with dilute sulphuric acid, it is merely split up into neurin and distearyl-glycerinphosphoric acid. Hence Diakonow[1] regards lecithin as the distearyl-glycerinphosphate of neurin, two atoms of hydrogen in the glycerinphosphoric acid being replaced by the radicle of stearic acid. It appears also that there probably exist other analogous compounds in which the radicles of oleic and palmitic acids take part.

Preparation.—Usually from the yolk of egg, where it occurs in union with vitellin. Its isolation is complicated, and the reader is referred to Hoppe-Seyler.[2]

Glycerinphosphoric acid. $C_3H_9PO_6$.

Occurs as a product of the decomposition of lecithin, and, hence, is found in those tissues and fluids in which this latter is present : in leukæmia the urine is said to contain this substance. It has not been obtained in the solid form. It has been produced synthetically by heating glycerin and glacial phosphoric acid ; it may be regarded as formed by the union of one molecule of glycerin with one of phosphoric acid, with elimination of one molecule of water. It is a dibasic acid ; its salts with barium and calcium are insoluble in alcohol, soluble in cold water. Solutions of its salts are precipitated by lead acetate.

Protagon. $(C_{160}H_{308}N_5PO_{35}?)$

A crystalline body, containing nitrogen and phosphorus, obtained by Liebreich[3] from the brain substance and regarded by him as its principal constituent. The researches of Hoppe-Seyler and Diakonow tended to show that protagon was merely a mixture of lecithin and cerebrin. A repetition of Liebreich's experiments has, however, led Gamgee and Blankenhorn[4] to confirm the truth of his results. Protagon appears to separate out from warm alcohol on gradual cooling in the form of very small needles, often arranged in groups ; it is slightly soluble in cold, more soluble in hot alcohol, and ether. It is insoluble in water, but swells up and forms a gelatinous mass. It melts at 200° C , and forms a brown sirupy fluid.

Preparation.—Finely divided brain substance, freed from blood and connective tissue, is digested at 45° C. with alcohol (85 per cent.) as long as the alcohol extracts anything from it. The protagon which separates out from the filtrate is well washed with ether to get rid of all cholesterin and other bodies soluble in ether, and finally purified by repeated crystallization from warm alcohol.

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[1] Hoppe-Seyler's Med. Chem. Untersuch., Heft ii. (1867) S. 221, Heft iii. (1868) S. 405. Centralb. f. d. med. Wiss., (1868) Nr. 1. 7 u. 28.

[2] Med. Chem. Untersnch., Heft ii. (1867) S. 215.

[3] Ann. d. Chem. u. Pharm., Bd. 134, S. 29.

[4] Zeitschr. f. physiol. Chem., Bd. iii. (1879) S. 260, and Jl. of Physiol., vol. ii. (1879) p. 113.

Neurin (Cholin). $C_5H_{15}NO_2$.

Discovered by Strecker[1] in pig's-gall, then in ox-gall. It does not occur in the free state except as a product of the decomposition of lecithin. It is a colorless fluid, of oily consistence, possesses a strong alkaline reaction, and forms with acids very deliquescent salts. The salts with hydrochloric acid and the chlorides of platinum and gold are the most important.

Neurin is a most unstable body, mere heating of its aqueous solution sufficing to split it up into glycol, trimethylamin, and ethylene oxide.

Preparation.—From yolk of egg. For this see Diakonow.[2]

Wurtz[3] has obtained it synthetically, first by the action of glycol hydrochloride on trimethylamin, and then by that of ethylene oxide and water on the same substance. The above, together with the mode of its decomposition, point to the idea that neurin may be regarded as trimethyl-oxy.ethyl-ammonium, hydrate, $N(CH_3)_3(C_2H_5O)OH$.

Cerebrin. $C_{17}H_{33}NO_3$ (?).

Is found in the axis cylinder of nerves, in pus corpuscles, and largely in the brain. In former times many names were given to the substance when in an impure state—*ex. gr.*, cerebric acid, cerebrote, etc. W. Müller[4] first prepared it in the pure form, and constructed the above formula from his analysis; the mean of these is, O 15.85, H 11.2, N 4.5, C 68.45. Great doubts are, however, thrown upon its purity by the researches of later observers. According to Liebreich[5] and Diakonow,[6] it is a glucoside.[7]

Cerebrin is a light, colorless, exceedingly hygroscopic powder, which swells up strongly in water, slowly in the cold, rapidly on heating. When heated to 80° C., it turns brown, and at a somewhat higher temperature melts, bubbles up, and finally burns away. It is insoluble in cold alcohol, or ether; warm alcohol dissolves it easily. Heated with dilute mineral acids, cerebrin yields a sugar-like body, possessing left-handed rotation, but incapable of fermentation.

Preparation.—For this see W. Müller.[8]

NITROGENOUS METABOLITES.

THE UREA GROUP, AMIDES, AND SIMILAR BODIES.

Urea. $(NH_2)_2CO$.

The chief constituent of normal urine in mammalia, and some other animals; the urine of birds also contains a small amount. Normal blood, serous fluids, lymph, and the liver, all contain the same body in traces. It is not found in the muscles, as a normal constituent, but may make its appearance there under certain pathological conditions.

[1] Ann. d. Chem. u. Pharm., Bd. 123, S. 353, Bd. 148, S. 76.
[2] Op. cit. (sub. Lecithin).
[3] Ann. d. Chem. u. Pharm., Sup. Bd. 6, S. 116 u. 127.
[4] Ann. d. Chem. u. Pharm., Bd. 105, S. 361.
[5] Arch. f. pathol. Anat., Bd. 39 (1867).
[6] Centralb. f, d. med. Wiss., 1868, Nr. 7.
[7] See also, Geogheghan, Zeitsch. f. physiol, Chem., Bd. iii. (1879) S. 332.
[8] Op. cit.

When pure. it crystallizes from a concentrated solution in the form of long, thin, glittering needles. If deposited slowly from dilute solutions, the form is that of four-sided prisms with pyramidal ends; these are always anhydrous. It possesses a somewhat bitter cooling taste, like saltpetre. It is readily soluble in water and alcohol, the solutions being neutral. In anhydrous ether it is insoluble. The crystals may be heated to 120° C. without being decomposed; at a higher temperature they are first liquefied and then decompose, leaving no residue. Heated with strong acids or alkalies, decomposition ensues, the final products being carbonic anhydride and ammonia. The same decomposition may also occur as the result of the action of a specific ferment on urea in an aqueous solution.[1] Nitrous acid at once decomposes it into carbonic anhydride and free nitrogen. It readily forms compounds with acids and bases; of these the following are of importance.

Nitrate of urea. $(NH_2)_2CO.HNO_3$.

Crystallizes in six-sided or rhombic tables. Insoluble in ether and nitric acid, soluble in water, slightly soluble in alcohol.

Oxalate of urea. $[(NH_2)_2CO]_2.H_2C_2O_4 + H_2O$.

Often crystallizes in long thin prisms, but under the microscope is obtained in a form closely resembling the nitrate; it is slightly soluble in water, less so in alcohol.

With mercuric nitrate urea yields three salts, containing, respectively, 4, 3, and 2 equivalents of mercuric oxide to one of urea. The first is the precipitate formed in Liebig's quantitative determination of urea, and may be represented by the formula $2N_2H_4CO.Hg(NO_3)_2 3HgO$. The exact constitution of these salts has not yet been determined.

Preparation.—Ammonic sulphate and potassic cyanate are mixed together in aqueous solution, and the mixture is evaporated to dryness. The residue when extracted with absolute alcohol yields urea. From urine, either by evaporating to dryness, having previously precipitated the urine with normal and basic lead acetate in succession, and removed the lead by sulphuretted hydrogen, and then extracting with alcohol; or concentrating only to a syrup, and then forming the nitrate of urea; this is washed with *pure* nitric acid and decomposed with baric carbonate.

Detection in Solutions.—In addition to the microscopic appearance of the crystals obtained on evaporation, the nitrate and oxalate should be formed and examined. Another part should give a precipitate with mercuric nitrate, in the absence of sodic chloride, but not in the presence of this last salt in excess. A third portion is treated with nitric acid containing nitrous fumes; if urea is present, nitrogen and carbonic anhydride will be obtained. To a fourth part nitric acid in excess and a little mercury are added, and the mixture is warmed. In presence of urea a *colorless* mixture of gases (N and CO_2) is given off. A fifth portion is kept melted for some time, dissolved in water, and cupric sulphate and caustic soda are added: a red or violet color, due to biuret, is developed.

[1] Musculus, Pflüger's Archiv, Bd. xii. (1876) S. 214. Jaksch. Zeitsch. f. physiol. Chem., Bd. v. (1881) S. 395.

Quantitative Determination.—For this some special manual must be consulted.[1] It will suffice here to point out that the determination is made either with a solution of mercuric nitrate of known strength (Liebig); by decomposing the urea by means of sodic hypobromite into nitrogen, carbonic anhydride and water, and measuring the nitrogen (Knop) [$N_2H_4CO + 3NaBrO = 3NaBr + CO_2 + 2H_2O + N_2$], or by heating the urea with caustic baryta in a sealed tube, the urea being determined by the weight of baric carbonate formed (Bunsen)

Urea is generally considered to be an amide of carbonic acid—*i. e.*, carbamide. The amide of an acid is formed when water is removed from the ammonium salt of the acid; if the acid be dibasic and two molecules of water be removed, the result is often spoken of as a diamide. Thus, if from ammonic carbonate, $(NH_4)_2CO_3$, two molecules of water, $2H_2O$, be removed, carbonic acid being a dibasic acid, the result is urea ; thus :

$$(NH_4)_2CO_3 - 2H_2O = (NH_2)_2CO,$$

which may be written either according to the ammonia type as

$$\left.\begin{matrix} CO \\ H_2 \\ H_2 \end{matrix}\right\} N_2 \quad \text{or as} \quad CO \left\{ \begin{matrix} NH_2 \\ NH_2 \end{matrix}\right.$$
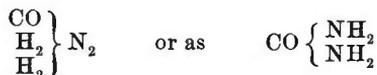
two atoms of amidogen (NH_2) being substituted for two atoms of hydroxyl (HO).

This connection between carbonic acid and urea is shown by the fact that ammonic carbonate may be formed out of urea by hydration, as when urea is subjected to the specific ferment mentioned above. Regarded then as a diamide of carbonic acid, urea may be spoken of as carbamide. But the theoretical derivation of urea from ammonic carbonate by dehydration cannot be realized in practice, whereas urea can readily be formed from ammonic carbamate, and Kolbe is inclined to regard it, not as the diamide of carbonic acid, but as the amide of carbamic acid. Ammonium carbamate, $CO_2N_2H_6$ *minus* H_2O, gives urea, CO,N_2,H_4— which, if carbamic acid be written as CO,OH,NH_2, may be written as CO,NH_2,NH_2, *one* atom of amidogen being substituted for *one* atom of hydroxyl, and not two, as when the substance is regarded as derived from carbonic acid. Drechsel's[2] experiments indicate a ready derivation of urea from ammonic carbamate. He has obtained urea by the electrolysis of a solution of this salt with rapidly alternating currents, thus removing the elements of water from the carbamate by such alternating processes of oxidation and reduction as may be supposed to take place in the body. The reaction is expressed as follows :

i. $NH_2.CO.O.NH_4 + O = NH_2.CO.O.NH_2 + H_2O.$
ii. $NH_2.CO.ONH_2 + H_2 = NH_2.CO.NH_2 + H_2O.$
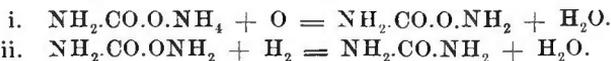
Wanklyn and Gamgee,[3] however, since urea when heated with a large excess of potassic permanganate gives off all its nitrogen in a free state, and not in the oxidized form of nitric acid, as do all other amides, conclude that it is not an amide at all, that it is isomeric only and not identical with carbamide.

It is important to remember that urea is also isomeric with ammonic cyanate, $C\left\{\begin{matrix} N \\ ONH_4, \end{matrix}\right.$ and, indeed, was first formed artificially by Wöhler

1 Neubauer and Vogel, Analyse des Harns., viii. Aufl. 1881, S. 264.
2 Arch. f. Physiol., 1880, S. 550.   3 Journ. Chem. Soc. 2, vol. vi. p. 25.

(1828) from this body. We thus have three isomeric compounds, ammonium cyanate, urea, and carbamide, related to each other in such a way that urea may be obtained readily either from ammonium cyanate or from ammonic carbamate, and may with the greatest ease be converted into ammonic carbonate.[1] Now urea is a much more stable body than ammonic cyanate, and in the transformation of the latter into the former, energy is set free; and it is worthy of notice that though the presence of sulphocyanides in the saliva probably indicates the existence of cyanic residues in the body, the nitrogenous products of the decomposition of proteids belong chiefly to the class of amides, cyanogen compounds being rare among them. Pflüger[2] has called attention to the great molecular energy of the cyanogen compounds, and has suggested that the functional metabolism of protoplasm by which energy is set free, may be compared to the conversion of the energetic unstable cyanogen compounds into the less energetic and more stable amides. In other words, ammonium cyanate is a type of living, and urea of dead nitrogen, and the conversion of the former into the latter is an image of the essential change which takes place when a living proteid dies.

Compound Ureas.—The hydrogen atoms of urea can be replaced by alcohol and acid radicles. The results are compound ureas or ureides when the hydrogen is replaced by an acid radicle. Many of them are called acids, since the hydrogen from the amide group, if not all replaced as above, can be replaced by a metal. Thus the substitution of oxalyl (oxalic acid) gives parabanic acid,

$$N_2 \begin{cases} CO \\ H_2 \\ C_2O_2 \end{cases} \text{ or } CO, NH_2, N . C_2O \; ;$$
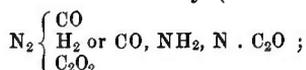
of tartronyl (tartronic acid), dialuric acid, $CO, N_2I_2, N.C_3H_2O_3$; of mesoxalyl (mesoxalic acid), alloxan, $CO, NH_2, N . C_3O_3$. These bodies are interesting as being also obtained by the artificial oxidation of uric acid. (See below.)

Uric acid. $C_5H_4N_4O_3$.

The chief constituent of the urine in birds and reptiles; it occurs only sparingly in this excretion in man and most mammalia. It is normally present in the spleen, and traces of it have been found in the lungs, muscles of the heart, pancreas, brain, and liver. Urinary and renal calculi often consist largely of this body, or its salts. In gout, accumulations of uric acid salts may occur in various parts of the body, forming the so-called gouty concretions.

It is when pure a colorless, crystalline powder, tasteless, and without odor. The crystalline form is very variable, but usually tends towards that of rhombic tables.[3] When impure it crystallizes readily, but then possesses a yellowish or brownish color. In water it is very insoluble (1 in 14,000 or 15,000 of cold water); ether and alcohol do not dissolve it appreciably. On the other hand, sulphuric acid takes it up without

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[1] The following literature is interesting in connection with the question of the cyanic or amide origin of urea. Drechsel: Ber. d. k. s. Gesell. d. Wiss. Leipzig: Sitz. 25, Juli. 1875; Arch. f. Physiol., 1880, S. 550. V. Knieriem: Zt. f. Biol., Bd. x. (1874) S. 263. Munk: Zt. f. physiol. Chem., Bd. ii. (1878) S. 29. E. Salkowski: Centralb. f. d. med. Wiss., 1875, No. 58; Ber. d. deutsch. Chem. Gesell., 1875, S. 116; Zeitsch. f. physiol. Chem., Bd. i. (1877), Sn. 1. u. 374; Bd. iv. (1880) Sn. 54, u. 103. Schmiedeberg: Arch. f. exp. Pathol., Bd. viii. (1877) S. 1.

[2] Pflüger's Archiv, Bd. x. (1875) S. 337.

[3] See Ültzmann and K. B. Hoffmann, Atlas der Harnsedimente, Wien, 1872.

decomposition, and it is also readily soluble in many salts of the alkalies, as in the alkalies themselves. Ammonia, however, scarcely dissolves it.

Salts of Uric Acid.—Of these, the most important are the acid urates of sodium, potassium, and ammonium. The sodium salt crystallizes in many different forms, these not being characteristic, since they are almost the same for the corresponding compounds of the other two bases. It is very insoluble in cold water (1 in 1100 or 1200), more soluble in hot (1 in 125). It is the principal constituent of several forms of urinary sediment, and composes a large part of many calculi; the excrement of snakes contains it largely. The potassium resembles the sodium salt very closely, as also does the compound with ammonium; the latter occurs generally in the sediment from alkaline urine.

Preparation.—Usually from guano, or snake's excrement. From guano by boiling with caustic potash (1 part alkali to 20 of water) as long as ammonia is evolved. In the filtrate a precipitate of acid urate of potassium is formed by passing a current of carbonic anhydride; this salt is then washed, dissolved in a caustic potash and decomposed by carefully pouring its solution into an excess of hydrochloric acid.

The presence of uric acid is recognized by the following tests. The substance having been examined microscopically, a portion is evaporated *carefully* to dryness with one or two drops of nitric acid. The residue will, if uric acid is present, be of a red color, which, on the addition of ammonia, turns to purple. This is the murexide test, and depends on the presence of alloxan and alloxantin in the residue. Schiff[1] has given a delicate reaction for uric acid. The substance is dissolved in sodic carbonate, and dropped on paper moistened with a silver salt. If uric acid be present, a brown stain is formed, due to the reduction of the carbonate of silver. An alkaline solution of uric acid can, like dextrose, reduce cupric sulphate, with precipitation of the cuprous oxide.

Uric acid resists very largely the action of even strong acids and alkalies, exhibiting in this respect a marked difference from urea. It might, therefore, perhaps be supposed that urea residues do not preëxist in uric acid; nevertheless, by oxidation, uric acid does give rise, not only to ordinary urea, but also, and at the same time, to the compound ureas (ureides) spoken of above. Thus by oxidation with acids,

<div align="center">

Uric acid.   Alloxan.   Urea.

$$C_5H_4N_4O_3 + H_2O + O = C_4N_2H_2O_4 + CN_2H_4O.$$

</div>
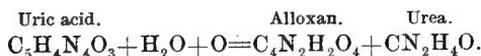
Now alloxan, as was stated above, is a compound urea, viz , mesoxalylurea, and by hydration can be converted into mesoxalic acid and urea, thus :

<div align="center">

Alloxan.   Mesoxalic acid. Urea.

$$C_4N_2H_2O_4 + 2H_2O = C_2H_2O_5 + CN_2H_4O ;$$

</div>
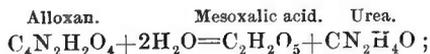
and by the action of chlorine uric acid can be split up directly into a molecule of mesoxalic acid and two molecules of urea :

<div align="center">

Uric acid.   Mesoxalic acid. Urea.

$$C_5H_4N_4O_3 + Cl_2 + 4H_2O = C_3H_2O_5 + 2CN_2H_4OC + 2HCl.$$

</div>
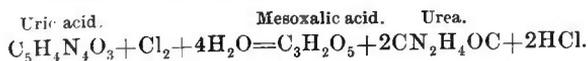
[1] Ann. d. Chem. u. Pharm., Bd. 109, S. 65.

By oxidation with alkalies, uric acid is converted into allantoin and carbonic acid,

Uric acid.   Allantoin.

$$C_5H_4N_4O_3 + H_2O + O = C_4H_6N_4O_3 + CO_2;$$
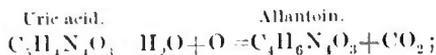
and allantoin, by hydration, becomes allanturic or lantanuric acid and urea,

Allantoin.   Urea.   Allanturic acid.

$$C_4H_6N_4O_3 + H_2O = CH_4N_2O + C_3H_4N_2O.$$

Now allanturic acid is a compound urea, with a residue of glyoxylic acid. By other oxidations of uric acid, parabanic acid (oxalyl-urea), oxaluric acid (which is hydrated parabanic acid), and dialuric acid (tartronyl-urea) are obtained. In fact, all these decompositions of a molecule of uric acid lead to the production of urea and of a carbon acid of some kind or other. The relation of uric acid to urea as illustrated by the above reactions is brought very prominently into view by the synthesis of uric acid which has recently been performed.[1] It is obtained by simply fusing together glycocine (amido-acetic acid) and urea at a temperature of 200°–230° C. The converse formation of glycocine from uric acid with the simultaneous production of ammonia and carbonic anhydride has been known for some time. Since in this latter reaction the ammonia and carbonic anhydride are in the proportions in which they would be obtained from cyanic or cyanuric acid, uric acid has been regarded as built up from residues of cyanuric acid and glycin, just as hippuric acid is formed from glycin and benzoic acid. It was also at one time supposed that uric acid might be regarded as tartronyl cyanamide.

$$N_2 \begin{cases} C_3H_2O_3 \\ (CN)_2 \\ H_2 \end{cases}$$
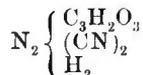
If the existence of some cyanogen residue is thus assumed in the molecule of uric acid, then it must be supposed that before urea can be obtained from it a molecular change takes place by which a portion at least of the nitrogen of the uric acid is converted into the same condition as the rest of the nitrogen, viz., into the amide state.

If this be so, since the metabolism of the animals in which uric acid replaces urea cannot be supposed to be fundamentally different from that of the urea-producing animals, we may infer that the antecedent of both uric acid and urea in the regressive metabolism of proteids is, as we suggested above, a body containing some at least of its nitrogen in the form of cyanogen.[2]

Kreatin. $C_4H_9N_3O_2$.

Occurs as a constant constituent of the juices of muscles, though possibly it may be formed during the process of extraction by the hydration of kreatinin. Kreatin is not a normal constituent of urine, but it is said to occur in traces in several fluids of the body. When found in urine its presence is probably due to the conversion of kreatinin, a constant constituent of urine, into kreatin during its extraction, since Dessaignes[3] has shown that the more rapidly the separation is effected, the less is the quantity of kreatin obtained, and the greater the amount of kreatinin.

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[1] Horbaczewski, Ber. d. deutsch. chem. Gesell. Jahrg. 1882, S. 2678.
   See V. Knieriem, Zeitsch. f. Biol.. Bd. xiii. (1877) S. 36. Schröder, Zeitsch. f. Physiol. Chem., Bd. ii. (1878) S. 228.
[3] J. Pharm. (3) Bd. xxxii. S. 41.

In the anhydrous form it is white and opaque, but crystallizes with one molecule of water in colorless transparent rhombic prisms. It possesses a somewhat bitter taste, is soluble in cold, extremely soluble in hot water, is less soluble in absolute than in dilute alcohol, and is soluble in ether.

It is a very weak base, scarcely neutralizing the weakest acids. It forms crystalline compounds with sulphuric, hydrochloric, and nitric acids.

Preparation.—From extract of muscle by precipitating completely with basic lead acetate, and crystallizing out the kreatin, mixed with kreatinin. From this latter it is separated by the formation of the zinc-salt of kreatinin, kreatin not readily yielding a similar compound.

Kreatin may he converted into kreatinin under the influence of acids, the transformation heing one of simple dehydration.

Kreatin may be decomposed into sarcosin (methyl-glycin) and urea :

$$C_4H_9N_3O_2 + H_2O = C_3H_7NO_2 + CH_4N_2O ;$$
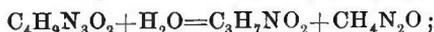
it may be formed synthetically[1] by the action of sarcosin and cyanamide :

$$C_3H_7NO_2 + CH_2N_2 = C_4H_9N_3O.$$

Sarcosin is glycin in which one atom of hydrogen has been replaced by the alcohol radicle methyl, thus :

$$\text{Glycin} \left. \begin{matrix} C_2H_3O \\ NH_2 \end{matrix} \right\} O \text{ becomes } \left. \begin{matrix} C_2H_2(CH_3)O \\ NH_2 \end{matrix} \right\} O ;$$
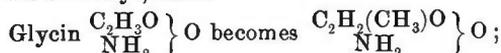
like glycin, sarcosin has not been found in a free state in the body.

Kreatinin. $C_4H_7N_3O.$

This, which is simply a dehydrated form of kreatin, occurs normally as a constant constituent of urine and of muscle extract. It crystallizes in colorless shining prisms, possessing a strong alkaline taste and reaction. It is readily soluble in cold water (1 in 11.5), also in alcohol, but is scarcely soluble in ether. It acts as a powerful base, forming with acids and salts compounds which crystallize well. Of these the most important is the salt with zinc chloride $(C_4H_7N_3O)_2ZnCl_2$. It is formed when a concentrated solution of the chloride is added to a not too dilute solution of kreatinin. Since the compound is very little soluble in alcohol, it is better to use alcoholic rather than aqueous solutions. It crystallizes in warty lumps composed of aggregated masses of prisms, or fine nedles.

Preparation.—Either by the action of acids or kreatin, or from human urine by concentrating, and precipitating with lead acetate; in the filtrate from this, a second precipitate is caused by the addition of mercuric chloride, and consists of a compound of this salt with kreatinin. The mercury is removed by sulphuretted hydrogen, and the kreatinin purified by the formation of the zinc salt, and washing with alcohol.

Kreatin-zinc chloride may be converted into kreatin, by the action of hydrated oxide of lead on its boiling aqueous solution.

Allantoin. $C_4H_6N_4O_3.$

The characteristic constituent of the allantoic fluid of the fœtus ; it occurs also in the urine of animals for a short period after their birth. Traces of it are sometimes detected in this excretion at a later period.

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[1] Sitzungsher. d. hayersch. Akad. 1868, Hft. 3, S. 472.

It crystallizes in small, shining, colorless prisms, which are tasteless and odorless. They are soluble in 160 parts of cold, more soluble in hot water, insoluble in cold alcohol and ether, soluble in hot alcohol. Carbonates of the alkalies dissolve them, and compounds may be formed of allantoin with metals but not with acids.

Allantoin, as already stated, is one of the products of the oxidation of uric acid, and by further oxidation gives rise to urea.

Preparation.—This is best carried out by the careful oxidation of uric acid either by means of potassic permanganate or ferrocyanide, or by plumbic oxide.

Hypoxanthin or Sarkin. $C_5H_4N_4O$.

Is a normal constituent of muscles, occurring also in the spleen, liver, and medulla of bones. In leukæmia it appears in the blood and urine. It crystallizes in fine needles which are soluble in 300 parts of cold, more soluble in hot water, insoluble in alcohol, soluble in acids and alkalies. It forms crystalline compounds with acids and bases. It is precipitated by basic acetate of lead, the precipitate being soluble in a solution of the normal acetate. Its preparation from muscle extract depends on its precipitation first by basic acetate of lead, and then by an ammoniacal solution of silver nitrate after the removal of kreatin.

Both hypoxanthin and the next body, xanthin, can also be obtained from proteids by the action of putrefactive changes, of water at boiling temperature, of dilute hydrochloric acid (0.2 per cent.) at 40° C., and by the action of gastric and pancreatic ferments.[1] Chittenden has noticed a peculiar difference between fibrin and egg-albumin when submitted to the above processes; he finds that the latter does not yield hypoxanthin when treated with boiling water, with dilute hydrochloric acid, or gastric ferment, while the former does. Egg-albumin on the other hand yields hypoxanthin by the action of pancreatic ferment in alkaline solution but not so readily as fibrin does.

Xanthin. $C_5H_4N_4O_2$.

First discovered in a urinary calculus, and called xanthic oxide. More recently it has been found as a normal, though scanty, constituent of urine, muscles, and several organs, such as the liver spleen, thymus, etc.

When precipitated by cooling from its hot, saturated, aqueous solution it falls in white flocks, but if the solution be allowed to evaporate slowly it is obtained in small scales. When pure it is a colorless powder, very insoluble in water, requiring 1500 times its bulk for solution at 100° C. Insoluble in alcohol and ether, it readily dissolves in dilute acids and alkalies, forming crystallizable compounds.

Hypoxanthin by oxidation becomes xanthin. Both these bodies, as well as the following, guanin and carnin, are evidently closely allied to uric acid; indeed, uric acid by the action of sodium-amalgam may be converted into a mixture of xanthin and hypoxanthin.

Preparation.—It is obtained from urine and the aqueous extract of muscle by a process similar to that for hypoxanthin, and is then

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[1] Salomon, Zeitschr. f. physiol. Chem., Bd. ii. (1878–1879) S. 60. Krause, Inaug. Diss., Berlin, 1878. Chittenden, Journ. of Physiol., vol. ii. (1879) p. 28. See also Drechsel, Ber. d. deutsch. Chem. Gesell. Jahrg. xiii. (1880) S. 240. Salomon, Ibid. S. 1160. Kossel, Zeitsch. f. physiol. Chem., Bd. v. (1881) Sn. 152 u. 267.

separated from the latter by the action of dilute hydrochloric acid; this separation depends on the different solubilities of the hydrochlorides of the two bodies. For further information, see Neubauer and Vogel.[1]

Carnin. $C_7H_8N_4O_3$.

Discovered by Weidel[2] in extract of meat, of which it constitutes about one per cent.

It crystallizes in white masses composed of very small, irregular crystals; it is soluble with difficulty in cold, more easily soluble in hot water, insoluble in alcohol and ether. Its aqueous solution is not precipitated by normal lead acetate, but is by the basic acetate of this metal. It unites with acids and salts forming crystalline compounds.

Preparation.—Is found in the precipitate caused in extract of meat by basic acetate of lead.[3]

This body possesses an interesting relation to hypoxanthin, into which it may be converted by the action either of nitric acid or, still better, of bromine.

Guanin. $C_5H_5N_5O$.

First obtained from guano, but recently observed as occurring in small quantities in the pancreas, liver, and muscle extract.

It is a white amorphous powder, insoluble in water, alcohol, ether, and ammonia. It unites with acids, alkalies, and salts to form crystallizable compounds.

Preparation.—From guano by boiling successively with milk of lime and caustic soda, precipitating with acetic acid, and purifying by solution in hydrochloric acid and precipitation by ammonia.

Guanin may, by the action of nitrous acid, be converted into xanthin. By oxidation it can be made to yield principally guanidine and parabanic acid, accompanied, however, by small quantities of urea, xanthin, and oxalic acid. Capranica has given several reactions characteristic of this body.[4]

Its separation from hypoxanthin and xanthin depends on its insolubility in water and behavior with hydrochloric acid.

Kynurenic acid. $C_{20}H_{14}N_2O_6+2H_2O$.

Found in the urine of dogs, and first described by Liebig.[5] When pure, it crystallizes in brilliant white needles, insoluble in cold, soluble in hot alcohol. The only salt of this body which crystallizes well is that formed with barium. For preparation and other particulars, see Liebig[6] and Schultzen and Schmiedeberg.[7]

Glycin. $C_2H_2(NH_2)O(OH)$. Also called Glycocoll and Glycocine.

Does not occur in a free state in the human body, but enters into the composition of many important substances, *ex. gr.*, hippuric and bile acids. It crystallizes in large, colorless, hard rhombohedra, which are

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1 Harn. Analyse, Ed. viii. (1881) S. 26. Also the literature quoted above on hypoxanthin.

2 Ann. d. Chem. u. Pharm., Bd. 158, S. 365.

3 See Weidel, op. cit.

4 Zeitsch. f. physiol. Chem., Bd. iv. (1880) S. 240.

5 Ann. d. Chem. u. Pharm., Bd. 86, S. 125, and Bd. 108, S. 354.

6 Op. cit. 7 Ann. d. Chem. u. Pharm., Bd. 164, S. 155.

easily soluble in water, insoluble in cold, slightly soluble in hot alcohol, insoluble in ether. It possesses an acid reaction, but a sweet taste. It has also the property of uniting with both acids and bases, to form crystallizable compounds. In this it exhibits its amide nature, and that it is an amide is rendered evident from the methods of its synthetic preparation; thus, mono-chlor-acetic acid and ammonia give glycin and ammonic chloride: $C_2H_3ClO_2 \quad 2NH_3 = C_2H_2(NH_2)O(OH) + NH_4Cl$. It is amido-acetic acid. Heated with caustic baryta it yields ammonia and methylamine.

Preparation.—From glutin by the action of acids or alkalies; from hippuric acid by decomposing it with hydrochloric acid at a boiling temperature and removing by precipitation the simultaneously formed benzoic acid.

Taurin. $C_2H_7NO_3S$.

In addition to entering into the composition of taurocholic acid (see p. 888), taurin is found in traces in the juices of muscle and in the lungs.

It crystallizes in colorless, regular, six-sided prisms; these are readily soluble in water, less so in alcohol. The solutions are neutral. It is a very stable compound, resisting temperatures of less than 240° C.; it is not acted on by dilute alkalies and acids, even when boiled with them. It is not precipitated by metallic salts.

Taurin is amido-isethionic acid; and may be synthetically prepared from isethionic (ethyl-sulphuric) acid by the action of ammonia; thus:

$$\left.\begin{array}{c}C_2H_5\\H\end{array}\right\} SO_4 + NH_3 = \left.\begin{array}{c}C_2H_5\\NH_2\end{array}\right\} SO_3 + H_2O.$$
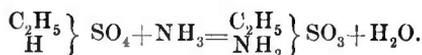
Preparation.—As a product of the decomposition of bile, and is purified by removing any traces of bile acids by means of lead acetate, and then successively crystallizing from water.

Leucin. $C_6H_{13}NO_2$.

Is one of the principal products of the decomposition of nitrogenous matter, either under the influence of putrefaction or of strong acids and alkalies. It occurs, however, normally in the pancreas, spleen, thymus, thyroid, salivary glands, liver, etc., and is one of the products of the tryptic (pancreatic) digestion of proteids; in acute atrophy of the liver it is present in the urine in large quantity, in company with tyrosin.

As usually obtained in an impure form it crystallizes in rounded lumps which are often collected together and sometimes exhibit radiating striation. When pure, it forms very thin, white, glittering flat crystals. These are easily soluble in hot water, less so in cold water and alcohol, insoluble in ether. They feel oily to the touch, and are without smell and taste. Acids and alkalies dissolve them readily, and crystallizable compounds are formed.

Carefully heated to 170° C. it sublimes, but at a higher temperature is decomposed, yielding amylamin, carbonic anhydride, and ammonia. In the presence of putrefying animal matter it splits up into valeric acid and ammonia.

Leucin is amido-caproic acid, and may be represented thus:

$$\left.\begin{array}{c}C_6H_{11}O\\NH_2\end{array}\right\} O.$$

Preparation.—From horn shavings by boiling with sulphuric acid, neutralizing with baryta and separating from tyrosin by successive crystallization. See also Kühne,[1] who prepares it by the action of the pancreatic ferment (trypsin) on proteids.

Scherer has given the following test for leucin. The suspected substance is evaporated carefully to dryness with nitric acid ; the residue, if it is leucin, will be almost transparent, and turn yellow or brown on the addition of caustic soda. If this be again very carefully concentrated with the alkali an oily drop is obtained, which is quite characteristic of this substance. Leucin if not too impure, may be easily recognized by its subliming on being heated ; a characteristic odor of amylamin is at the same time evolved.

Asparagine. $C_4H_8N_2O_3$.

Is not found as a constituent of the animal body but appears to be formed by the decomposition of proteids, notably during the germinative changes of the proteids in leguminous seeds.[2] It is a crystalline body, and when boiled with acids or alkalies is readily converted into aspartic acid.

Aspartic (*or asparaginic*) acid. $C_4H_7NO_4$.

This acid has been obtained in small quantities among the products of the pancreatic digestion of fibrin[3] and vegetable glutin,[4] although not occurring as a constituent of any animal tissue or secretion. It is on the other hand found normally in plants, notably in beet-sugar molasses. It arises also as a constant product of the action of alkalies and other reagents on both vegetable and animal proteids, and of acids on gelatine.[5] It thus possesses considerable interest in respect of its relation to the proteids. It crystallizes in rhombic prisms which are but sparingly soluble in cold water or alcohol, readily soluble in boiling water. Its acid solutions are dextrorotatory, its alkaline laevorotatory and reduce Fehling's fluid. It forms a characteristic readily crystallizable compound with copper. Nitrous acid converts it into malic acid.

Glutaminic acid. $C_5H_9NO_4$.

The circumstance and conditions under which this body occurs are in general the same as for the aspartic acid, and hence as a product of proteid decomposition it acquires some importance. It has not, however, as yet been obtained by the action of pancreatic ferments on proteids and in this it differs from the preceding body.

It crystallizes in rhombic tetrahedra or octahedra; is not very soluble in cold, but readily soluble in hot water ; insoluble in alcohol and ether. Its acid solutions possess a strong dextrorotatory power, and it reduces Fehling's fluid.

Cystin. $C_3H_7NSO_2$.

Is the chief constituent of a rarely occurring urinary calculus in men and dogs. It may also occur in renal concretions, and in gravel, and is occasionally found in urine.

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1 Virchow's Archiv, Bd. 39, S. 130.
2 Landwirthsch. Versuchs Stationen., Bd. xviii. 1.
3 Radziejewski u. Salkowski, Ber. d. deutsch. chem. Gesell. Jahrg. vii. (1874) S. 1050.
4 V. Knieriem, Zeitsch. f. Biol., Bd. xi. (1875) S. 198.
5 Horbaczewski, Sitzb. d. k. Akad. d. Wiss. Wien, 1880. 2 Abth. Juni-Heft.

From calculi it is obtained, by extraction with ammonia, as colorless six-sided tables or rhombohedra, which are neutral and tasteless. It is insoluble in water, alcohol, and ether, soluble in ammonia and the other alkalies, and also in mineral acids. The fact that this body is one of the few crystalline substances, occurring physiologically, which contain sulphur, renders its detection very easy. Apart from its insolubility in water, etc., it yields with caustic potash and salts of either silver or lead, a brown coloration due to the presence of the sulphides of these metals.

According to Dewar and Gamgee[1] cystin is amido-sulpho-pyruvic acid, and its formula is $C H_6 NSO$ —pyruvic being lactic acid minus two atoms of hydrogen.

THE AROMATIC SERIES.

Benzoic acid. $HC_7H_5O_2$.

This is not found as a normal constituent of the body, but owes its presence in urine to the fermentative decomposition of hippuric acid, whereby glycin and benzoic acid are formed :

$$\overset{\text{Hippuric acid.}}{C_2H_4(C_7H_5O)NO_2} + H_2O = \overset{\text{Glycin.}}{C_2H_5NO_2} + \overset{\text{Benzoic acid.}}{C_7H_6O_2}.$$
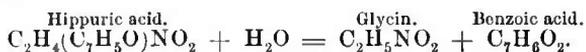
The sublimed acid is generally crystallized in fine needles, which are light and glistening ; any odor they possess is not due to the acid, but to an essential oil, with which they are mixed. When precipitated from solution, the crystalline form is always indistinct. This acid is soluble in 200 parts cold, or 25 parts of boiling water, but is easily soluble in alcohol or ether. It sublimes readily at 145° C. ; it also passes off in the vapors arising from its heated solutions.

Preparation.—Either as above from hippuric acid by fermentation, by boiling the hippuric acid with acids or alkalies, or by sublimation from gum-benzoin.

Tyrosin. $C_9H_{11}NO_3$.

Generally accompanies leucin, and is perhaps found normally in small quantities in the pancreas and spleen. It is also usually obtained in large quantities by the decomposition of proteid matter, either by putrefaction or the action of acids.

The researches of Radziejewsky[2] render it probable that tyrosin does not occur normally in any part of the human organism, except as a product of pancreatic digestion.

All attempts to synthetize tyrosin were for some time fruitless, although evidence was obtained sufficient to indicate the probable existence in its molecule of some aromatic (phenyl) radicle.[3] More recently the synthesis has been performed,[5] and we now have every reason for regarding tyrosin as para-hydroxl-phenyl-*a* alanine. This synthesis as well as that of uric acid, referred to above, is of considerable importance, since the more definite the knowledge which is possessed of the true molecular

[1] Journ. of Anat. and physiol., Nov. 1870, p. 143.
[2] Archiv. f. path. Anat., Bd. 36, S. 1.   Zeitsch. f. anal. Chem., Bd. 5, S. 466.
[3] Barth., Chem. Centralh. 1865.   S. 1029, 1869.   S. 761, 1872, S. 830.   Hüffner. Ibid. 1869, S. 159.   Beilstein u. Kühlberg, Ibid. 1872, S. 830.
[4] Erlenmeyer u. Lipp., Ber. d. deutsch. Chem. Gesell. Jahrg. xv. (1882) S. 1544.

structure of the products of proteid decomposition the more reason is
there for expecting that the synthesis of a proteid itself may be realizable
in the not very remote future.

Tyrosin crystallizes in exceedingly fine needles which are usually col-
lected into feathery masses. The crystals are snow-white, tasteless, and
odorless, almost insoluble in cold water, readily soluble in hot water,
acïds, and alkalies, insoluble in alcohol and ether. If crystallized from
an alkaline solution tyrosin often assumes the form of rosettes composed
of fine needles arranged radiately.

Tyrosin does not sublime by heating, but is decomposed with an odor
of phenol and nitrobenzol. On boiling with Millon's reagent it gives a
reaction almost identical with, but much more marked than, that for
proteids (Hoffman's test). If tyrosin is treated on a watch-glass with
one or two drops of strong sulphuric acid, then diluted with a little water,
neutralized with calcic carbonate, and the solution filtered, a character-
istic violet color is obtained on the addition of a drop of acid-free ferric
chloride (Piria's test).

Preparation.—By means similar to those employed for leucin, the
separation of the two depending on their widely differing solubilities.
According to Kuhne's method[1] large quantities are easily obtained as the
result of pancreatic digestion.

Hippuric acid. $C_9H_9NO_3$. Or Benzoyl-glycin. $C_2H_4(C_7H_5O)NO_2$.

Is found in considerable quantities in the urine of herbivora, and also,
though to a much smaller amount, in the urine of man. It is formed in the
body by the union with dehydration of glycin and benzoic acid, see p. 521.

Crystallized from a saturated aqueous solution, it assumes the form of
fine needles; if from a more dilute solution, white, semitransparent four-
sided prisms are obtained. These when pure are odorless, with a some-
what bitter taste. They are soluble in 600 parts of cold water, readily
soluble in boiling water, readily soluble in alcohol, less so in ether. All
the solutions redden litmus.

Hippuric acid is monobasic, and forms salts which are readily soluble
in water (except the iron salts); from these, if in sufficiently concen-
trated solutions, excess of hydrochloric acid precipitates the acid in fine
needles. When heated with concentrated mineral acids it is resolved
into benzoic acid and glycin. The same decomposition occurs in pres-
ence of putrefying bodies. Strong nitric acid produces an odor of nitro-
benzol.

Preparation.—*Fresh* urine of horses or cows is treated with milk of
lime, in order to form calcic hippurate, and thus prevent the decomposi-
tion of the hippuric acid, filtered, and the filtrate evaporated to a small
bulk; the hippuric acid is then precipitated by adding an excess of
hydrochloric acid; the acid is then purified by several crystallizations
from boiling water.

When heated in a small tube, hippuric acid gives a sublimate of ben-
zoic acid and ammonic benzoate, accompanied by an odor like that of
new hay, while oily, red drops are observed in the tube. This is very
characteristic, and distinguishes it from benzoic acid.

Phenylic (*Carbolic*) acid or *Phenol.* C_6H_6O.

This body is undoubtedly obtained as the result of the putrefactive
decomposition of proteids, notably in putrefactive pancreatic digestions.[2]

[1] Op. cit. (sub Leucin).
[2] Baumann, Zeitsch. f. physiol. Chem., Bd. i. (1877) S. 60.

It may be obtained from the distillate of such digestive mixtures. It is also found in the contents of the alimentary canal under the same conditions which give rise to indol. When so occurring, a portion of it may be obtained from the feces while the rest reappears in the urine.[1]

Buliginsky[2] says that the urine of many animals, of cows and horses always, contains a substance insoluble in alcohol, and not precipitated by lead acetate and ammonia, which by the action of dilute mineral acids gives carbolic acid. The same acid applied to the body externally or internally also passes into the urine.[3] Similarly benzol (C_6H_6) when taken into the stomach appears as carbolic acid in the urine.[4]

The pure acid crystallizes in long, colorless, prismatic needles; they melt at 35° C., and boil at 180° C. It is readily soluble in alcohol and ether, slightly soluble in water (I part in 20). In most cases it acts as a weak acid, forming crystalline salts with the alkalies. With nitric acid it yields picric acid. Its solutions reduce silver and mercury salts.

Preparation.—By the dry distillation of salicylic acid, also from the acid products of the distillation of coal. It is obtained in the last portions of the distillate when preparing indol, and is separated by forming a compound with bromine, $C_6H_3Br_3O$.

The Bile Series.

Cholalic (*or cholic*) acid. $H.C_{24}H_{39}O_5 + H_2O.$

Occurs in traces in the small intestine, in larger quantities in the contents of the large intestine, and the feces of men, cows, and dogs. In icterus, the urine often contains traces of this acid. But its principal interest lies in its being the starting-point for the various bile acids (see below). The pure acid may be amorphous, or crystalline, in the latter case crystallizing from hot alcoholic solutions in tetrahedra. These crystals are insoluble in water and ether. In the amorphous form, it is somewhat soluble in water and ether. Heated to 200° C., it is converted into water and dyslysin ($C_{24}H_{43}O_3$).

This acid possesses, in the anhydrous condition, a specific rotatory power of -50° for the yellow light; when it crystallizes with H_2O, the rotation is -35°. The rotatory power of the alkali salts is always less than the above, and when in solution in alcohol, the rotation is independent of the concentration. For the alcoholic solution of the sodium salt, the rotation is + 31.4°.

Preparation.—By the decompositions of bile acids by means of acids, alkalies, or fermentative changes.

Bayer[5] has examined the bile acids obtained from human bile, and has prepared from them cholalic acid. To this he assigns the formula $C_{18}H\ O_4$. If this he so, then cholalic acid of human bile would seem to be a body entirely different from that obtained from ox-bile, and analyzed by Strecker. Bayer's results, however, require further confirmation.

[1] Salkowski, Ber. d. deutsch. Chem. Gesell., ix. (1876) S. 1595. Centralb. f. d. med. Wiss., 1876, S. 818. Ber. d. deutsch. Chem. Gesell., x. (1877) S. 842. Virchow's Arch., Bd. lxxii. (1878) S. 409. See also Centralb. f. d. med. Wiss., 1878, Nos. 30, 31, 34, 42, and Zeitsch. f. physiol. Chem., Bd. ii. (1878) S. 241.

[2] Hoppe-Seyler. Med. chem. Untersuch. Heft 2 (1867) S. 234.

[3] Almén, Neues Jahrb. d. Pharm., Bd. 34, S. 111. Salkowski, Pflüger's Archiv, Bd. v. (1871-72) S. 335.

[4] Schultzen and Naunyn, Reichert u. Du Bois-Reymond's Archiv, 1867, Heft 3, S. 349.

[5] Zeitschr. f. physiol. Chem., Bd. ii. (1878-79) S. 358.

Pettenkofer's test.[1]

This well-known test for bile acids depends on the reaction of cholalic acid in presence of sugar and sulphuric acid. If to a solution of the acid a little sugar be added, and then sulphuric acid, keeping the temperature below but not much below 70° C., a beautiful reddish-purple is obtained. If diluted with alcohol, this solution gives a characteristic spectrum with two absorption bands, one between D and E, nearest to E, the other close to F on the red side of F.

The reaction is much impeded by the presence of coloring matters; moreover, proteids, and other bodies easily decomposed by sulphuric acid, such as amyl-alcohol and oleic acid, give a similar result; the coloring matter produced from these bodies does not, however, give the absorption bands described above.[2]

Glycocholic acid. $C_{26}H_{43}NO_6$.

This body was first obtained in the crystalline form and described by Gmelin (1826), who gave it the name of "cholic" acid.

To avoid confusion it is now best to use the word "cholic" as a synonym for "cholalic," Demarçay, who first (1838) described the cholalic acid as a product of the decomposition of the bile acids, having given it the name of cholic acid. The name cholalic is perhaps the best, since it indicates the method by which the bile acids are split up, viz., by treatment with alkali.

This is the principal bile-acid of ox-gall; it is also present in the bile of man, but has so far not been observed in that of carnivora. In icterus, the urine may contain traces of this acid.

It crystallizes in fine, glistening needles. These are slightly soluble in cold water, readily so in hot water and alcohol, but insoluble in ether. They possess a bitter and yet sweet taste, and a strong acid reaction.

The salts of this acid are readily soluble in water and crystallize well. The salts, as well as the free acid, exert right-handed polarization amounting to $+29.0°$ for the acid, and $+25.7°$ for the sodium salt, both measured for yellow light.

Glycocholic acid is a compound of glycin and cholalic acid; thus:

$$\underset{\text{Cholalic acid.}}{C_{24}H_{40}O_5} + \underset{\text{Glycin}}{C_2NH_5O_2} - H_2O = \underset{\text{Glycocholic acid.}}{C_{26}H_{43}NO_6}.$$
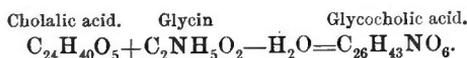
Prolonged boiling with dilute mineral acids or caustic alkalies decomposes glycocholic acid into glycin and cholalic acid; if dissolved in concentrated sulphuric acid and then warmed, glycocholic acid by the removal of one molecule of water yields cholonic acid, $C_{26}H_{41}NO_5$. The barium salt of this last acid is insoluble in water, which fact is of importance, since cholonic acid possesses nearly the same specific rotatory power as glycocholic acid.

Preparation.—From ox-gall, by evaporating to a syrup, decolorizing with animal charcoal, extracting with strong alcohol, and precipitating by a large excess of ether. Its separation from taurocholic acid depends on its precipitation by normal lead acetate, taurocholic acid not being precipitated by this reagent.

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[1] Pettenkofer, Annalen. d. Chem. u. Pharm., Bd. lii. (1844) S. 90.

[2] For further information on this subject see Bischoff, Zeitsch. f. rat. Med., Ser. 3, Bd. 21, S. 126. Schulze, Ann. d. Chem. u. Pharm., lxxi. (1849) S. 266. Schenk, Anatom. physiol. Untersuch. Wien, 1872, S. 47. Adamkiewicz, Pflüger's Arch., Bd. ix. (1874) S. 156.

Taurocholic acid. $C_{26}H_{45}NSO_7$

Occurs also in ox-gall, but is found especially plentiful in human bile and that of carnivora, notably of the dog.

It crystallizes with difficulty in very fine needles which are exceedingly deliquescent. When dried it is an amorphous powder, with pure bitter taste, easily soluble in water and alcohol, insoluble in ether. All its salts are soluble in water, and are precipitated by basic lead acetate in the presence of free ammonia. The sodium salt dissolved in alcohol has a specific rotatory power of + 24.5°; if dissolved in water this rotation is less, and in this respect it resembles glycocholic acid.

This acid is far more unstable than the preceding one, being decomposed if boiled with water. The products of decomposition are taurin and cholalic acid.

Taurocholic acid is a compound of taurin and cholalic acid; thus:

<div style="text-align:center">

Cholalic acid.   Taurin.   Taurocholic acid.

$$C_{24}H_{40}O_5 + C_2H_7NO_3S - H_2O = C_{26}H_{45}NO_7S.$$

</div>
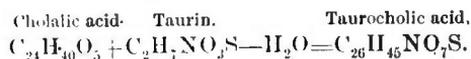
Preparation.—From the bile of dogs by a process similar to that for glycocholic acid. It is separated from traces of this latter and from cholalic acid by precipitation with basic lead acetate and ammonia.[1]

BILE PIGMENTS.

These have been very briefly described on p. 303.

Bilirubin. $C_{16}H_{18}N_2O_3.$

It is found chiefly in the fresh bile of man and carnivora, to which it gives the characteristic dark golden-red color. It frequently constitutes a considerable part of some kinds of gall-stones; not, however, as free bilirubin, but as a compound with earthy matter, chiefly chalk; the gall-stones of oxen and pigs often contain 40 per cent. of this compound.[2] These are, therefore, the best material from which to prepare bilirubin.

Preparation.—The gall-stones are treated with strong acetic or dilute hydrochloric acid to separate the earthy matter, and the residue is thoroughly washed with water and alcohol and dried. From this residue the prolonged action of hot chloroform extracts the bilirubin, which may either be obtained in the amorphous form by precipitation with alcohol of its solution in chloroform, or as well-defined crystals by the slow evaporation of the chloroform solution.

The most usual form of the crystals is that of rhombic prisms; they are readily soluble in chloroform and alkaline solutions only.

By treatment with oxidizing agents, such as nitrous acid bilirubin takes up oxygen and becomes biliverdin, the color at the same time changing to green. The possible oxidation does not end here, and if continued a series of products are obtained, each with a characteristic color, as in the well-known Gmelin's test.[3] Of these, only the final product of the oxidation has been obtained in a state of sufficient purity to enable any definite statements to be made of its characteristics.[4] This is the body known as Choletelin (see below).

Parke, Tübing. Med.-chem. Unters., Bd. i. S. 160.
Maly, Sitzber. d. Wien. Akad., lvii. 1868, ii. Abth. Febr. Hft.
[3] Tiedemann und Gmelin, Die Verdauung, 1826, S. 79.
[4] Heynsius und Campbell, Pflüger's Arch., Bd. iv. (1871) S. 497.

Biliverdin. $C_{16}H_{18}N_2O_4$.[1]

This product of the oxidation of bilirubin gives the characteristic color to the bile of herbivora, and to biliary vomits. It occurs, also, probably, at times in the urine of jaundice and in the pigmentary matter of the placenta. It is not found, or occurs in traces only, in gall-stones.

Preparation.—An impure product is obtained by precipitating ordinary herbivorous bile with baric chloride, washing the precipitate with water and alcohol and decomposing it with hydrochloric acid. The biliverdin thus obtained is washed with ether and dissolved in alcohol. From its solution in the latter it is obtained as an amorphous green powder by slow evaporation. Pure biliverdin is best prepared by the slow oxidation in the air of bilirubin dissolved in dilute caustic soda.

It does not crystallize, and is insoluble in ether or chloroform; readily soluble in alcohol. When oxidized it gives the same play of colors as does bilirubin, with the formation of the same final and intermediate products.

Neither this body nor bilirubin gives any characteristic absorption bands.

There seems now no reason for doubting that the bile pigments are derived ultimately from the coloring-matter of the blood.

Virchow has described[2] the gradual changes of old blood-clots, as of cerebral hemorrhage, which lead to the presence of the so-called hæmatoidin crystals. Though these have not been obtained in sufficient quantities to enable their composition to be finally fixed by a chemical analysis,[3] still the identity of their crystalline form with that of bilirubin and the fact that they both give the same play of colors when oxidized as in Gmelin's test, justify the assumption that hæmatoidin and bilirubin are identical.[4] Moreover, the balance of experimental evidence distinctly supports the view that a liberation from the corpuscles of the coloring-matter of the blood in the bloodvessels by an injection of chloroform, water, etc., leads generally to the appearance of bile pigments in the urine.[5] The occurrence of bilirubin crystals in the urine has frequently been observed after the operation of transfusion of blood in man. The chemical possibility of the conversion of hæmoglobin into biliverdin is readily seen by a comparison of the formulæ of hæmatin (see p. 408) and bilirubin. The former has, according to Hoppe-Seyler,[6] the composition indicated by the formula $2(C_{34}H_{35}N_4FeO_5)$, while that of bilirubin is $C_{16}H_{18}N_2O_3$. Although the conversion has not as yet been directly effected, the following facts are significant. If bilirubin is treated with sodium amalgam the substance known as hydrobilirubin (see below) is obtained. If hæmatin is dissolved in caustic soda and treated with sodium amalgam or in hydrochloric acid solution with zinc dust, a substance is obtained which is now recognized as identical with hydrobilirubin.[7] This is the most direct chemical evidence of the relation of the coloring-matters of the blood and bile.

1 Maly, Sitzb. d. Wien. Akad., lxx. (1874) iii. Abth. Arch. f. path. Anat., Bd. i. S. 383.
3 Rohin, Ann. d. Chem. u. Pharm., Bd. cxvi. S. 89.
4 But see also Preyer, Die Blutkrystalle, 1871, S. 187.
5 Tarchanoff, Pflüger's Arch., Bd. ix. (1874) S. 53. See also Bd. x. (1875) S. 208.
6 Physiologische Chemie, 1879, S. 395.
7 Hoppe-Seyler, Med.-chem. Untersuch., Hft. iv. 1871, S. 523. Ber. d. deutsch. chem. Gesell., vii. (1874) S. 1065.

Choletelin. $C_{16}H_{18}N_2O_6(?)$.[1]

This substance is obtained as the final product of the oxidation of either bilirubin or biliverdin. It is best prepared by acting upon bilirubin with nitrous acid in the presence of alcohol; the various colors of Gmelin's reaction are observed and the final reddish-yellow solution, if poured into water, yields a precipitate of choletelin. It is not crystalline and is soluble in alcohol, ether, and chloroform. When freshly prepared it seems to give an uncertain absorption band if examined in an *acid* solution. On this account some observers[2] have been led to regard it as identical with hydrobilirubin (urobilin). There is, however, no doubt that they are quite distinct bodies.[3]

Hydrobilirubin. $C_{32}H_{40}N_4O_7$.

This body was first described by Maly[4] as resulting from the action of sodium amalgam on an alkaline solution of bilirubin. When the reaction is complete, the solution is precipitated with hydrochloric acid, the precipitate dissolved in ammonia, again precipitated by acid, and the substance thus finally obtained is washed with water. It is readily soluble in alcohol, less so in ether. Its alkaline solutions are yellow, and these turn pink on the addition of acid. Both its acid and alkaline solutions, the latter especially on the addition of a few drops of chloride of zinc, give a characteristic absorption band betwen b and F.[5] In the colors of its alkaline and acid solutions and the greenish fluorescence of its ammoniacal solution on the addition of chloride of zinc, and in its absorption spectrum hydrobilirubin shows its close relation to urobilin (see below), with which indeed it is now considered to be identical. It is also identical with a body named stercobilin[6] which had previously been described as a product of the alteration of the bile pigments in the alimentary canal, occurring in feces. There is no difficulty in seeing how this change (hydrogenation) can be brought about in the intestine, since it is known that a considerable quantity of hydrogen may make its appearance by fermentative processes in the intestine, and in its nascent state might readily produce the simple change which is known to occur when bilirubin is converted into hydrobilirubin.

PIGMENTS OF URINE.

Our knowledge of these bodies is at present limited and imperfect. Most probably[7] they are numerous, but only two appear sufficiently well characterized to deserve mention here.

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[1] Maly. Sitz. d. Wien Akad., Bd. lvii. (1868) 2 Abth. Febr. und Bd. lix. 1869, 2 Abth, April. See also Heynsius and Campbell, loc. cit.

[2] Heynsius and Campbell, loc. cit. Stokvis, Centralb. f. d. med. Wiss., No. 14, (1873) S. 211.

[3] Maly, Centralb. f. d. med. Wiss., No. 21 (1875) S. 321. Liebermann, Pflüger's Arch., Bd. xi. (1875) S. 181.

[4] Centralb. f. d. med. Wiss., No. 54, 1871. Annal. d. Chem., Bd. clxiii. (1872) S. 77.

[5] Vierordt, Zeitsch. f. Biol., Bd. ix. (1873) S. 160.

[6] Vanlair and Masius, Centralb. f. d. med. Wiss., No. 24, 1871.

[7] Vierordt, Die quantitative Spectralanalyse, etc., Tübingen, 1876, S. 81.

Urobilin. $C_{32}H_{40}N_4O_7$.

As stated above, this is now regarded as identical with hydrobilirubin. It was first described by Jaffé[1] as a well-characterized normal urinary pigment, and its identity with hydrobilirubin subsequently determined.[2]

Normal urine contains only small quantities of urobilin, but there is present a substance (chromogen) which under the influence of acids, with absorption of oxygen, yields urobilin. The urine of fever frequently contains a considerable amount of actual urobilin as such.

The properties described above for hydrobilirubin are identical with those of urobilin. Its preparation from urine is somewhat difficult, and for this some special manual must be consulted.[3]

Uroerythrin

Is considered to be the substance which gives to the urine of rheumatism its characteristic color. Very little is known of its chemical properties.[4] It appears to be an amorphous reddish body with an acid reaction, slowly soluble in water, alcohol, and ether. When treated with caustic alkali it turns green. Urine containing this body takes on a characteristic reddish-yellow color on the addition of concentrated hydrochloric acid.

Thudichum considers that normal urine contains only one pigment, which he calls urochrome.[5] Maly is inclined to regard this as the same as urobilin.[6] More recently Thudichum has upheld his former views.[7]

THE INDIGO SERIES.

Indican. $C_8H_7NSO_4$.

A body was long ago described[8] as occurring in the urine and sweat of men and other animals which yielded by the action of acids the blue coloring matter indigo as one of the products of its decomposition. Schunk considered this substance to be identical with the indican known to occur in several plants (Indigofera, Isatis). Hoppe-Seyler,[9] on the other hand, having regard to the greater ease with which the indican from plants undergoes decomposition, regarded them as most probably different substances. Baumann has shown[10] that the two are really different, and has confirmed his earlier statements in a more recent publication.[11] According to him, the indican obtained from urine is not a glucoside (so also Hoppe-Seyler) and yields sulphuric acid by the action of hydrochloric acid. He assigns to it the formula $C_8H_6N.O.SO_2.OH$,

[1] Centralb. f. d. med. Wiss., 1868, S. 243. Virchow's Arch., Bd. xlvii. (1869) S. 405.

[2] Maly, Ann. d. Chem. u. Pharm., Bd. clxiii. (1872) S. 77.

[3] Vide Neubauer and Vogel. Harnanalyse, ed. viii (1881) S. 81.

[4] Heller's Archiv, (2) Bd. iii. (1854) S. 361.

[5] Brit. Med. Jl., N. S., No. 201, 1864, p. 509.

[6] Maly, Ann. d. Chem. u. Pharm., loc. cit. 1872, S. 90.

[7] Jl. Chem. Soc., Ser. 2, vol. xiii. (1875) pp. 397, 401.

[8] Schunk, Phil Mag., vol. x. p. 73; xiv. p. 228; xv. pp. 29, 117, 183. Chem. Centralb., 1856, S. 50; 1857, S. 957; 1858, S. 225. Hoppe-Seyler, Arch. f. path. Anat., Bd xxvii. S. 388. Jaffé, Pflüger's Arch., Bd. iii. (1870) S. 448.

[9] Handb. d. path. chem. Anal. Ed. iv. (1875) S. 191.

[10] Pflüger's Arch., Bd. xiii. (1876) S. 301. Zeitsch. f. physiol. Chem., Bd. i. (1877–78) S. 60.

[11] Zeitschr. f. physiol. Chem., Bd. iii. (1879) S. 254.

and regards it as indoxylsulphuric acid. The acid itself is not yet known in the free state, but it yields stable salts such as that of potassium, $C_8H_6N.SO_4K$. It occurs largely in the urine as the result of the presence of indol in the alimentary canal. In this way Baumann and Brieger[1] were enabled to obtain large quantities by giving indol to a dog. For its preparation their original paper must be consulted.

When treated in aqueous solution with hydrochloric acid in presence of oxygen, it yields indigo-blue

$$2C_8H_6NSO_4K + O_2 = 2C_8H_5NO + 2KHSO_4.$$
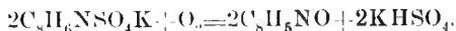
It is always estimated in urine by conversion into indigo-blue.

Indigo. C_8H_5NO.

It is formed, as stated above, from indican, and gives rise to the bluish color sometimes observed in sweat and urine.

It may, by slow formation from indican, be obtained in fine crystals; these are insoluble in water, slightly soluble, with a faint violet color, in alcohol and ether. Chloroform also dissolves them to a slight extent. Indigo is soluble in strong sulphuric acid, forming at the same time two compounds with this acid; these are soluble in water. It possesses a pure blue color; when pressed with a hard body a reddish copper-colored mark is left, and the crystals exhibit the same color if seen in reflected light.

The soluble compounds with sulphuric acid give an absorption band in the spectrum which lies close to the D line, and to the red side of it. This may be used to detect indigo.

Treated with reducing agents, indigo is decolorized, being reduced to indigo-white. The latter contains two atoms more hydrogen than indigo.

Indol. C_8H_7N.

To this body the specific odor of the feces is partly due. It is obtained as the final product of the reduction of indigo; and also by the distillation of proteid matter with caustic alkalies.[2]

It often occurs among the products of the action of pancreatic ferment on proteids; its presence in such cases appears, however, to be due, not to the action of the trypsin, but to a simultaneous putrefaction under the influence of bacteria, etc.[3] If the pancreatic digestion be carried on in the presence of salicylic acid, indol does not make its appearance. Indol is a crystalline body, soluble in boiling water, alcohol, and ether. It passes over in the steam when its aqueous solution is boiled. It is characterized by the following reactions. A strip of pinewood moistened with hydrochloric acid is colored bright crimson when dipped into a solution of indol. Its alcoholic solution turns red when treated with nitrous acid, and its aqueous solution gives a copious red precipitate with the same reagent. It also yields a characteristic crystalline compound with picric acid.

[1] Zeitsch. f. physiol. Chem., Bd. iii. (1879) S. 254. See also Ber. d. deutsch. Chem. Gesell., xii. (1879) Sn. 1098, 1192, 2166; and xiii. (1880) S. 408.

[2] Kühne, Ber. d. deutsch. chem. Gesel., viii. (1875) S. 206.

[3] Kühne, Verhand. d. Heidlb. naturhist med. Ver., N. S. Bd. i. Hft. 3. Bericht d. Deutschen chem. Gesellschaft, 1875, S. 206.

Skatol. C_9H_9N (?). Noticed by Brieger[1] as one of the products of putrefactive changes in the small intestine. Secretan[2] had previously described a similar substance as arising from the putrefaction of albumin.

Skatol is crystalline and contains nitrogen; it is more soluble in water than indol, and does not give rise to any red coloration with nitrous acid.

Skatol readily passes into the urine when it occurs in the alimentary canal, and then gives a violet-red reaction with strong hydrochloric acid.

V. Nencki[3] prepares this substance by the putrefaction of a mixture of finely divided pancreas and muscle substance. After the addition of acetic acid the mass is distilled, when the skatol readily passes over. From the distillate it is precipitated by picric acid, and the precipitate when again distilled with ammonia gives off pure skatol which may be finally purified by crystallization.

[1] Ber d. Deutsch. chem. Gesell., Jahrg. x. (1877) S. 1027.
[2] Recherches sur putrefaction de l'albumine. Geneva, 1876.
[3] Centralb. f. d. med. Wiss., 1878, S. 849.

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