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### **Publication/Creation**

London : Macmillan, 1888-1891.

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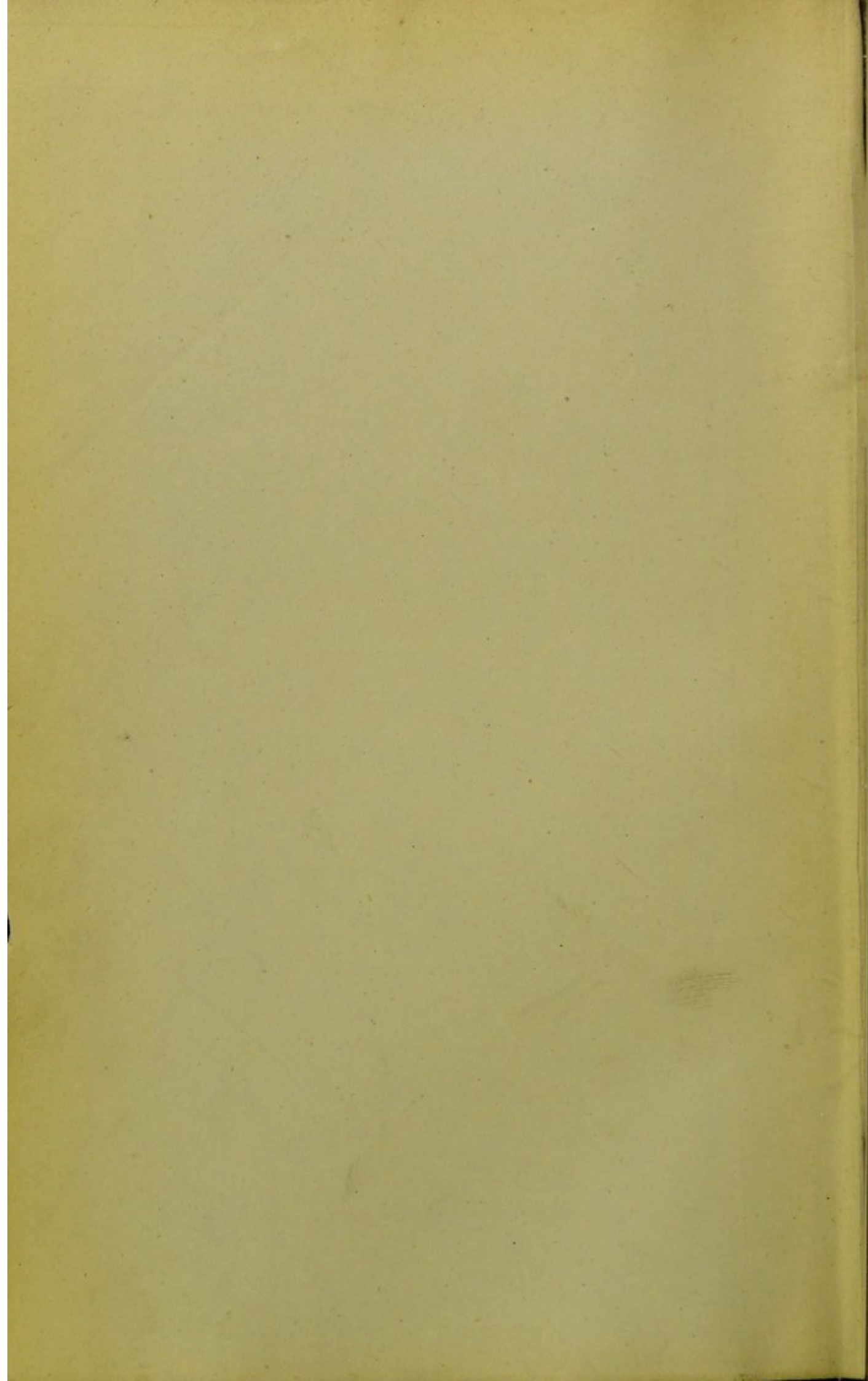
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A TEXT BOOK  
OF  
PHYSIOLOGY



THE HISTORY OF

THE CITY OF LONDON

FROM THE FOUNDATION



BY JOHN STOW



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57

A TEXT BOOK  
OF  
PHYSIOLOGY

LEEDS & WEST RIDING  
MEDICO-CHIRURGICAL SOCIETY

BY

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CAMBRIDGE.

WITH ILLUSTRATIONS.

FOURTH EDITION, REVISED.

London:  
MACMILLAN AND CO.

1883

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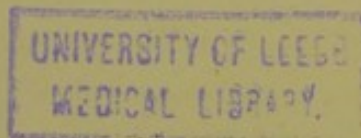
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Cambridge :

PRINTED BY C. J. CLAY, M.A. & SON,  
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PREFACE TO THE FOURTH EDITION.

IN previous Editions of this work I endeavoured, 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 favour 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 labours 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 textbook, 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 labours.

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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## 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 protoplasm, in the midst of which lies a nucleus, though this is sometimes 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 differentiation 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 economise 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 pre-eminently 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 manifestations of these protoplasmic qualities in varied sequence and subordination.

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 similarly the results of these fundamental qualities of protoplasm peculiarly associated together. The dominant principle of this association is the physiological division of labour 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 amoebiform 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, metabolism 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 automatism, 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 protoplasm, 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 corresponding to one of the fundamental qualities of protoplasm, to the development of which it is specially devoted by the division of labour. It must however be remembered that there is probably a distinct limit to the division of labour. 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. " " irritable and automatic: the nervous system.
3. " " secretory, or excretory: digestive, urinary, and pulmonary, &c., epithelium.
4. " " metabolic: fat-cells, hepatic cells, lymphatic and ductless glands, &c.
5. " " reproductive: ovary, testis.
6. The indifferent or mechanical: cartilage, bone, &c.

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 coordinating 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 imbedded 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 coordinating 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 operations. 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 mechanisms, 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 elements. 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 muscular machines, some serving for locomotion, others for special manœuvres of particular members and parts, others as an assistance 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 correspondingly 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 fundamental tissues have in all animals the same properties, being, it is true, more acute and perfect in one than in another, but remaining 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 particulars only as are wholly subordinate. In the nervous tissues of the higher animals, on the contrary, we find properties unknown 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 physiology very much according to the views which have been just sketched out. The fundamental properties of most of the elementary 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 coordinating 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 functions 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.



SWITCH-BOARD

TYPE 12 JAPANESE

LEEDS & WEST-RIDING  
MEDICO-CHIRURGICAL SOCIETY

CHAPTER I.

BLOOD.

BLOOD, when flowing in a normal condition through the blood-vessels, consists of an almost colourless 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 labours 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 received 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.



## SECT. 1. THE COAGULATION OF BLOOD.

Blood, when shed from the blood-vessels of a living body, is perfectly fluid. In a short time it becomes viscid; it flows less readily from vessel to vessel. The viscosity 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. If the blood in this jelly stage be left untouched in a glass vessel, a few drops of an almost colourless fluid soon make their appearance on the surface of the jelly. Increasing in number, and running together, the drops after a while form a superficial layer of pale straw-coloured 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 firmer consistency, now forms a clot or *crassamentum*, floating in a perfectly fluid *serum*. 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 generally 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*. 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 viscosity sets in. In consequence there appears on the surface of the blood an upper layer of colourless plasma, containing in its deeper portions many colourless corpuscles (which are lighter 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  $0^{\circ}\text{C}$ ., coagulation may be almost indefinitely postponed. Under these circumstances a more complete descent of the corpuscles takes place, and a considerable quantity of colourless 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 colourless shrunken clot and serum. This shews 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 p.c. solution of sodium chloride<sup>1</sup> 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 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

<sup>1</sup> A solution of sodium chloride of this strength will hereafter be spoken of as 'normal saline solution.'



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 coloured clot and the colourless serum.

Fibrin, whether obtained by whipping freshly-shed blood, or by washing either a normal clot, or a clot obtained from colourless 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<sup>1</sup>. 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<sup>2</sup>.

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 blood-vessels 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 colourless 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 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 colourless 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

<sup>1</sup> See Appendix.

<sup>2</sup> For further details see Appendix.



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<sup>1</sup>, and the solution rapidly filtered gives a clear colourless filtrate, which is at first perfectly fluid. Soon however the fluidity gives way to viscosity, 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<sup>2</sup>, the 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*<sup>3</sup> 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

<sup>1</sup> 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.

<sup>2</sup> See Appendix.

<sup>3</sup> See Appendix for the distinction between the coagulation of proteids by heat, and the coagulation due to the appearance of fibrin.



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<sup>1</sup>. So also the serous fluid removed from the pericardial, pleural, or peritoneal cavities some hours after death in most cases shews no disposition to clot<sup>2</sup>. 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 unmistakeable manner<sup>3</sup>. 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.

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

<sup>1</sup> In some specimens, however, a spontaneous coagulation, generally slight, but in exceptional cases massive, may be observed.

<sup>2</sup> If it be removed immediately after death it generally clots readily and firmly, giving a colourless clot consisting of fibrin and white corpuscles only.

<sup>3</sup> In a few cases no coagulation can thus be induced.



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 for ever 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<sup>1</sup> teaches that fibrin arises from some mutual action of fibrinogen and paraglobulin induced by the fibrin ferment; the other<sup>2</sup> 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 these 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 favour 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

<sup>1</sup> That of Alexander Schmidt, and his pupils and others.

<sup>2</sup> That of Hammarsten, Fredericq and others.



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 favour 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 cooperation of paraglobulin to form fibrin; and another body, which may be thrown down from solutions of plasmin or from blood at the temperature of  $55^{\circ}$ — $60^{\circ}$  (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 conclude that fibrin is formed by the conversion, through the agency of a ferment, of a substance fibrinogen, which forms part of the plasmin 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 favourable 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 vessel into which blood is shed, the more quickly coagulation comes on, for contact with surfaces favours 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 approximative 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 favours 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 blood-vessels, 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 blood-vessels 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 blood-vessels 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, shewing 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 favourable 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 blood-vessels; the following shew 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 blood-vessel 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 blood-vessel 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 neighbourhood of the ligature, gradually thinning away from thence and reaching usually as far as 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 favour 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 blood-vessel causes a coagulation at the spot of injury. Any treatment of a blood-vessel tending to injure its normal condition causes local coagulation.

7. Disease involving the inner coat of a blood-vessel 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 dilation 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 blood-vessels and the blood is maintained, coagulation does not take place; but when this relation is disturbed by the more or less gradual death of blood-vessels, 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 favours coagulation within the blood-vessels, apparently because the blood-vessels, 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 blood-vessels, 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 from 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 blood-vessels 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 blood-vessels 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 blood-vessels 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 blood-vessel, 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 blood-vessels 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 blood-vessels 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 pre-existent 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 blood-vessels 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 blood-vessels 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 .2 p. c., 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.

**Composition of serum.** In 100 parts of serum there are in round numbers

Water	... ..	90 parts
Proteid Substances	... ..	8 to 9 „
Fats, Extractives <sup>1</sup> , and Saline Matters	2 to 1	„

The proteid substances present in serum are<sup>2</sup>:—(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<sup>3</sup>. 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 *paraglobulin* 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.

<sup>1</sup> 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.

<sup>2</sup> There seems no longer any reason to distinguish a serum-casein from *paraglobulin*, see Appendix.

<sup>3</sup> For further details see Appendix.



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<sup>1</sup> and cholesterin occur in very small quantities only. Among the extractives present in serum may be put down all the nitrogenous and other substances which form the extractives of the body and of food, such as urea, kreatin, sugar, lactic acid, &c. 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 odour of blood-serum is probably due to the presence of volatile bodies of the fatty acid series. The faint yellow colour 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 the serum offers a marked contrast to the corpuscles (see below). 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.

**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 p. c. The solids are almost entirely organic matter, the inorganic salts in the corpuscles amounting to less than 1 p. c. Of the organic matter again by far the larger part consists of hæmoglobin. In 100 parts of the dried organic matter of the corpuscles of human blood, Hoppe-Seyler and JüdeU found, as the mean of two observations,

Hæmoglobin	90·54	Lecithin	·54
Proteid Substances	8·67	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 corpuscles differ under different circumstances. Malassez, by comparing the tint of a quantity of blood the numbers 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

<sup>1</sup> For detailed accounts of the characters of the several chemical substances mentioned in this and succeeding chapters consult the Appendix under the appropriate headings.



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.

**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 paroglobulin. 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 in-



crease 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 hæmorrhage 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) in 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 recognised 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 shew 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 mesh-work 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 ensured 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 believes 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, from 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 hæmorrhage) 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<sup>1</sup> 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 coloured 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 ascertained by

<sup>1</sup> See Chapter on Changes of Blood in Respiration.



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<sup>1</sup>.

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 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

<sup>1</sup> Klein, *Hdb. Phys. Lab.*, p. 8.



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. 22) 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 are 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 labours 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,

“ “ “ “ liver,

“ “ “ “ skeletal muscles,

“ “ “ “ other organs.

Since in the heart and great blood-vessels 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 &c. 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 shewn 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.



## 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 be 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 shewn 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 blood-vessels), 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 recognisable 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<sup>1</sup>, Figs. 1 and 2, be laid on the electrodes of an induction-machine<sup>2</sup>,

<sup>1</sup> 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.

<sup>2</sup> 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 &c. of copper, platinum, or carbon, &c.) is called the *negative* element. A galvanic action is set up when the positive (zinc) and the negative (copper) elements are connected outside the battery



the passage of a single induction-shock, which may be taken as a convenient form of an almost momentary stimulus, will produce no visible change in the nerve, but the muscle will give a short sharp contraction, *i.e.* will for an instant shorten itself, becoming 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

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 re-established 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. 1 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. 9. p. 51) the direction of the current from  $x$  to  $y$  through the primary coil *P* is shewn 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 "induced" current is, for an exceedingly brief period of time, set up in the secondary coil. Thus in Fig. 1 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  $y' x'$  &c., 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*.



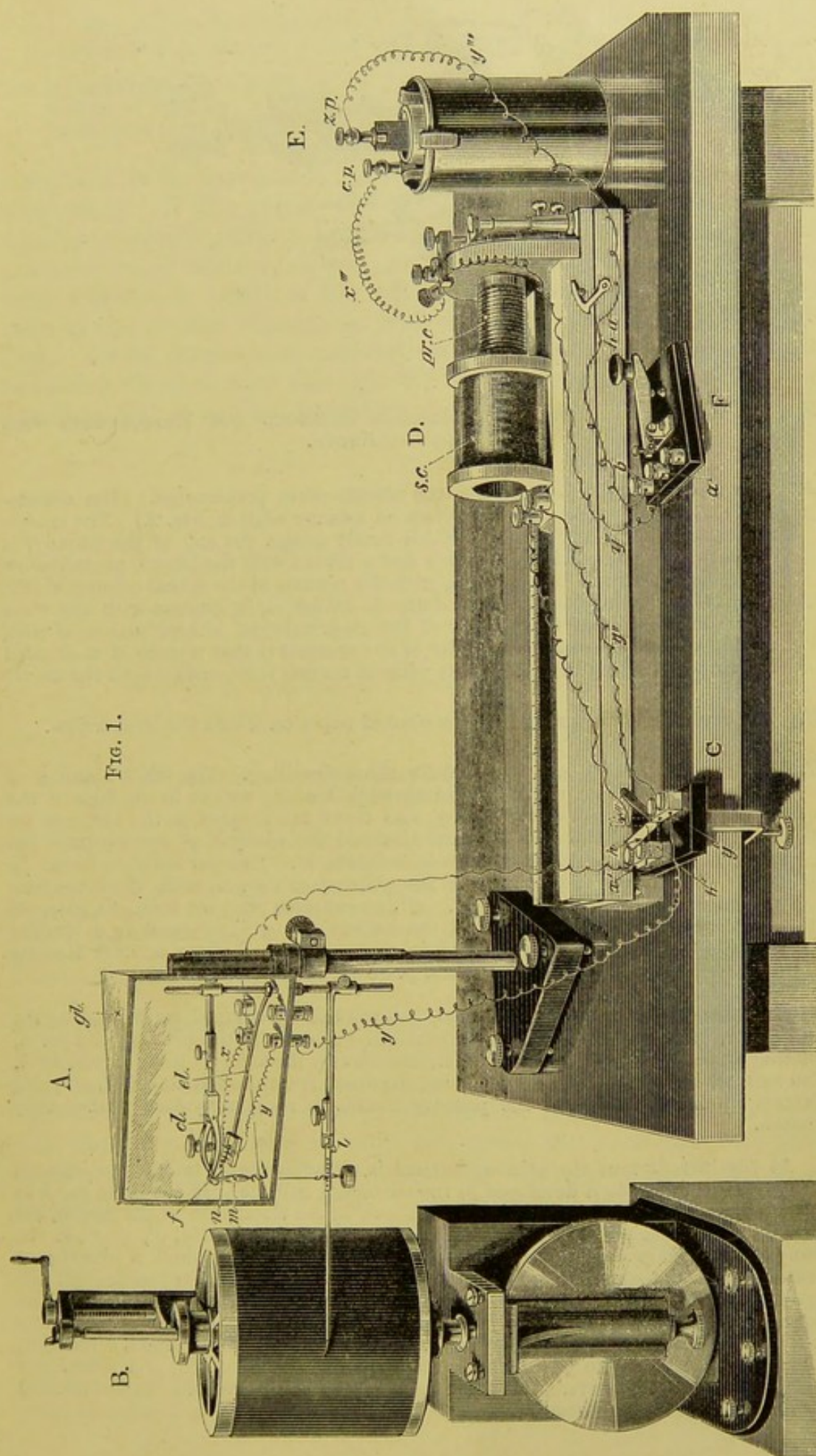


FIG. 1.



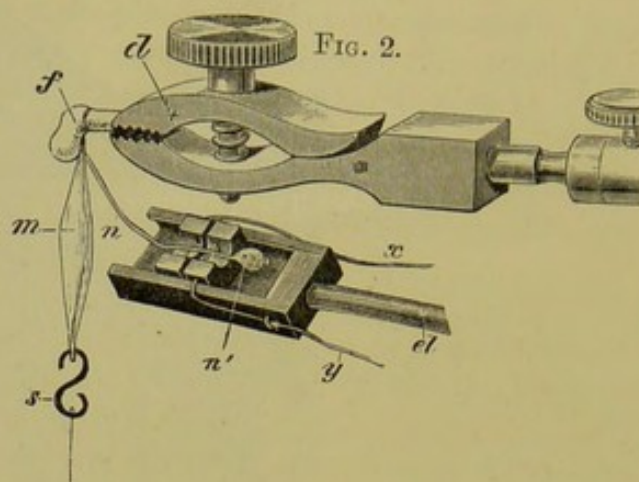


FIG. 1. DIAGRAM ILLUSTRATING APPARATUS ARRANGED FOR EXPERIMENTS WITH MUSCLE AND NERVE.

- A. The moist chamber containing the muscle-nerve preparation. (The muscle-nerve and electrode-holder are shewn on a larger scale in Fig. 2.) 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''*, *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<sup>iv</sup>* from another binding screw *b* of the key to the zinc pole *z. p.* of the battery.

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<sup>iv</sup>* 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 current is for the instant developed in the secondary coil *s. c.* If the cross bar *h* in the du-Bois Reymond's key be raised (as shewn 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. 2. The muscle-nerve preparation of Fig. 1, with the clamp, electrodes, and electrode-holder, are here shewn on a larger scale. The letters as in Fig. 1.

The apparatus figured in Figs. 1 and 2 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.

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 shewn in Fig. 3 will be described, the lever rising with the shorten-

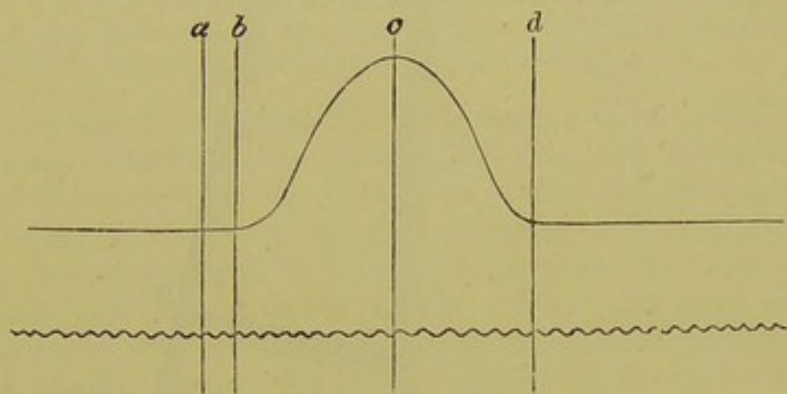


FIG. 3. A MUSCLE-CURVE OBTAINED BY MEANS OF THE PENDULUM MYOGRAPH.  
To be read from left to right.

*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  $\frac{1}{360}$  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 shewn by the greater length of the vibration-curves.

ing 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. 4.

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



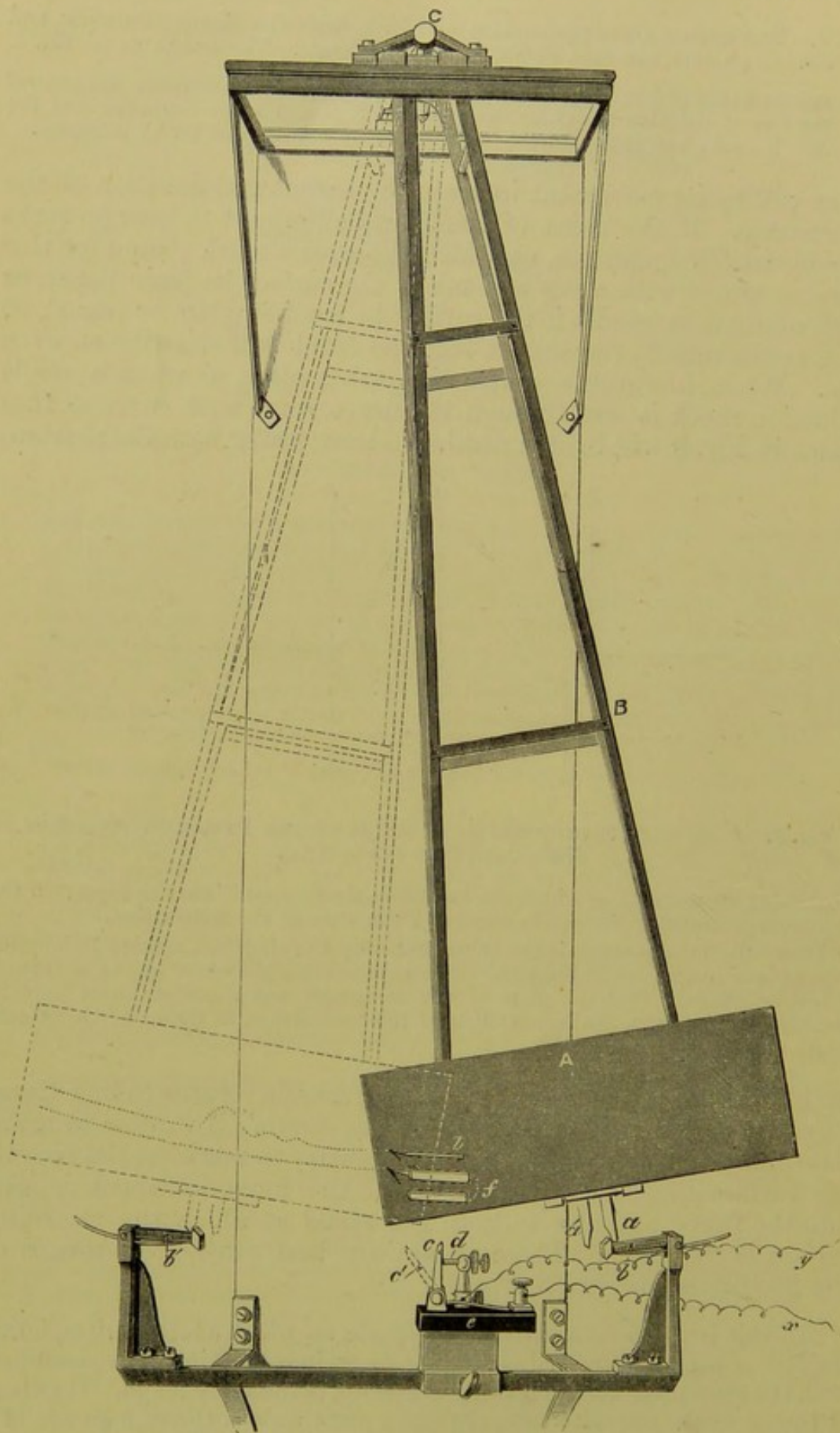


FIG. 4. THE PENDULUM MYOGRAPH.

The figure is diagrammatic, the essentials only of the instrument being shewn. The smoked glass plate *A* swings with the pendulum *B* on carefully adjusted



bearings at *C*. The contrivances by which the glass plate can be removed and replaced at pleasure are not shewn. 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 shewn 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 shewn in the figure placed immediately below the lever, serves to mark the time.

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 shewn in Fig. 3, 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  $\frac{1}{10}$  sec.

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  $\frac{2\frac{1}{2}}{180}$  i.e. about  $\frac{1}{77}$  sec., that the shortening begins. The shortening as shewn 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  $\frac{1}{20}$  sec.

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  $\frac{1}{30}$  sec.

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

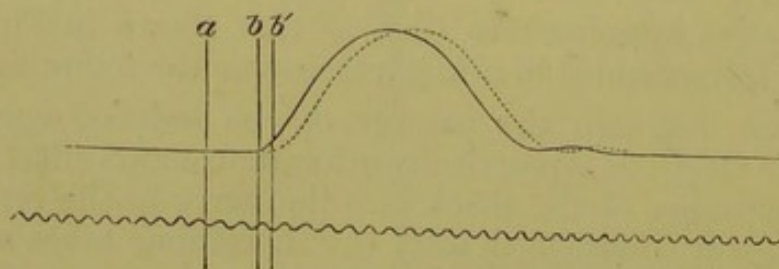


FIG. 5. CURVES ILLUSTRATING THE MEASUREMENT OF THE VELOCITY OF A NERVOUS IMPULSE. (Diagrammatic.) To be read from left to right.

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, shewn 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, shewn 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.



exactly the same point of the travelling surface as before, a curve like that shewn by the plain line in Fig. 5 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 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 shews 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 accurately 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  $\frac{1}{100}$ th sec.

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



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

We have given what may be considered the average duration<sup>1</sup> of each phase chiefly for the sake of shewing 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 coloured 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.

### *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

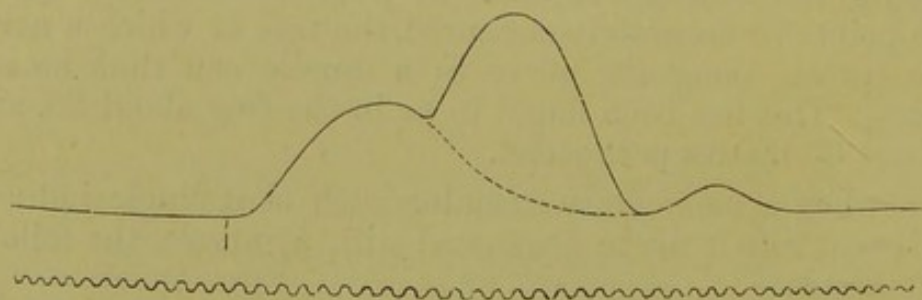


FIG. 6. TRACING OF A DOUBLE MUSCLE-CURVE. To be read from left to right.

While the muscle<sup>2</sup> 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.

<sup>1</sup> 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.

<sup>2</sup> In this and the other curves of this section the tracings figured were taken from *frog's* muscle.



contraction or spasm will be followed by a second spasm, the two bearing some such relation to each other as that shewn 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 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.

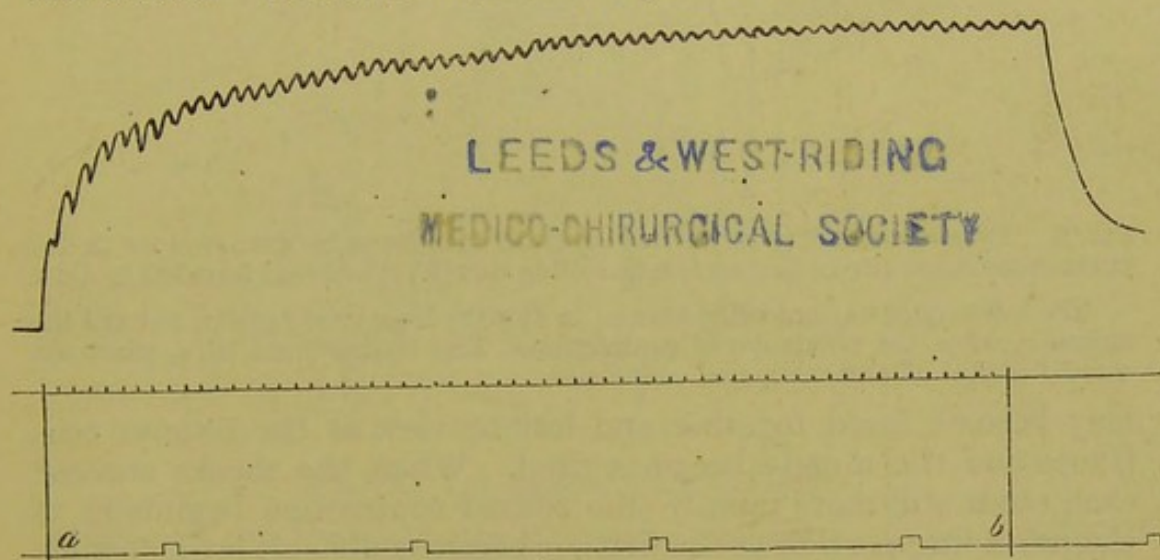


FIG. 7. MUSCLE THROWN INTO TETANUS, WHEN THE PRIMARY CURRENT OF AN INDUCTION-MACHINE IS REPEATEDLY BROKEN AT INTERVALS OF SIXTEEN IN A SECOND.

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 shews 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.



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 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 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,

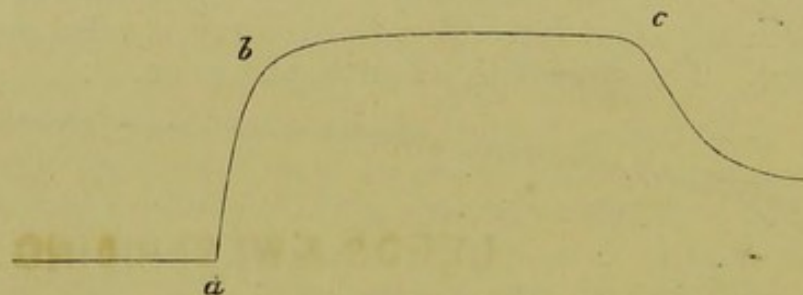


FIG. 8. TETANUS PRODUCED WITH THE ORDINARY MAGNETIC INTERRUPTOR OF AN INDUCTION-MACHINE. (Recording surface travelling slowly.) To be read from left to right.

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.

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 portion 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 shewn in Fig. 8, where the primary current of an induction-machine was rapidly made and broken by the magnetic interruptor, Fig. 9. 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 shewn 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.

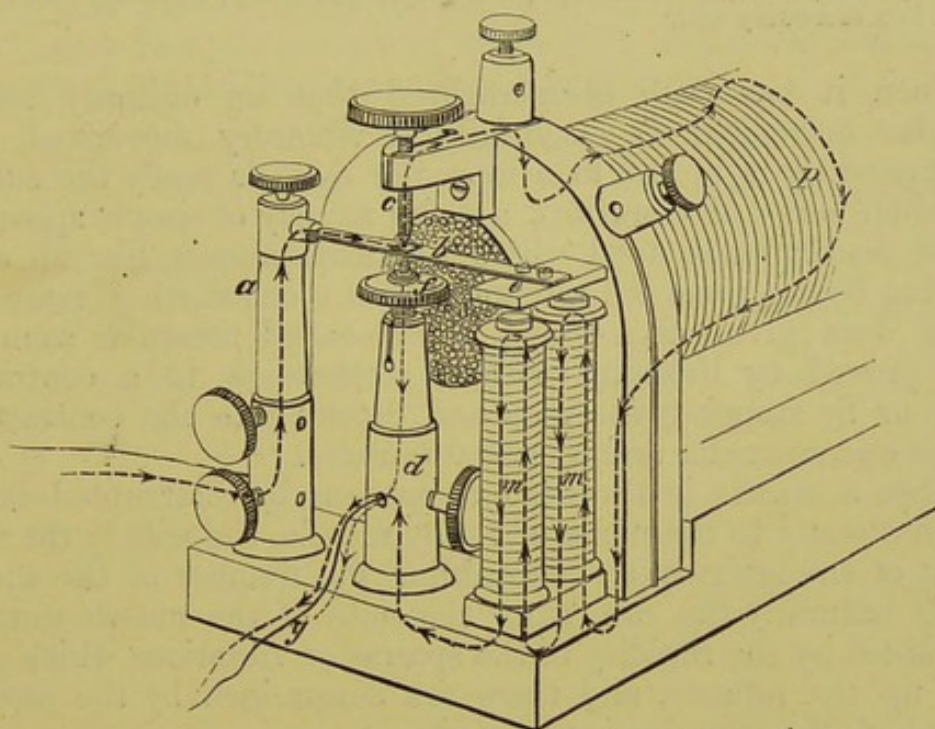


FIG. 9. THE MAGNETIC INTERRUPTOR.

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 shewn 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 magnetised, 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 re-establishes 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.

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 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 the 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. 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 vigour 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 .1 sec. for the contraction to pass over any point of the fibre, the wave-length 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 con-



dition in the living body, it is probably somewhat greater, and the wave also probably travels with undiminished velocity and vigour 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 unarised 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

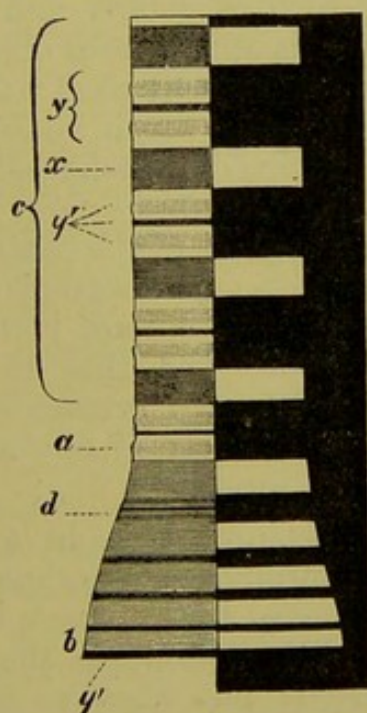


FIG. 10. MUSCULAR FIBRE UNDERGOING CONTRACTION.

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 shews the same fibre as seen in polarized light. (After Engelmann.)



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. 10, 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 disc 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.

When the fibre is examined in polarised 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 shewn in Fig. 3, 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. 6 and 7, shew 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 is however a complicated and difficult subject, and it will be sufficient to reassert that it is essentially a vital property, 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-polarisable electrodes<sup>1</sup>, con-

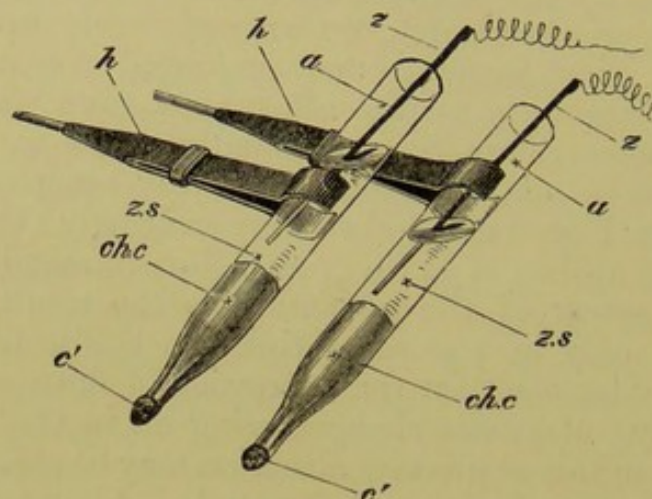


FIG. 11. NON-POLARISABLE ELECTRODES.

*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 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

<sup>1</sup> These (Fig. 11) consist essentially of a slip of thoroughly amalgamated zinc dipping into a saturated solution of zinc sulphate, which in turn is brought into 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 polarisation 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.



called the 'equator,' containing all the points of the surface midway between the two ends. Fig. 12 is a diagrammatic representation of such 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

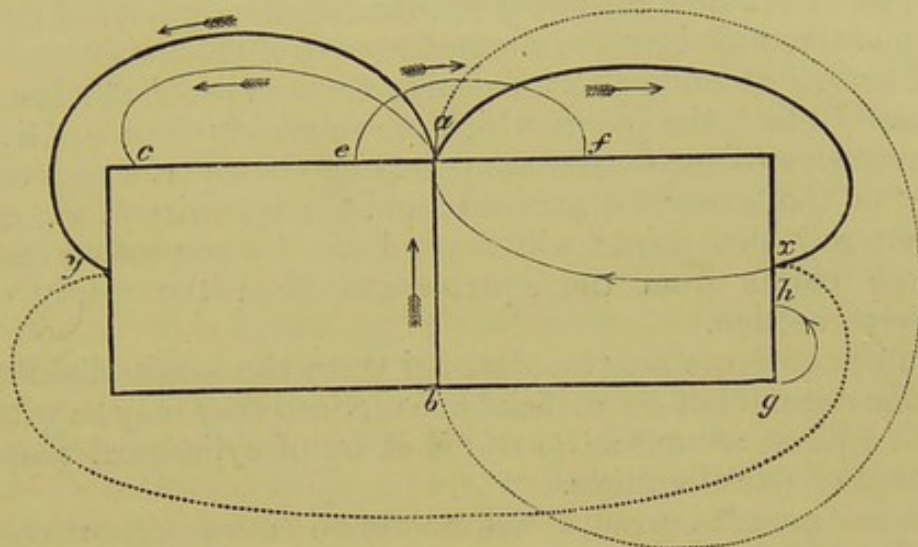


FIG. 12. DIAGRAM ILLUSTRATING THE ELECTRIC CURRENTS OF NERVE AND MUSCLE.

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 shewn in a nerve. The arrows shew the direction of the current through the galvanometer.

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

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 shew 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. 12, the arrows indicate the direction of the currents. If the 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 farther 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 one cut end  $x$ , and the other on the other 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 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 points will depend on the respective distances 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 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 in 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 shewn that the surface of the uninjured inactive<sup>1</sup> 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 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 favour 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 variation 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

<sup>1</sup> The necessity of its being inactive will be seen subsequently.



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 shewn 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 tetanizing current is shut off.

Not only may this negative variation be shewn by the galvanometer, 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 the 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 shews 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. 61) that the surface of the uninjured inactive ventricle of the frog's heart is isoelectric, 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 shewn 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 preexisting 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 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 shewn 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<sup>1</sup>.

<sup>1</sup> 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.



*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 muscle 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, 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, and becomes firmer and more resistant. The entrance into rigor mortis is characterised 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 connective 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 p. c. solution of a neutral salt, ammonium chloride being the best, a large portion of it will become imperfectly 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 proteid, 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 proteid<sup>1</sup>, and it is worthy of notice that it coagulates at a lower temperature, viz. 55°—60° C., than does serum-albumin, paraglobulin and many other proteids; it is precipitated and after long action coagulated by alcohol, and is precipitated by an excess of sodium chloride. By the action of dilute acids it is very readily converted into what is called syntonin or acid-albumin<sup>2</sup>, by the action of dilute alkalis 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<sup>3</sup>, and while frozen, minced, and rubbed up in a mortar with four times its weight of snow containing 1 p.c. 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<sup>4</sup> 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

<sup>1</sup> See Appendix.

<sup>2</sup> Ibid.

<sup>3</sup> 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.

<sup>4</sup> 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 characterised 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<sup>1</sup>; 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 produced, 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

<sup>1</sup> See Appendix.



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 are 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 shewn 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 shewn 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 kreatin, which occurs to the extent of about .2 to .3 p. c., 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 kreatinin into which kreatin 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<sup>1</sup>.

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 adult that it may fairly be considered as a normal constituent of muscle to a variable extent, possibly from .5 to 1 p. c. 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 characterised by the preponderance of potassium salts and of phosphates; these form in fact nearly 80 p. c. of the whole ash.

The general composition of human muscle is shewn in the following table of v. Bibra.

Water ... ..	744.5
Solids	
Myosin and other matters, elastic elements, &c., insoluble in water ...	155.4
Soluble proteids ... ..	19.3
Gelatin ... ..	20.7
Extractives and Salts ... ..	37.1
Fats ... ..	23.0
	255.5

<sup>1</sup> See Appendix.



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

Helmholtz shewed 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<sup>1</sup> 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 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 shew 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

<sup>1</sup> The micro-unit being a milligramme of water raised one degree centigrade.



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 shew 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. 12, and the description which it was used on p. 59 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 shewn 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, iso-electric; 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 shewn either by the galvanometer or by the rheoscopic frog. If the nerve of the 'muscle-nerve preparation' *B* (see p. 62) 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 'pre-existing' current, is an essential feature of a nervous impulse is shewn 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 shewn (p. 47) 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 .0007 sec. 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 sec. 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 sec.). 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 considerable 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 neighbourhood of the two electrodes respectively.

Suppose that on the nerve of a muscle-nerve preparation are placed two (non-polarizable) electrodes (Fig. 13, *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.

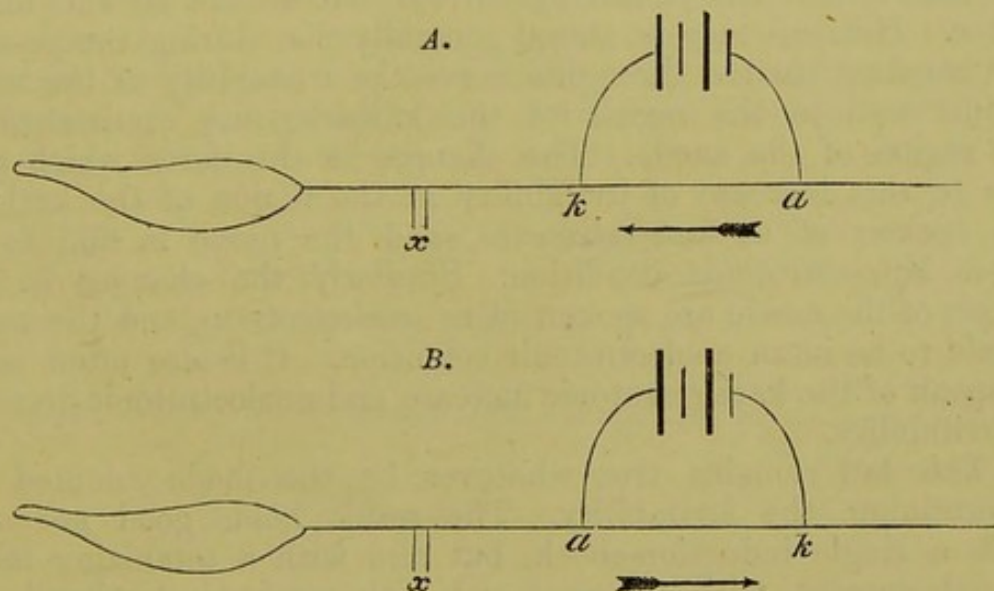


FIG. 13. MUSCLE-NERVE PREPARATIONS, with the nerve exposed in *A* to a *descending* and in *B* to an *ascending* constant current.

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.

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. 13 *A*. If while the current is passing, the same induction-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. 13 *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). The same result, *mutatis mutandis*, and with some qualifications which we need not discuss, would be gained if *x* were placed not between the muscle and the polarizing current, but on the far side of the latter. 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 neighbourhood 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 katelectro-



tonic 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. 14).

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 elsewhere is affected by the electrotonic condition. At all events anelectrotonus 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 shew 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 co-called "law of contraction")

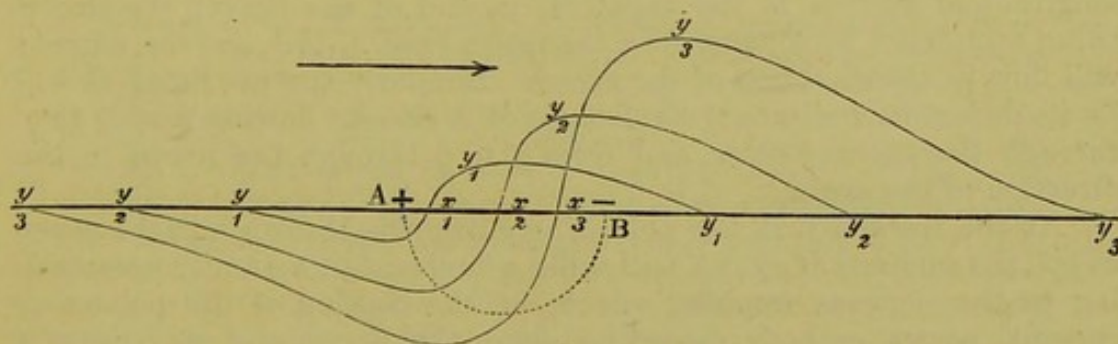


FIG. 14. DIAGRAM ILLUSTRATING THE VARIATIONS OF IRRITABILITY DURING ELECTROTONUS, WITH POLARIZING CURRENTS OF INCREASING INTENSITY (from Pflüger).

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 near 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.



go far to shew that a nervous 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 in as much as they shew 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. 15) 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 neighbourhood of the anode (*p*) as those in the neighbourhood 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 of *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 in 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.

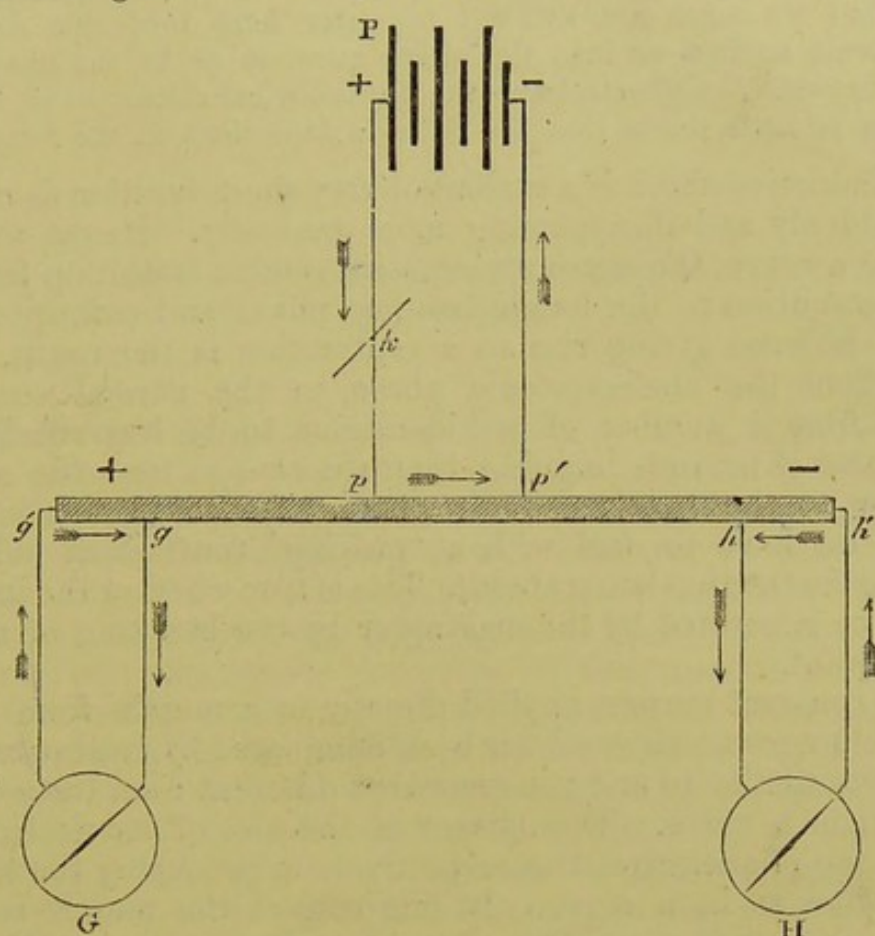


FIG. 15. DIAGRAM ILLUSTRATING ELECTROTONIC CURRENTS.

*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.

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* electrotonus 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.

An induction-shock is a current of very short duration developed very suddenly and disappearing more gradually. Hence, when it falls into a nerve, the nerve undergoes a 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 favourable 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 shew 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 <sup>the</sup> 28 inches per sec., 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 farther 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<sup>1</sup>; 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 shocks 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 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. 1, *sc.*) a certain distance from 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

<sup>1</sup> 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.



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<sup>1</sup> 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 contractions 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 fatigue lowers them. Sometimes however, after the contractions have for some time remained of the same height, in spite of the stimulus, at each fresh stimulation, being increased in strength, a point is reached at which, with a further increase in the strength of the stimulus, a new increase of contraction sets in; but we must not attempt to explain here this paradoxical *super-maximal* contraction as it is called.

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

It may here be remarked that in order for a stimulus to be effective, a certain abruptness in its action is necessary. Thus we have seen that the constant current when it is passing through a nerve with uniform intensity does not give rise to a nervous impulse and that it may be increased or diminished to almost any extent without generating nervous impulses, provided that the change be made gradually enough; it is only when there is a sudden change that the current becomes effective as a stimulus. The current which is induced in the secondary coil of an induction-machine at the breaking of the primary circuit, is more rapidly developed, and has a steeper rise than the current which appears when the primary circuit is made; and accordingly we find that the breaking induction shock is more potent as a stimulus than the making shock. Similarly a sharp tap on a nerve will produce

<sup>1</sup> 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.



a contraction, when a gradually increasing pressure will fail to do so; and in general the efficiency of a stimulus of any kind will depend in part on the suddenness or abruptness of its action.

A stimulus, in order that it may be effective, must have an action of a certain duration, the time necessary to produce an effect varying according to its strength and being different in nerve from what it is in muscle. It would appear that an electric current applied to a nerve must have a duration of at least about  $\cdot 0015$  sec. to cause any contraction at all, and needs longer than this to produce its full effect. When the current is applied directly to a muscle, whose nervous elements are placed *hors de combat* by the action of urari, or by degeneration of the nerve-fibres this period of necessary duration seems to be still longer, and to be especially increased by deficient nutrition. And this may be offered as an explanation of the well-known clinical fact that in various cases of paralysis, muscles which have by degeneration of their nerves, lost their nervous supply, more readily 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 farther 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 farther 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' shews 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 tetanus, 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 tetanus 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 muscles require at least twenty stimuli in a second.

When the stimulus is repeated more frequently than is required to bring about a complete tetanus the constituent contractions are still proportionately increased in frequency. This is shewn 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 stimulated 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 contraction, 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 favourable action of the resistance. As the load continues 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*<sup>1</sup>.

*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,

<sup>1</sup> This is perhaps the best equivalent of the German *überlastet*.



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 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 the 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 grms.

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 favourable 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 gram-metres 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 the warm-blooded than in the 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 favourable 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 neighbouring 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. 78) how the constant current produces the variations in irritability known as katelectrotonus 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. 86) 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<sup>1</sup> may be either cooled to 0° C. or below, or heated to 50° or even 100° C., without discharging any nervous impulses, as shewn by the absence of contraction in the attached muscle. The contractions moreover may be absent even when the heating has not been very gradual.

A muscle may be cooled to 0° C. or below without any contraction being caused; but when it is heated to a limit, which in the case of frog's 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., favours 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 sec. At about 0° the irritability of the nerve disappears altogether.

When a muscle is exposed to similar cold, *ex. gr.* 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,

<sup>1</sup> The action of cold and heat on sensory nerves will be considered in the later portion of the work.



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 of 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 blood-vessels 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 favourable 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 shew that the nutrition of a muscle is favourably 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 blood-vessels 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 favourable 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 con-



tractions, 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 5 or 10 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 shewn 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 blood-vessels; 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 "intramolecular 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, kreatin, &c., 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 suppose 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 knowledge 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 characteristic 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 existence 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 contractile 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 essentially 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 substance 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, has suggested the view 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.



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SEC. 7. OTHER FORMS OF CONTRACTILE TISSUE.

*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, &c. 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 cm. 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 (p. 86), 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  $12^{\circ}\text{C}$ ., and are most active at a temperature above  $21^{\circ}\text{C}$ . So also the movements of the intestine cease at a temperature below  $19^{\circ}\text{C}$ .

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 reaction. 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 Engelmann 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; Engelmann 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, &c. 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 temperature and chemical media. Moderate heat quickens the movements, but a rise of temperature beyond a certain limit (about 40°C. in the case of the pharyngeal membrane of the frog) becomes injurious; cold retards. Very dilute alkalis are favourable, 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. Chloroform or ether in slight doses diminishes or suspends the action temporarily, in excess kills and disorganises the cells.

*Migrating Cells.* We have already (p. 35) 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, &c., 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

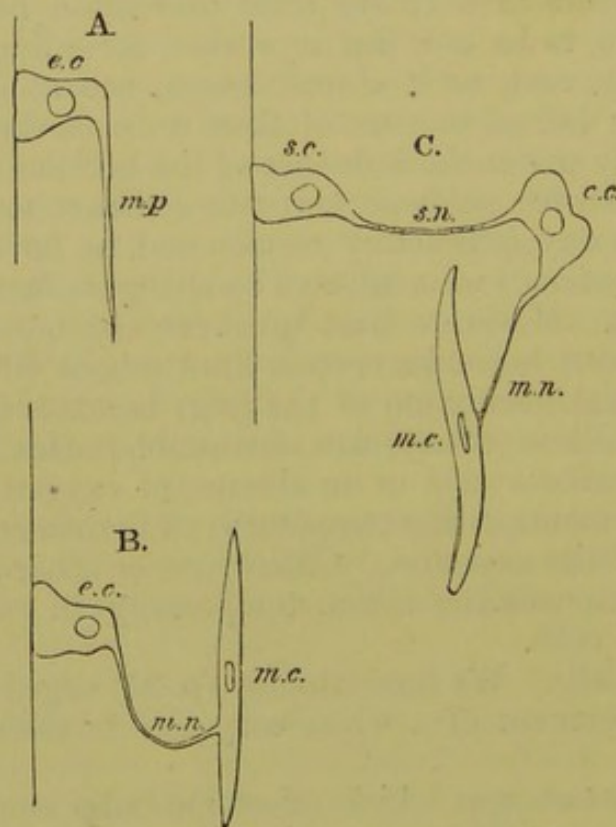


FIG. 16. DIAGRAM TO ILLUSTRATE THE SIMPLEST FORMS OF A NERVOUS SYSTEM.

- 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.*



vital communication between a sensitive ectodermic cell exposed to extrinsic accidents, and a muscular, highly contractile cell (or a muscular process of the same cell) buried at some distance from the surface of the body, and thus less susceptible to external influences. (Fig. 16, 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 co-ordinated 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 labour, 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. 16 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 vigour 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 profoundly modifying 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 electrotons (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. 52), 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 grey 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 automatism is a muscular automatism like that of a ciliated cell, or the automatism of a differentiated 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 excited 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 referred. 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 Engelmann, 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 grey 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 machinery it demands is (*a*) a sentient surface (external or internal), connected by (*b*) a sensory, or—to adopt the more general and better term—afferent nerve, with (*c*) a central nerve-cell or group of connected nerve-cells, which is in relation by means of (*d*) a motor, or efferent, nerve, or nerves, with (*e*) 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. The afferent impulses started in *a*, passing along *b*, reach the centre *c*, are there transmuted into efferent impulses, which, passing along *d*, finally reach *e*, and there produce a cognisable 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<sup>1</sup>. 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

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



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 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 co-ordinated 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.

**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 shew that these possess no power whatever of reflex action. Of the larger ganglia visible to the naked eye, such as the ciliary, otic, &c., 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, &c. 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, co-ordinated 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 have already referred to an automatic respiratory centre in the medulla oblongata. We may here premise, what we shall shew 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 co-ordinated 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 are 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.

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 co-ordination 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, &c.), 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.]

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.

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. Their walls are elastic (as shewn by their behaviour during the passage of blood-corpuscles through them), exceedingly thin and permeable. They are permeable both in the sense of allowing fluids to pass through them by osmosis, and also in the sense of allowing 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, 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 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.



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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. 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 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  $\cdot 75$  mm. per sec. 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 coloured 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 corpuscles. 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 frequently 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 corpuscles, 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 distinctly 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.

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



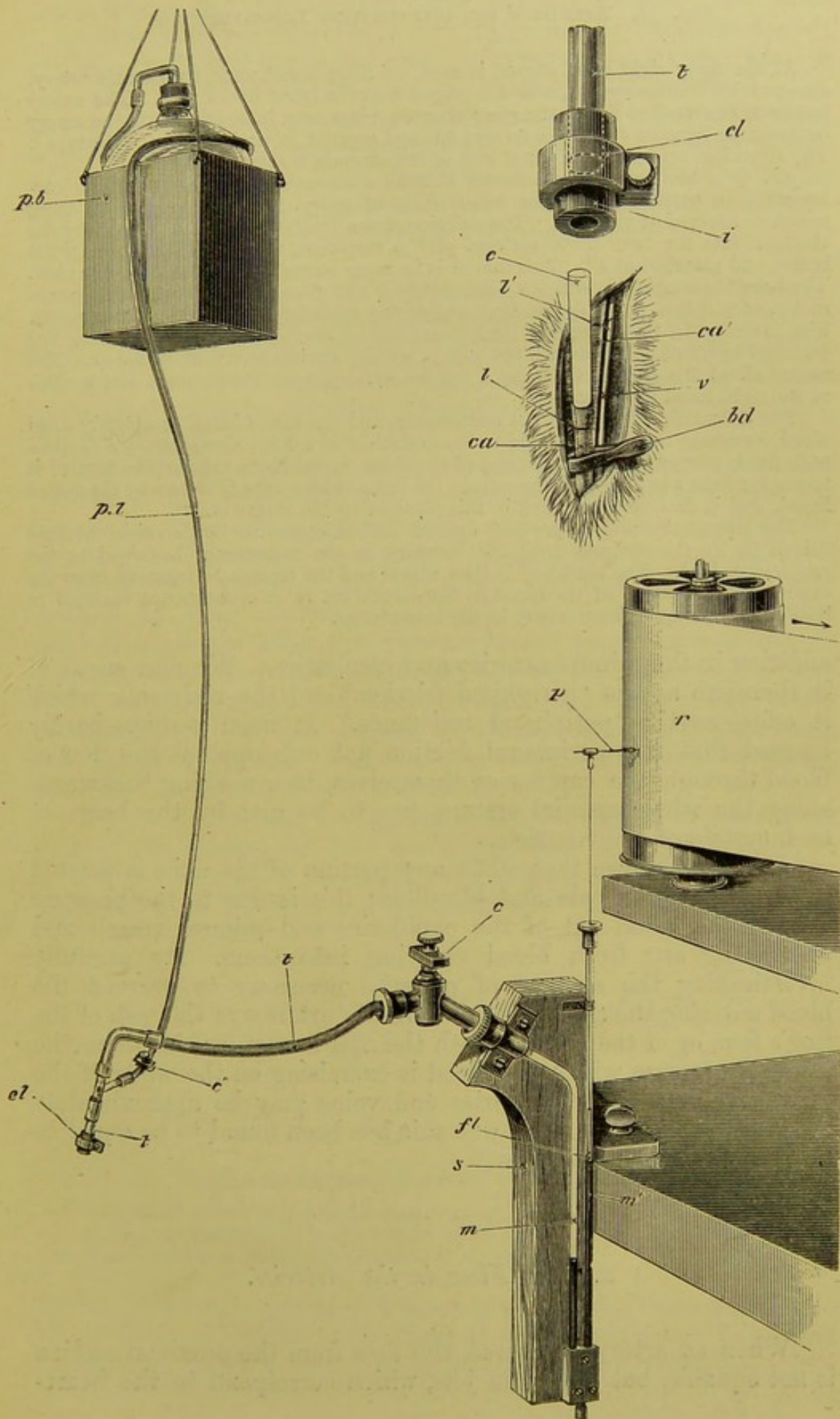




FIG. 17. APPARATUS FOR INVESTIGATING BLOOD-PRESSURE.

At the upper right-hand corner, is seen, on an enlarged scale, the carotid artery, clamped by the forceps *bd*, with the vagus nerve *v* lying by its side. The artery has been ligatured at *l'* and the glass cannula *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 cannula 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 stop-cock, 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 shewn 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 cannula *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 shewn 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.

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' 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. 17 *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 manometer, 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. 18 will be described. Each of the smaller

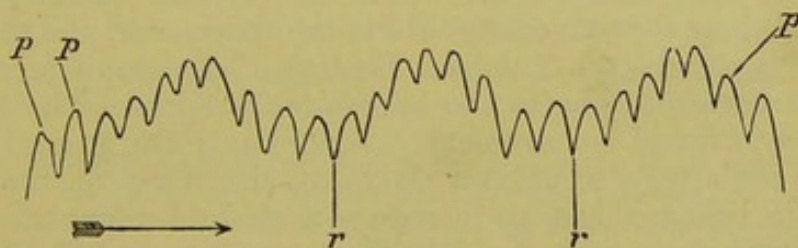


FIG. 18. TRACING OF ARTERIAL PRESSURE WITH A MERCURY MANOMETER.

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.

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 millimeters of mercury. In this lateral pressure we have further to distinguish between the slighter oscillations 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 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 T-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 T-piece. Some passes into the side limb of the T-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 T-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 T-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 cannula, Fig. 17 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 cannula has been placed, but of the vessel (aorta &c. 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. 1), or by means of a brush and ink on a continuous roll of paper, as in the more complex kymograph (Fig. 19).



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, other methods have to be adopted.

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.

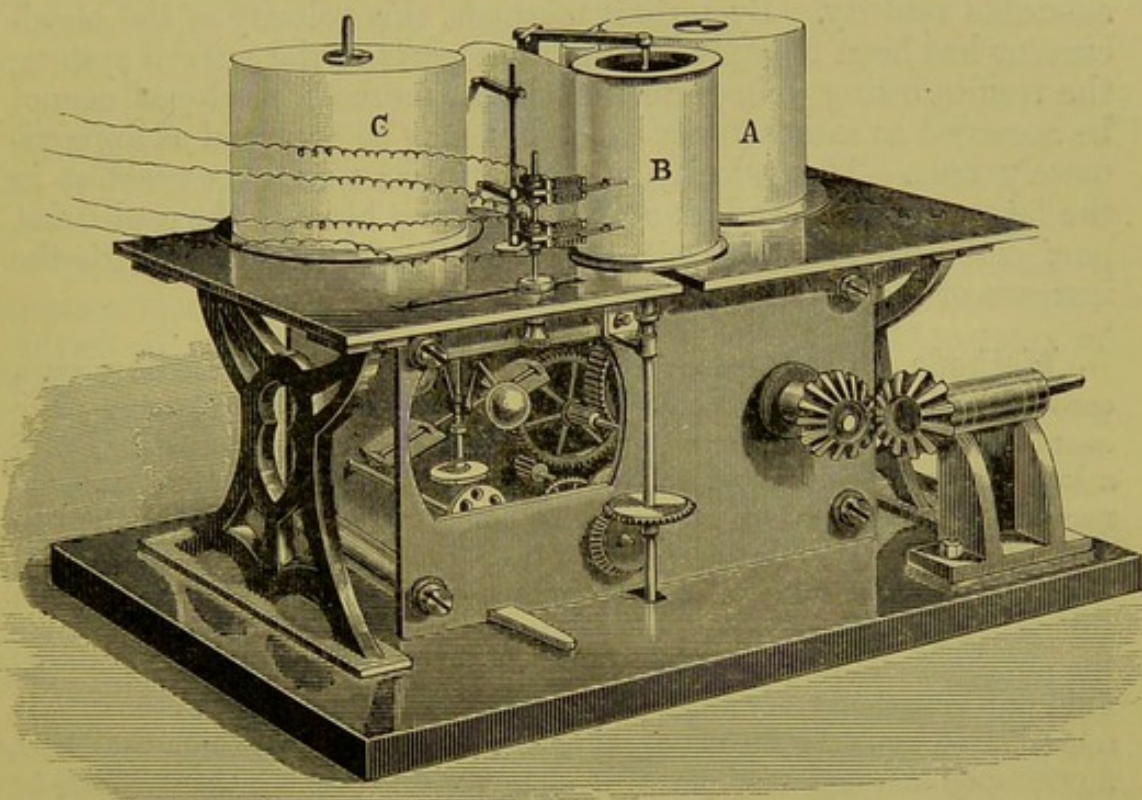


FIG. 19. LARGE KYMOGRAPH WITH CONTINUOUS ROLL OF PAPER.

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.

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 distension, 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 distension 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. An artery, *e.g.* a carotid, is clamped in two places, and divided between the clamps. Two cannulæ, 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 cannulæ 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 coloured 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 cannulæ 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.

The Rheometer (Stromuhr) of Ludwig. This consists of two glass bulbs *A* and *B*, Fig. 20, 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 disc *D*, which can be made to rotate, through two right angles, round the lower disc *E*. In the upper disc are two holes *a* and *b* continuous with *A* and *B* respectively, and in the lower disc are two similar holes *a'* and *b'*, similarly continuous with the tubes *H* and *G*. Hence, in the position of the discs shewn in the figure, the tube *G* is continuous through the two discs with the bulb *A* and the tube *H* with the bulb *B*. On turning the disc *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 disc *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.

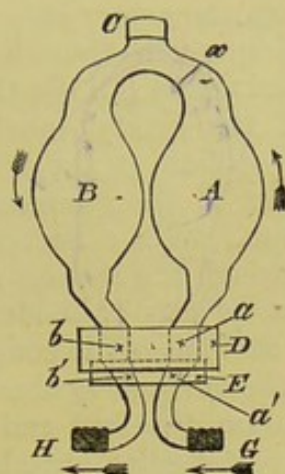


FIG. 20. DIAGRAMMATIC REPRESENTATION OF LUDWIG'S STROMUHR.

The ends of the tubes *H* and *G* are made to fit exactly into two cannulae inserted into the 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 disc *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 cannula 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 disc *D* into the position shewn 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 disc *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 disc 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 disc *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



cannula 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 *x* 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 .5 c.c. of blood had flowed from the proximal section of the artery in one second. Hence supposing that the diameter of the cannula (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 .5 c.c. or 500 c.mm. in a second would give ( $\frac{500}{3.14}$ ), a velocity of about 159 mm. in a second.

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 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 for 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 sec. 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 sec., and in the carotid of the dog from 200 to 500 mm. per sec., both these limits were 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 farther 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 neighbourhood 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 shew 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 recognised 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 sec. 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 accumulate 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 resistance, 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 condition, press on this extra quantity of fluid which they contain and tend to drive it past the resistance. Thus in the rigid system (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 remainder 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 distension of that part of the system, at the close of each stroke—an accumulation and distension, 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 resistance. 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 resistance, an additional distension 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 continually repeating the strokes a state of things will be at last arrived at, in which the elastic force, called into play by the continually increasing distension 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 intermittent 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 over-distension of the tubes on the near side of the resistance; the cause of the continuous flow lies in the over-distension 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 considerable 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 over-distension, as indicated by the arterial pressure. The over-distended 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 over-distended. This is what is meant by the high arterial pressure. On the other hand, the veins are much less distended. This is shewn by the low venous pressure. The distended 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 emptying 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 favoured by a variety of circumstances. We have seen moreover that, besides the very sudden decrease in the immediate neighbourhood 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 shews 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 farthest 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 sub-maxillary 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<sup>1</sup>. A like result occurs when, the peripheral resistance 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. ( $\cdot 5$  to  $\cdot 75$  mm.), and in the large veins at about 200 mm. in a sec. 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 secs. In the dog Vierordt found it to be 15·2 secs.; in the rabbit 7 secs.

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  $\cdot 5$  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

<sup>1</sup> See Book II cap. i. sec. 2, on the Secretion of the Digestive Juices.



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 compared 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. 127) 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.



## SEC. 2. THE HEART.

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 neighbourhood 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 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, shewing 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 behaviour 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 behaviour 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 shew 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. 21, of which the upper curve is a tracing taken

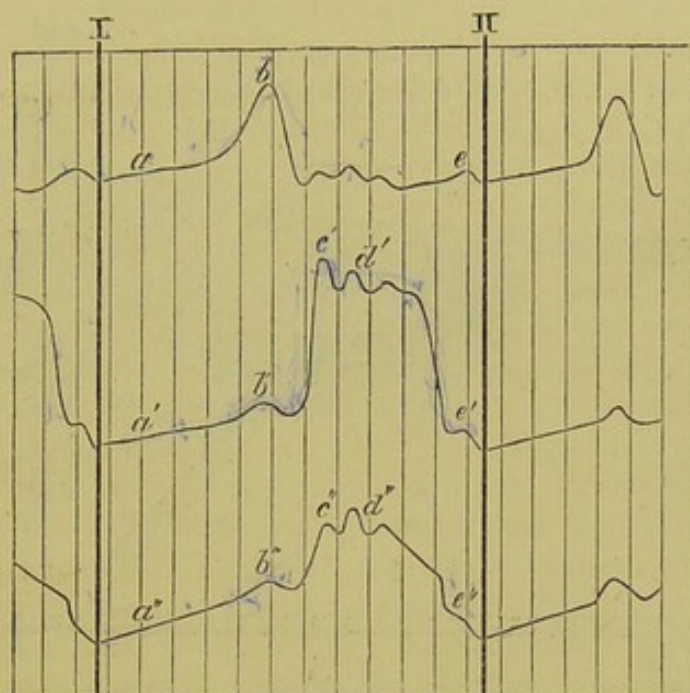


FIG. 21. SIMULTANEOUS TRACINGS FROM THE INTERIOR OF THE RIGHT AURICLE, FROM THE INTERIOR OF THE RIGHT VENTRICLE, AND OF THE CARDIAC IMPULSE, IN THE HORSE. (AFTER CHAUVEAU AND MAREY.) To be read from left to right<sup>1</sup>.

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.

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. 22 A) or 'ampulla' communicates by a separate air-tight tube with an air-tight tambour (Fig. 22 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

<sup>1</sup> 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 shew 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.



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

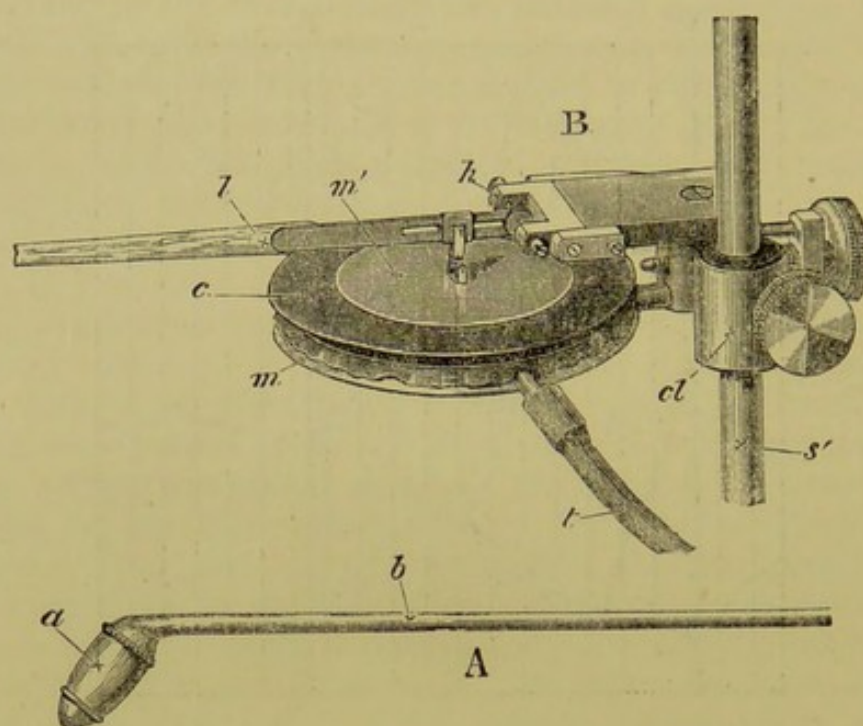


FIG. 22. MAREY'S TAMBOUR, WITH CARDIAC SOUND.

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.

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 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.

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 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 meaning 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  $\frac{1}{10}$ 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 shewn 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 figure ends, and a new cycle begins, repeating the same changes. The meaning of the features on the curves marked *e* and *d*, &c., 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. The 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; 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 commencing 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, lübb, dūp, so that the cardiac cycle, as far as the sounds are concerned, might be represented by :—lübb, dūp, 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 favour 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 to completely 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 recognisable. 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 shew 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. 138) 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

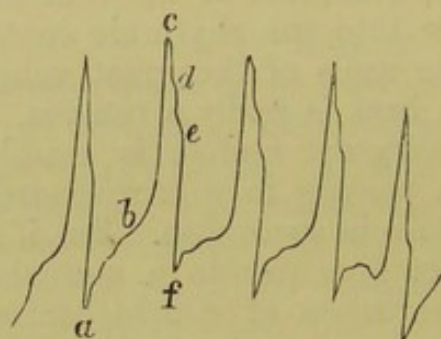


FIG. 23. CARDIOGRAPHIC TRACING OF CARDIAC IMPULSE IN MAN (from Landois).

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.

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. 22; 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. 23.

Curves of the variations in internal pressure may be obtained by passing a tube connected with a mercurial manometer (as in the investigation of arterial pressure, p. 122) 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<sup>1</sup> taken by this method is shewn in Fig. 24.

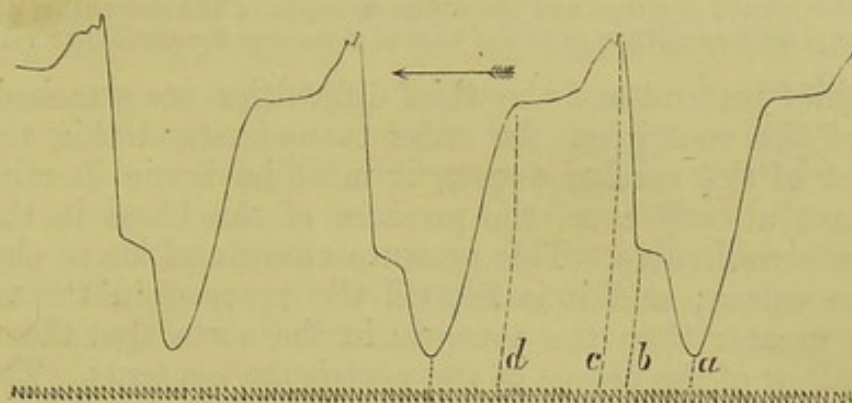


FIG. 24. Normal heart curve shewing changes in the antero-posterior diameter of the ventricle obtained from the cat by a light recording lever moved by a button which pressed gently on the anterior surface of the ventricle. The time curve gives 50 double vibrations per sec. and lines have been drawn to shew the duration of the different phases of the ventricular movement. *a* to *b* corresponds to the distension 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

<sup>1</sup> The majority of cardiographic, sphygmographic and other tracings shew 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 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. 29, p. 166. 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. 24 the intervals between *a*, *b*, *c*, *d*.) thus directly measured off.



period in this case is only about 3-50ths of a sec. 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 distension. The tracing gives no evidence as to the time of closure of the semilunar valves.

The chief interest and the chief difficulties are attached to the systole of the ventricles. In order to understand this, the most 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 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. 24 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. 21) 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, that is a tracing of the expansion of an artery, we find that the ventricle continues contracted after its contents have entirely left the cavity. 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. 24.

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. 25, 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.

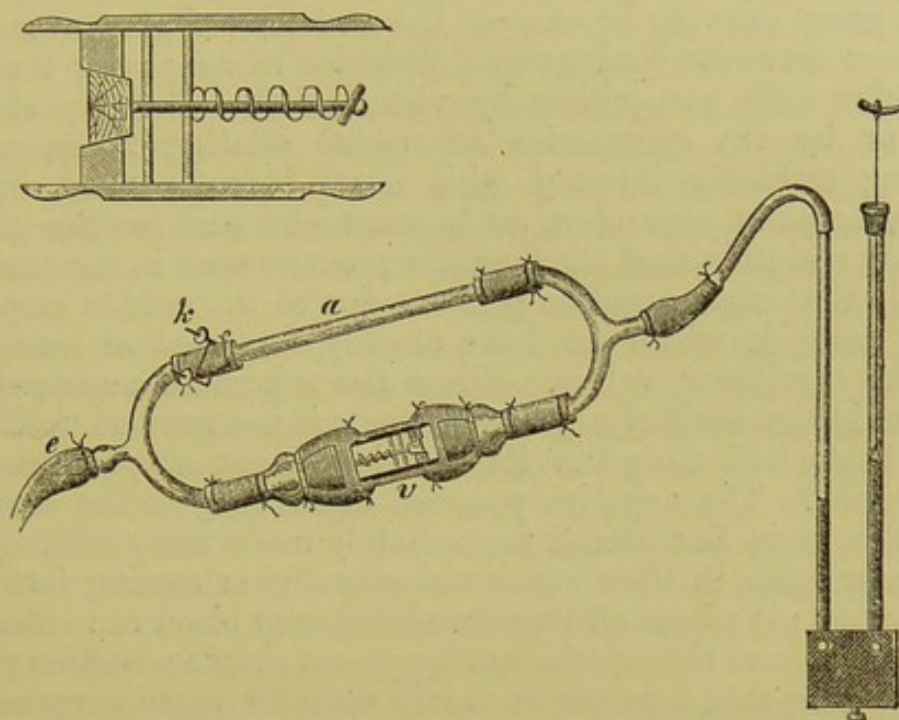


FIG. 25. THE MAXIMUM MANOMETER OF GOLTZ AND GAULE.

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 shewn 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.

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.<sup>1</sup> Part of this diminution of pressure in the cardiac cavities may 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 shews most distinctly 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 time at which it takes place. Goltz and Gaule, to

<sup>1</sup> These numbers are to be considered merely as instances which have been observed, and not as averages drawn from a large number of cases.



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. 21 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  $\frac{6}{10}$  sec.) 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  $\frac{4}{10}$  sec.), and the shortest (viz. rather less than  $\frac{2}{10}$  sec.) 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 .301 to .327 sec.,



occupying from 40 to 46 p. c. 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 .3 sec. 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 .085 sec. 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 sec.

Deducting these two periods from the total period of 0.3 sec., there would be left a period of 0.115 sec., 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 sec., and taking 0.3 sec. as the duration of the systole, the deduction of this would leave 0.5 sec. 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 sec. 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.

	secs.	secs.
Systole of ventricle <sup>le</sup> 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 ven- tricle 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  $\frac{8}{10}$  sec. occupying the whole cardiac cycle,  $\frac{3}{10}$  sec. or possibly rather more are taken up by the systole, and  $\frac{5}{10}$  sec. 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 shew merely the general relations of the several events and not to represent exact measurements.

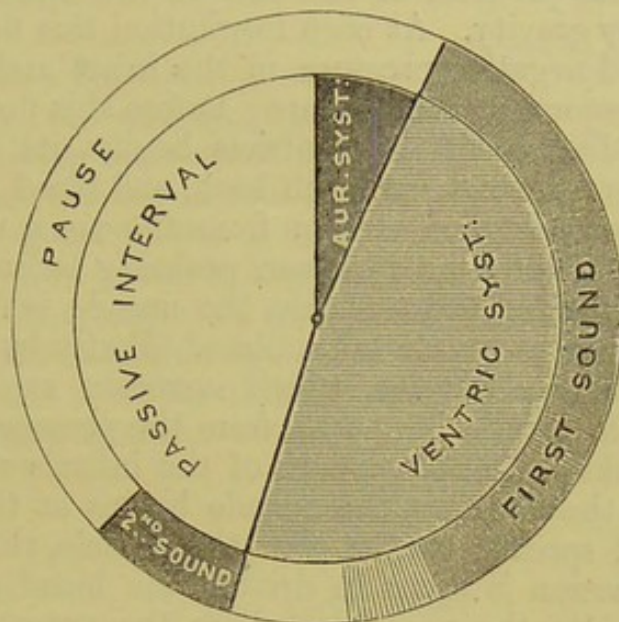


FIG. 26. DIAGRAMMATIC REPRESENTATION OF THE MOVEMENTS AND SOUNDS OF THE HEART DURING A CARDIAC PERIOD. (After Dr SHARPEY.)

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 favoured 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. Coincidentally 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 perhaps the most important factor of all in the determination of the work of the vascular mechanism, the quantity ejected from the ventricle into the aorta at each systole, cannot be accurately determined; we are obliged 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 ventricle 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  $\cdot 0025$  p. c. of 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 grm., and in a second case at 77 grm.

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.<sup>1</sup> 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 ascent of Snowdon by a tolerably heavy man. A calculation of more practical value is the following. Taking the quantity of blood as  $\frac{1}{13}$  of the body weight, the blood of a man weighing 75 kilos would be about 5,760 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.

<sup>1</sup> A high estimate is purposely taken here.



*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 some or other of the 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 .327 to .301 sec., 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 is placed on the artery, the lever is 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 distension 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.

If two levers be placed on the arterial tubes of an artificial<sup>1</sup> 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.

<sup>1</sup> 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.



1. With each stroke of the pump, each lever (Fig. 27, I. and II.) rises to a maximum, 1a, 2a, and then falls again, thus describing a curve,—the pulse-curve. This shews that the expansion of the

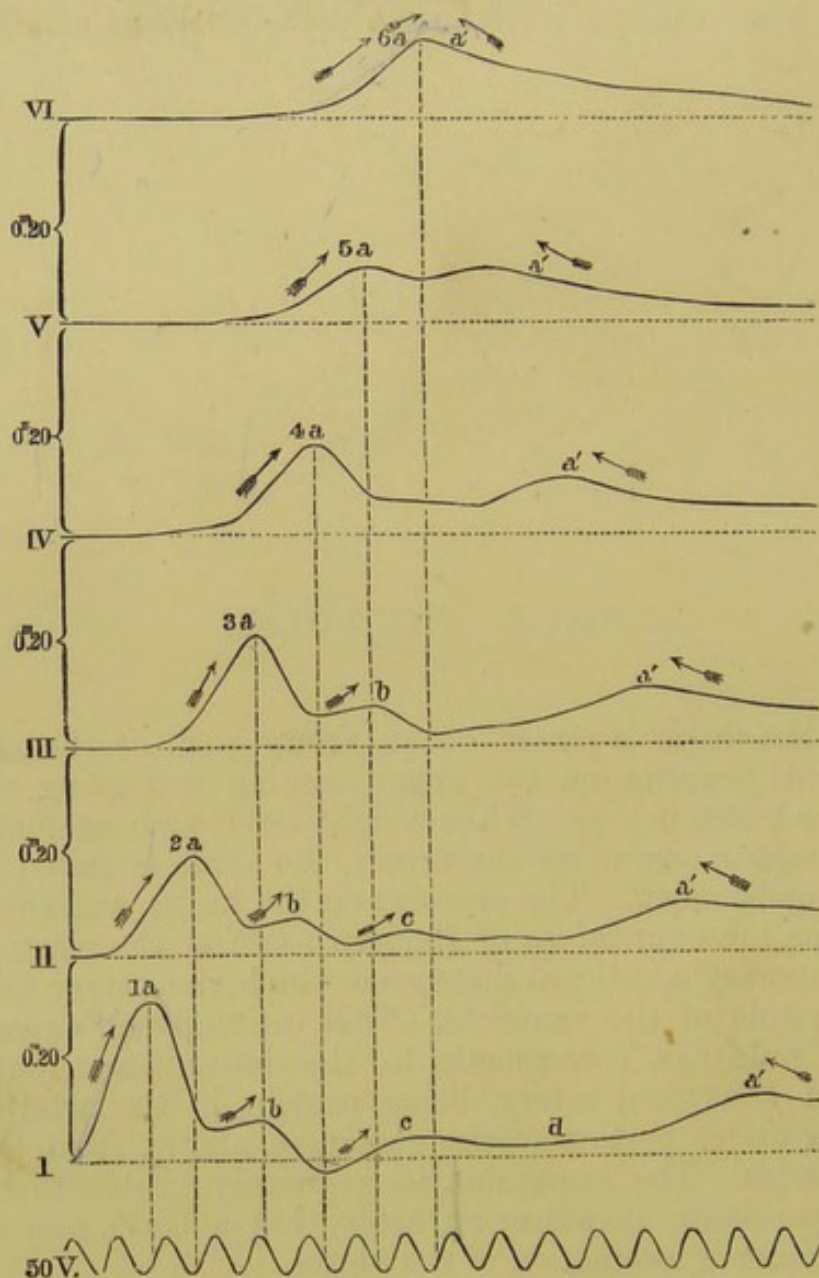


FIG. 27. Pulse-curves described by a series of sphygmographic levers placed at intervals of 20 cm. from each other along an elastic tube into which fluid is forced by the sudden stroke of a pump. The pulse-wave is travelling from left to right, as indicated by the arrows over the primary (a) and secondary (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  $\frac{1}{50}$  sec., allow the time to be measured which is taken up by the wave in passing along 20 cm. of the tubing. The waves a' are waves reflected from the closed distal end of the tubing; this is indicated by the direction of the arrows. It will be observed that in the more distant lever VI. the reflected wave, having but a slight distance to travel, becomes fused with the primary wave. (From Marey.)

tubing passes the point on which the lever rests in the form of a wave. At one moment the lever is quiet: the tube beneath it is simply distended to the normal permanent amount 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 with 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 shewn 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. 27, II.) commences later than the near one (Fig. 27, I.), the farther apart the two levers are, the greater is the interval in time between their curves. Compare the series I. to VI. (Fig. 27). 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. 27. 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 gradually flatten out 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 sec., while that of the current of blood is not more than half a metre per sec. 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 sec., will before it is completed have reached a point  $\frac{4}{10}$  of 5m. = 2 m. distant from the ventricle. But even in the tallest man the tips of the toes are not 2 m. 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 that 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

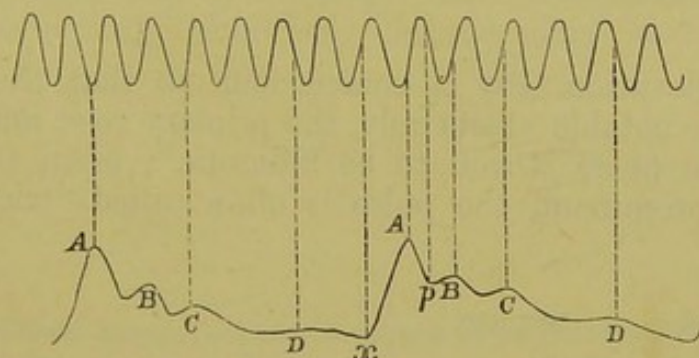


FIG. 28. PULSE-TRACING FROM CAROTID ARTERY OF HEALTHY MAN<sup>1</sup> (from Moens).

x, 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.

<sup>1</sup> 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, &c.—and are some from man, others from animals. They are introduced simply to illustrate points treated of successively in the text.



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. 28 and 29 and in many of the other tracings given, these secondary elevations are marked as B, C, D. When one such

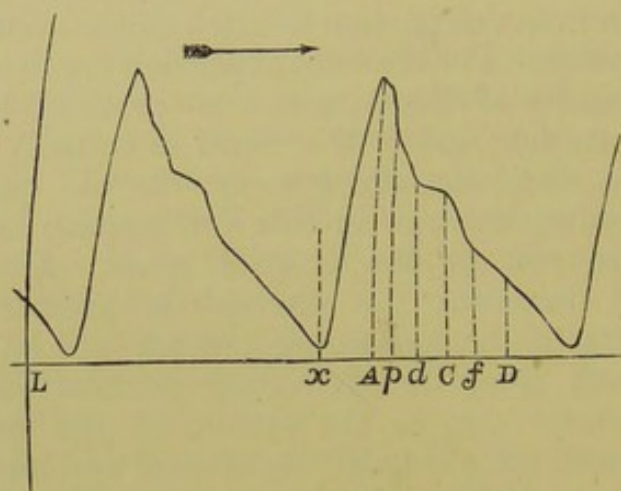


FIG. 29. PULSE-CURVE FROM RADIAL OF MAN.

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 shew 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.

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

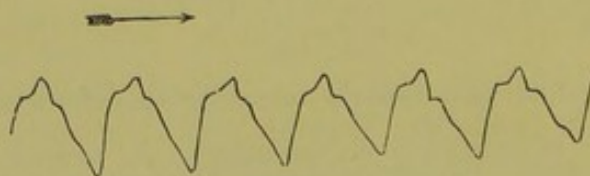


FIG. 30. ANACROTIC PULSE-TRACING FROM THE CAROTID OF RABBIT.

several "polycrotic." As a general rule, the secondary elevations 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 not the highest but



appears on the ascending portion of the main curve as in Fig. 30 and Fig. 33: 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 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. 31), *i.e.* a pulse which can be felt as double 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

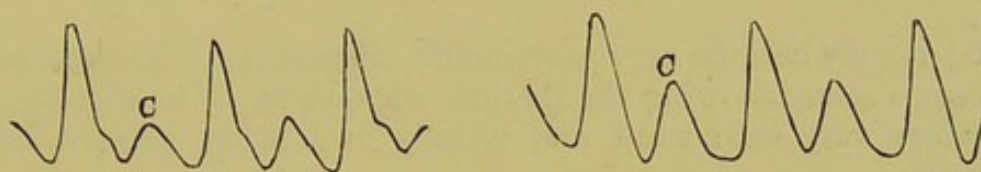


FIG. 31. TWO GRADES OF MARKED DICROTISM IN RADIAL PULSE OF MAN.  
(Typhoid Fever.)

notch." Neither it nor any other secondary elevations can be recognised in the tracings of blood-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 delicately 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

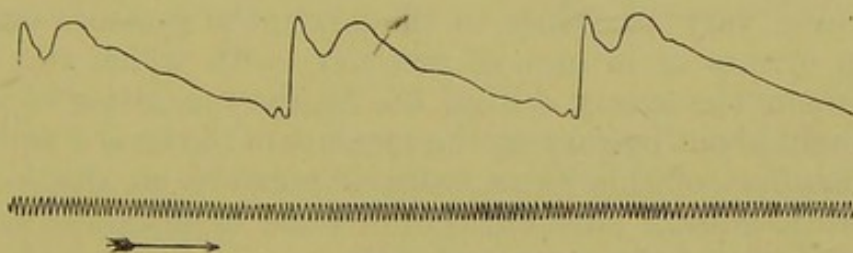


FIG. 32. NORMAL PULSE-CURVE IN THE AORTA FROM THE DOG.

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, shewed in an unmistakeable 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 higher up on the descending limb of the main wave; it is marked B on some of the curves and is frequently called the *predicrotic*

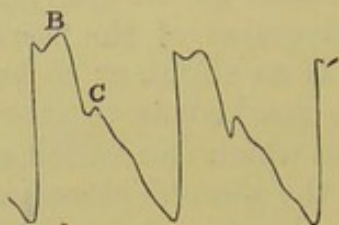


FIG. 33. ANACROTIC SPHYGMOGRAPH TRACING FROM THE ASCENDING AORTA (Aneurism).

wave; it may become very prominent. Sometimes other secondary waves are seen following the dicrotic wave as at D in Fig. 28; 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 many characteristic forms of pulse-curve. Moreover in the same artery,

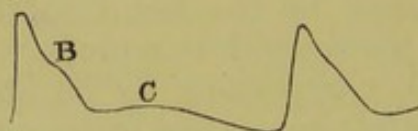


FIG. 34. PULSE-TRACING FROM THE DORSALIS PEDIS.

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. 35, 36 shew a series of changes thus brought about by varying the pressure of the lever; and Fig. 37 shews 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, 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

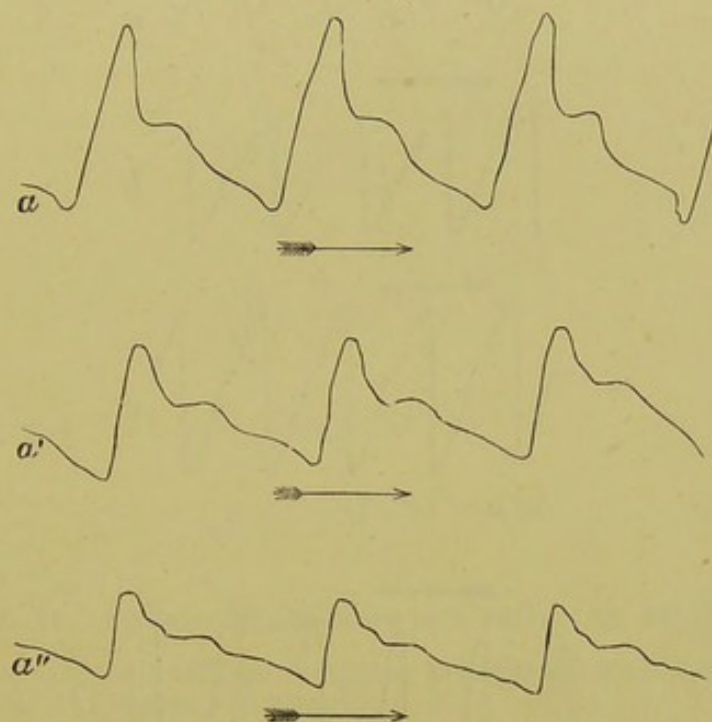


FIG. 35. INFLUENCE OF CHANGES IN THE PRESSURE APPLIED TO THE EXTERIOR OF THE VESSEL ON THE FORM OF THE CURVE.

*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.

(Fig. 27, VI. *a'*), but at the near lever is at some distance from it (Fig. 27, I. *a'*), being the farther 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 farther back we trace it. Now this is not the case with the dicrotic wave. Careful measurements shew that the distance between the primary and dicrotic crests is either greater

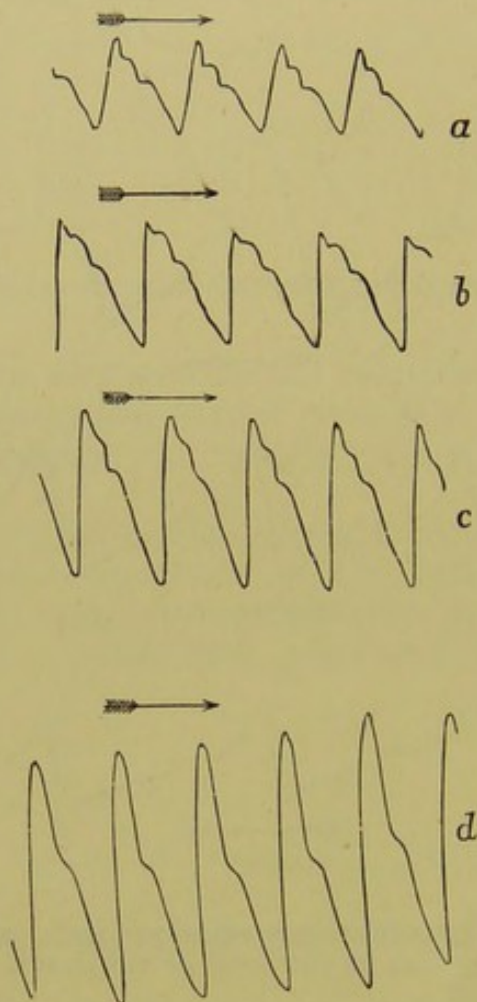


FIG. 36. NORMAL PULSE-CURVE FROM CAROTID OF RABBIT;

shewing 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 *d* 50 mm. of mercury.

or certainly not less in the smaller or more distant arteries 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 favourable 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.

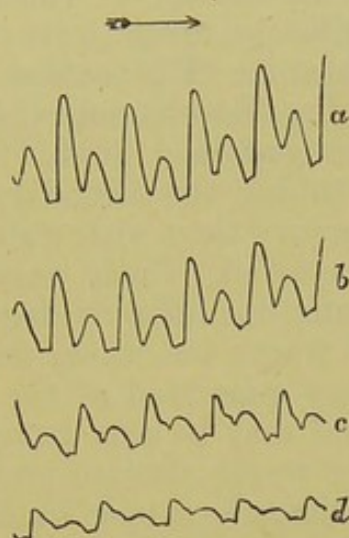


FIG. 37. DICROTIC PULSE-CURVE DUE TO LOSS OF BLOOD.

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.

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 diminution of pressure. This diminution will appear on a graphic record of the pressure as a depression or notch; and will be followed by a secondary rise as a reflux of fluid takes place towards the point where the pressure has become diminished. Both the 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 movement of expansion some little time after the actual expanding force has ceased to act. This leads to a falling back or contraction, 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 oscillations 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 than with water, and disappear almost wholly when air is employed. Such waves of oscillation may be supposed to be generated in different degrees, in each and 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 in 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 contraction of the arterial walls following up so to speak the arterial beat.

We have dwelt at so great a length on these secondary 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 finally settled, all interpretations 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 origin 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 favoured 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. 31) 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 shewn in Fig. 38. It may similarly be induced by

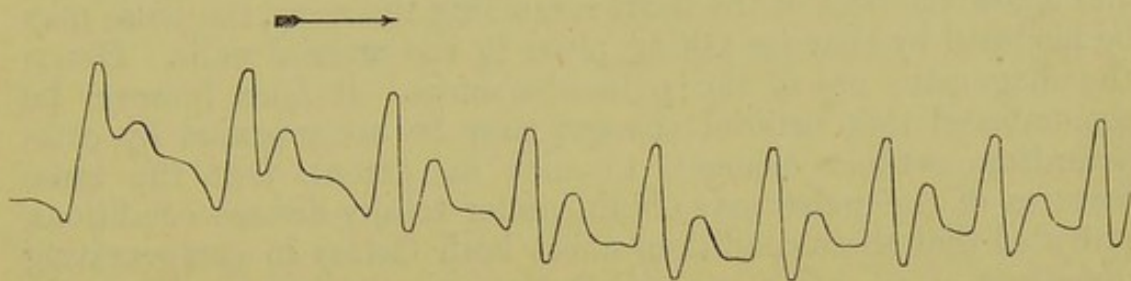


FIG. 38. TRACING FROM RADIAL IN MAN;

shewing 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 condition known as hyperdicrotism, where the dicrotic notch reaches a level lower than that from which the primary rise started.

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.

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 associated 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 insufficient 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 vaso-motor nerves, of which we shall presently speak, to a dilation of the small arteries of the gland. This dilation 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. 129), 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 neighbourhood of the heart shew 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 distension travelling backwards from the heart be-



comes 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 blood-vessels, 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 two first 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 affecting 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, &c.) and changes of form, due either to distension 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 cannula 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' cannula, Fig. 39 I., with a double tube, one inside the other, and tying the ventricle on to the cannula 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. 39 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

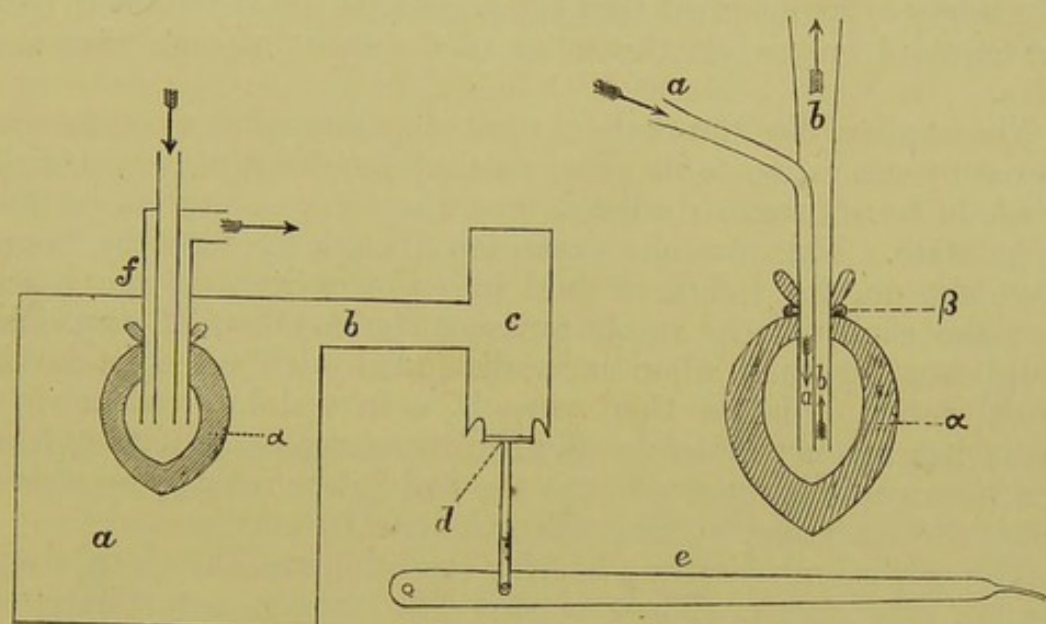


FIG. 39. PURELY DIAGRAMMATIC FIGURES OF

I. Perfusion cannula tied into frog's ventricle. *a*, entrance, *b*, exit, tube; *α*, 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 cannula *f*. *b*, tube leading to cylinder *c*, in which moves piston *d*, working the lever *e*.

of the 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 recognised 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. 57) under certain circumstances is readily developed.

Under the influences of certain poisons, veratrin, digitalin, &c., 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. 85). 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. 96) 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 (see p. 87), 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 favourable 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 the 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 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 vigour 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, from 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 independently 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" cannula 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 cannula, 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 shew 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. 40) 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 vigour 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 tumour 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. 40), when the current is

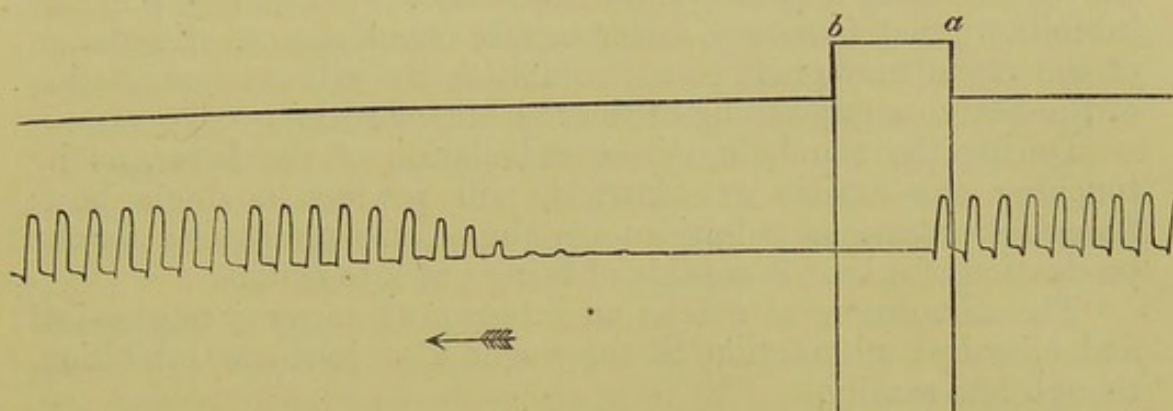


FIG. 40. INHIBITION OF FROG'S HEART BY STIMULATION OF THE VAGUS.

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.

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 .16 sec. The inhibitory effect is at a maximum soon after the moment of application of the current, and diminishes gradually onward; so much so is this the 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 vigour, 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 shewn in Fig. 40, 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 vigour 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 paralyse 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 in-



ferred that atropin, unlike urari, paralyses this intrinsic inhibitory mechanism itself.

After the application of muscarin<sup>1</sup> 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 paralyses 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 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. 183. 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

<sup>1</sup> The poisonous effects of many mushrooms are probably in large measure due to a similar action on the heart.



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 shews 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 in 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 shewing 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 processes originating in certain nerve cells, or reflex, that is, maintained 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 permanent 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 inhibitory 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 lessening 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 vertebral 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. 41 and 42, 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

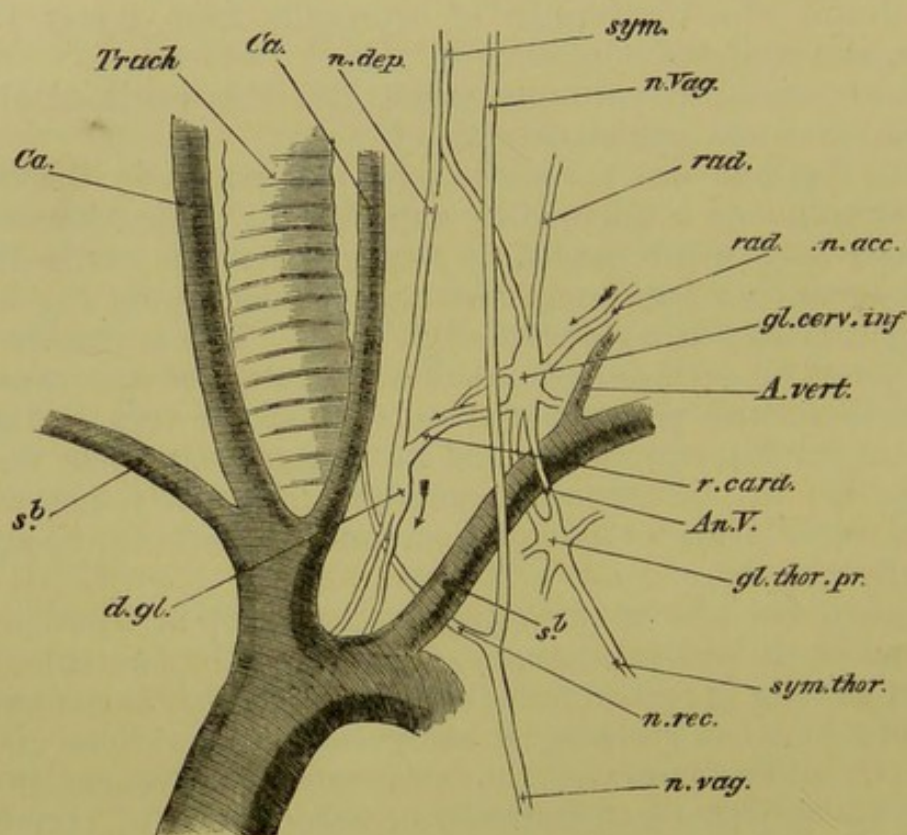


FIG. 41. THE LAST CERVICAL AND FIRST THORACIC GANGLIA IN THE RABBIT. (Left side.) (Somewhat diagrammatic, many of the various branches being omitted.)

*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 shewn, *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 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.



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.

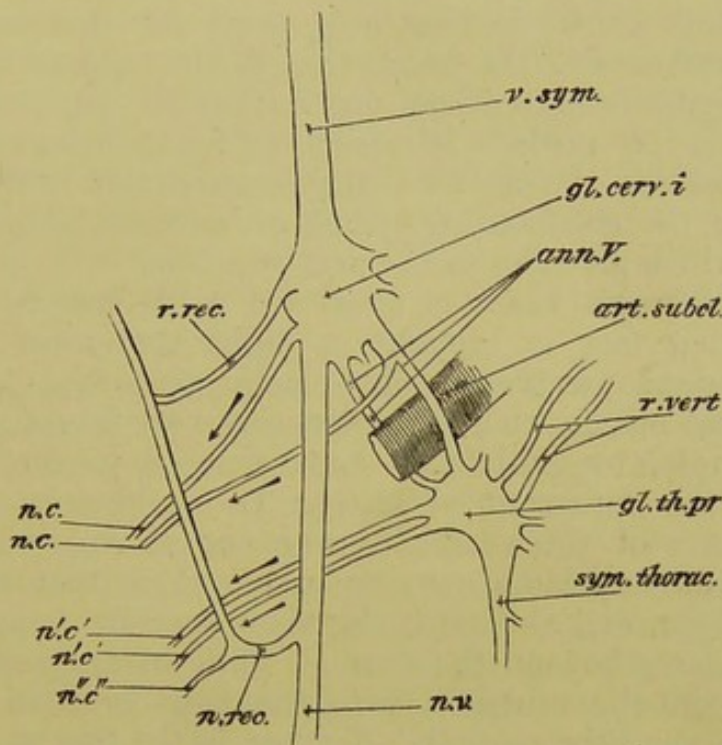


FIG. 42. THE LAST CERVICAL AND FIRST THORACIC GANGLIA IN THE DOG.

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. *r. vert.* communicating branches from the cervical nerves running alongside 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.

After a while however the beats diminish and disappear; 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. 179, with diluted blood (of the rabbit, sheep, &c.) it may be restored to functional activity. A similar but less complete restoration may be witnessed if serum be used 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 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 distension of its cavities. The contractions of cardiac muscle, like those of ordinary muscle (see p. 87), 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 increased quantity would be ejected with greater force. Further, since the distension 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. 43 will be obtained. It will be observed that immediately after the last beat, there is a sudden rapid fall of the blood pressure.

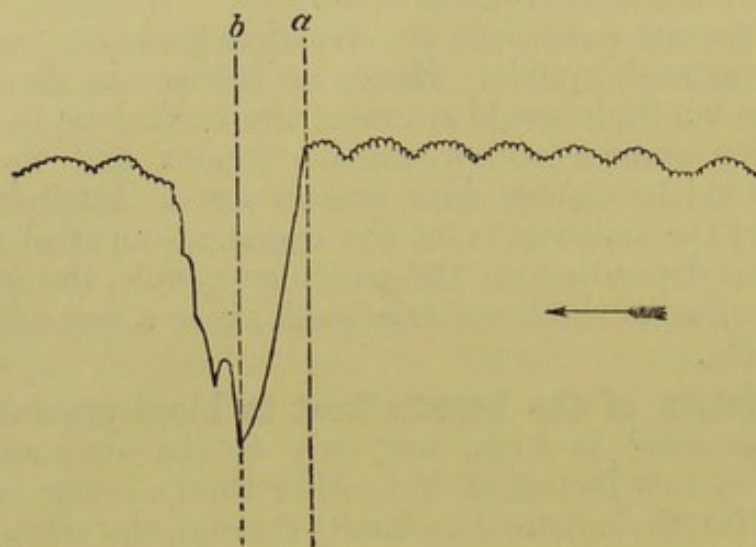


FIG. 43. TRACING, SHEWING THE INFLUENCE OF CARDIAC INHIBITION ON BLOOD-PRESSURE. FROM A RABBIT.

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.

At the pulse due to the last systole, the arterial system is at its maximum of distension; 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



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.

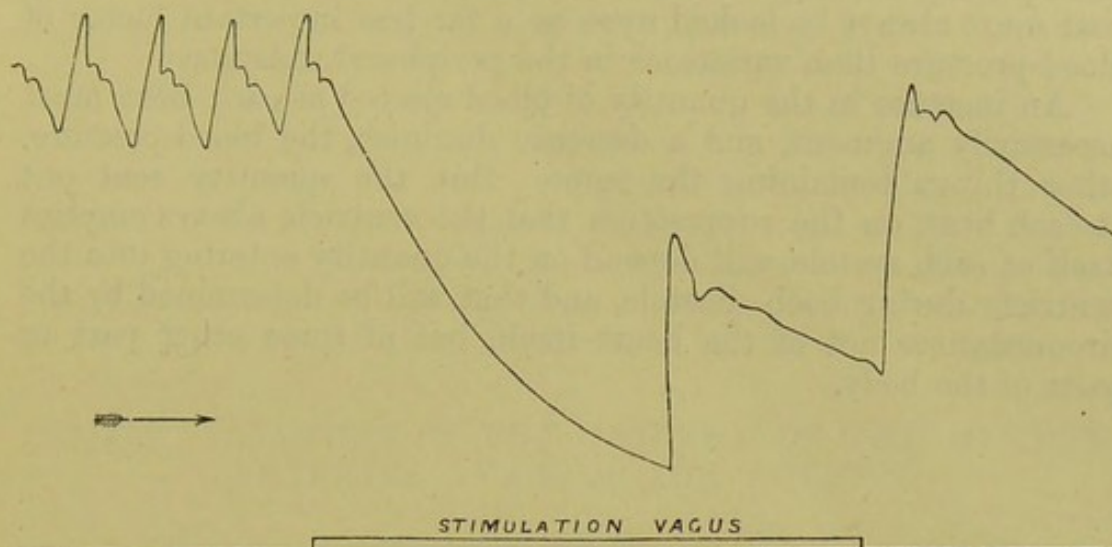


FIG. 44. VAGUS STIMULATION.

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. Shews the fall of blood-pressure, and the character of the first recommencing beats.

Complete arrest of the heart-beats is not necessary to produce a fall of pressure. As is seen in Fig. 45, mere slowing of the beats will lower the mean pressure. And, speaking generally, we may say

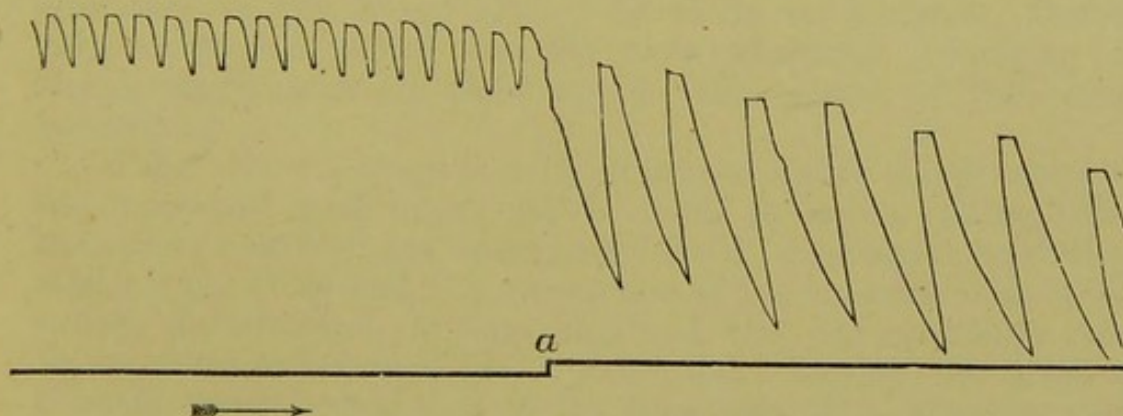


FIG. 45. STIMULATION OF VAGUS.

Blood-pressure curve taken with mercury manometer. The effect is to slow the rhythm rather than to bring about complete standstill. With the slow pulse the pressure still continues to fall. The beginning of stimulation is marked by *a*.

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 case; but obviously it is quite possible that the beats might, while more frequent, so lose in force, or while less frequent, so increase in force, that no difference in the mean pressure should result. And this indeed is not unfrequently the case. So much 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 blood-vessels, 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 somewhat 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 shew 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 on the same side, shewn 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 shews a rise of temperature amounting, it may be, to several degrees.

The quantity of blood present in the blood-vessels 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 blood-vessels of the front limb. Division of the splanchnic nerve produces a dilation of the blood-vessels 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 shew 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. 129) 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 shew.



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. 46. 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 blood-vessels 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 blood-vessels of the hind limb and of the brachial nerves governing those of the fore limb. 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 blood-vessels, 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. 41, *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. 46). 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

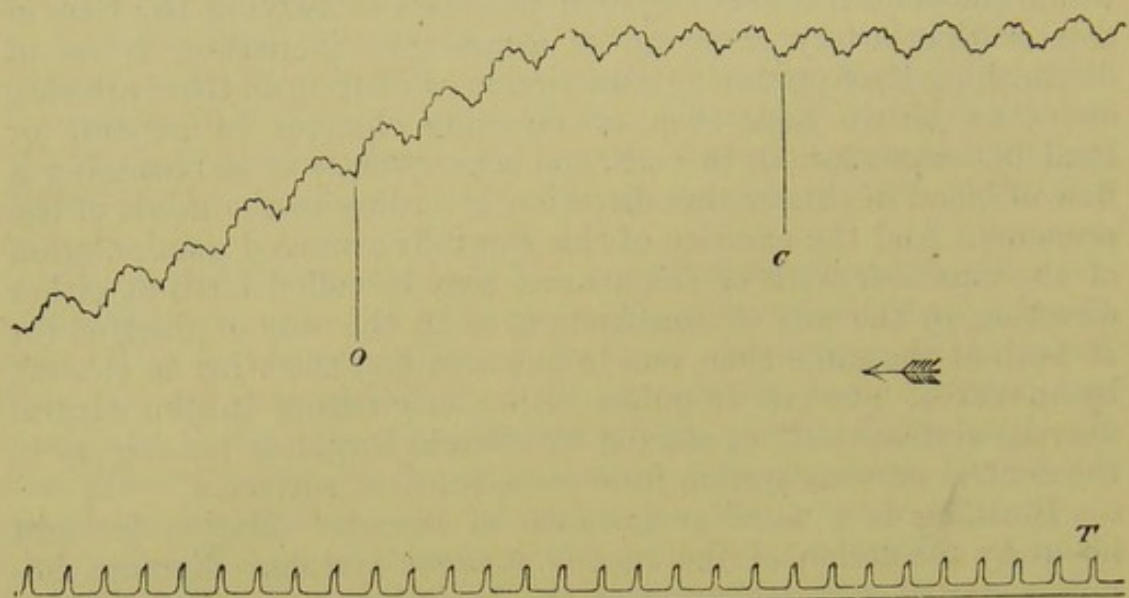


FIG. 46. TRACING, SHEWING THE EFFECT ON BLOOD-PRESSURE OF STIMULATING THE CENTRAL END OF THE DEPRESSOR NERVE IN THE RABBIT.

(To be read from right to left.)

*T* indicates the rate at which the recording surface was travelling; the intervals marked corresponds 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.

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 vasomotor fibres is in the direction of constriction leading to a rise, or of dilation leading to a fall of blood-pressure.

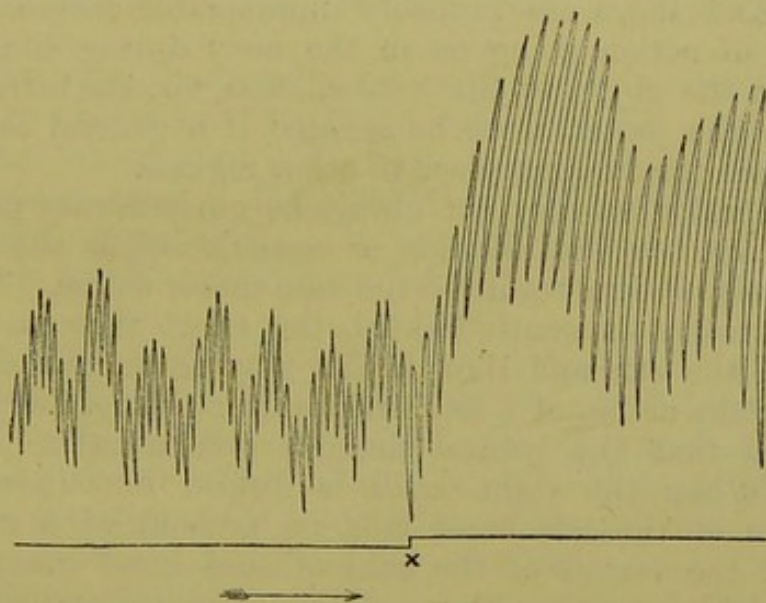


FIG. 47. RISE OF BLOOD-PRESSURE FROM STIMULATION OF NOSTRIL WITH SMOKE.

The respiration and cardiac rhythm are at the same time rendered more slow.  
The mark x indicates the time of stimulation.

Stimulation of a sentient surface in many cases causes a similar rise in blood-pressure as shewn in Fig. 47, 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 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 shewn 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 constriction 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 shews 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 shew 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. 198, 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 mylo-hyoid 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 experi-



menter 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 unmistakeable; 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 shewn 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, &c.; of the second, in the cervical sympathetic, the splanchnic, &c. 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 4mm. 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 grey 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. 188, need not be discussed here. Granting even the existence of such automatic functions, 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 impulses 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-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 re-established; 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 favour 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 word and governs the work of the whole organ, so the medullary vaso-motor centre rules and co-ordinates 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 pulsations 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 sub-maxillary 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 differently, 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 oxy-hæmoglobin of the corpuscles is deoxidised 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 increase 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. 116) 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 intra-vascular 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 shewn 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 increase 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 inflammation 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 forerunner 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 observed that the red 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 enormously distended, the stream becomes slower and slower, until at last the movement of the blood in the affected area ceases altogether. The phase of accelerated flow has given place to stasis. The capillaries, veins and small arteries are choked with corpuscles, 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 neighbouring currents, little by little the whole obstruction is removed, the current through the area is re-established, 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 shewn 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 blood-vessels 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 blood-vessels; 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 blood-vessels 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 shew 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 blood-vessels,



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 adhesion, 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 shews 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<sup>1</sup>, 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 hæmorrhage, is witnessed so long as the loss of blood does not amount to more than about 3 per cent. of

<sup>1</sup> 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.



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 blood-vessels 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.

These facts shew, 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 shew that a much greater quantity of blood can be lodged in the blood-vessels 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 shew 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 distension 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 distension 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, &c. &c.

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. 225).

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,

a. 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 blood-vessels 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-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.

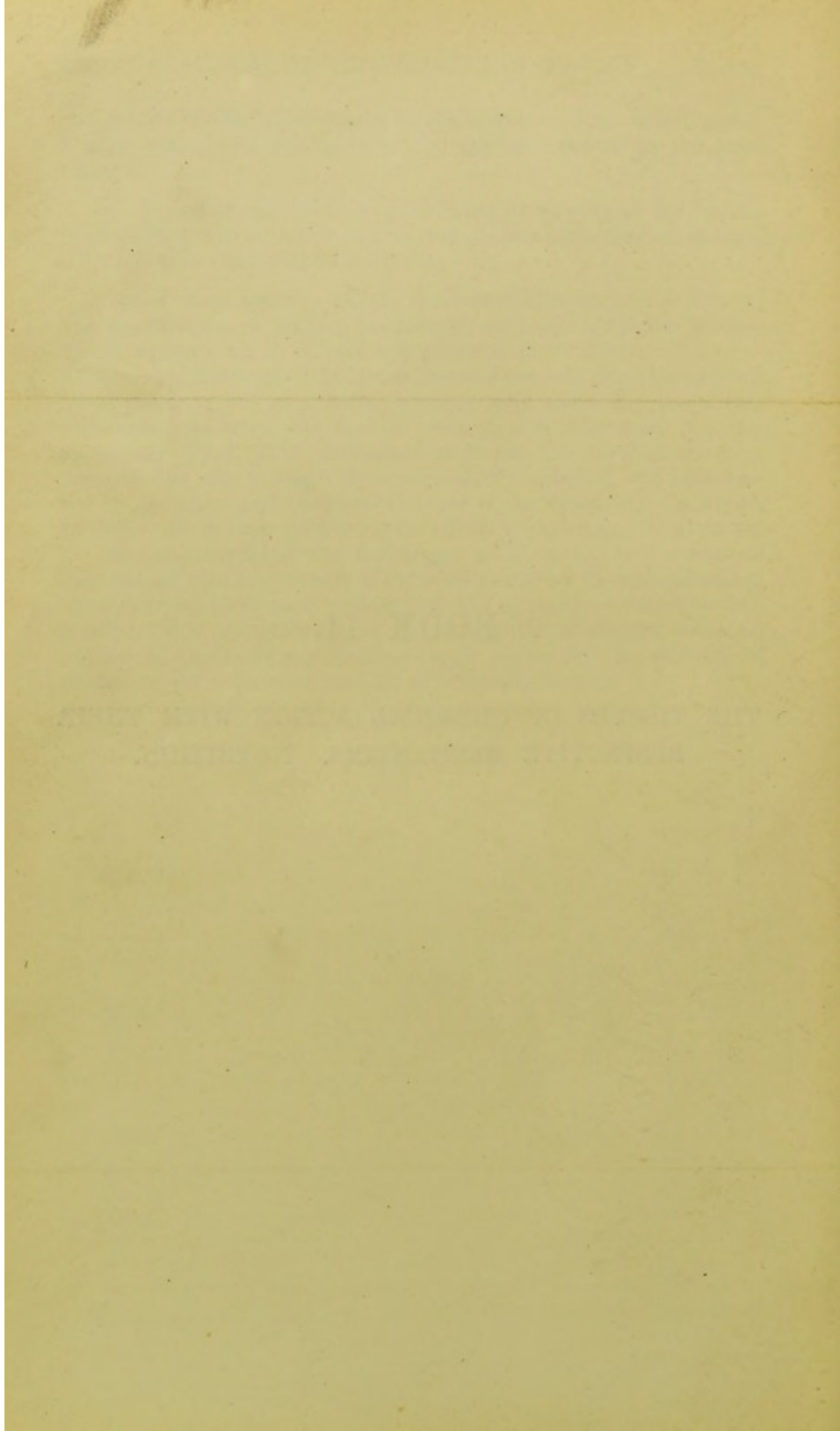
On the other hand, the turbulence which would be the natural outcome of all these events is softened down, by the compensating effects of which we have spoken, into the smoothness which we call health. Still, the greatness of the possibilities of change which lie hidden in the body are clearly enough shewn by the violence of disease, when compensation fails of accomplishment.



## BOOK II.

THE TISSUES OF CHEMICAL ACTION WITH THEIR  
RESPECTIVE MECHANISMS. NUTRITION.







## CHAPTER I.

### THE TISSUES AND MECHANISMS OF DIGESTION.

THE food in passing along the alimentary canal is subjected to the action of certain juices which are produced by the secretory activity of the epithelium-cells lining the canal itself or forming part of its glandular appendages. These juices (*viz.* saliva, gastric juice, bile, pancreatic juice, and the secretions of the small and large intestines), 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—First, the properties of the various juices, and the changes they bring about in the food eaten. Secondly, 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. Thirdly, 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. Fourthly and lastly, the means by which the nutritious digested material is separated from the undigested or excremental material, and absorbed into the blood.



## SEC. 1. THE PROPERTIES OF THE DIGESTIVE JUICES.

### *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, besides the molecular débris of food (and frequently cryptogamic spores), epithelium-scales, mucus-corpuscles and granules, and the so-called saliva corpuscles. Its reaction 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 acid. Saliva contains but little solid matter, on an average probably about .5 p. c., the specific gravity varying from 1.002 to 1.006. Of these solids, rather less than half, about .2 p. c., are salts (including a small quantity of potassium sulphocyanate). The organic bodies which can be recognised 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 characteristic 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 viscosity 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 carbohydrates: 1. *Starch*, which forms with water not a true solution but a more or less viscid mixture, and gives a characteristic blue colour with iodine. 2. *Dextrin*, differing from starch in forming a clear solution and in giving a red colour with iodine. 3. *Dextrose*, also called glucose or grape-sugar, giving no colouration with iodine, but characterised by the power of reducing cupric and other metallic salts; thus, when dextrose is boiled with a fluid often known as Fehling's fluid, 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, give 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 colouration 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 colour 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 colour 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 gives no blue colour at all, or very much less colour, shewing 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, shewing 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 colour instead of a pure blue, but when the conversion is complete no colouration at all is observed. The appearance of this red or violet colour indicates the presence of dextrin.

The temporary appearance of dextrin shews 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 amyolytic 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°—40°, or even a little higher, favours 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 amyolytic 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. 2nd, the close dependence of its activity on temperature. 3rd, its permanent and total destruction by a high temperature 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*<sup>1</sup>; and we may henceforward speak of the amylolytic ferment of saliva.

<sup>1</sup> Ferments may, for the present at least, be divided into two classes, commonly called *organised* and *unorganised*. Of the former, yeast may be taken as a well-



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 cannula into the opening of the Stenonian duct, and submaxillary saliva, or rather a mixture of submaxillary and sublingual saliva, by similar catheterisation of the Whartonian duct. In animals the duct may be dissected out and a cannula 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 albumin, 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 viscosity, 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 p.c.), 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 sub-

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.



maxillary 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.

### *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 colourless fluid with a sour taste and odour.

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 abdominal 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, &c.

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 shewn 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 .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 a free acidity corresponding to .2 p. c. 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 .2 p. c. 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, &c.), arising from the digestion of the mucous membrane itself<sup>1</sup>.

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 .2 p. c. (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 of gastric juice, and the mixture be exposed to a temperature of from

<sup>1</sup> These however may be removed by concentration at 40° C., and subsequent dialysis.



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 debris, 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 pieces 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, *ceteris 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 shewn 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, boiling produces no coagulation whatever. By neutralisation, 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 neutralisation 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 neutralisation 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



neutralisation, 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 neutralisation; 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 neutralisation, it is not, like the other similarly soluble proteids, coagulated by heat.

2nd. 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 the other less important reactions see Appendix.)

The neutralisation 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 gastric 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 Grützner's method is the most convenient.

Portions of well washed fibrin are stained with carmine and again washed to remove the superfluous colouring matter. A fragment of this coloured fibrin thrown into an active juice on becoming dissolved, gives up its colour to the fluid, and if the same stock of coloured 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 coloured 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 favour 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. Neutralisation of the juice wholly arrests digestion; fibrin may be submitted for an almost indefinite time to the action of neutralised gastric juice without being digested. If the neutralised juice be properly acidified, it may again become active; in gastric juice however which has been made alkaline, and kept at a temperature of  $35^{\circ}$ , the solvent powers are not only suspended but actually destroyed. Digestion is most rapid with dilute hydrochloric acid of .2 p.c. (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, &c. 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  $35^{\circ}$ — $40^{\circ}$  C.; at the ordinary temperature it is much slower, and at about  $0^{\circ}$  C. ceases altogether. The juice may be kept however at  $0^{\circ}$  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  $40^{\circ}$  or  $45^{\circ}$  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 p.c.), 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 shew 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 gelatinisation 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*<sup>1</sup>, 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 favoured 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 pre-

<sup>1</sup> See Appendix.



precipitate thus formed, readily curdles milk, but even when acidified has no peptic action on proteids, shewing 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.

### *Bile.*

The quality 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 colour 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, &c. ... ..	9.2
Cholesterin ... ..	2.6
Mucus and Pigment ... ..	29.8
Inorganic Salts ... ..	7.8
	<hr/> 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 (.2 to .27 per cent.), the presence of phosphates, of iron (about .006 p. c.), 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 colour 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-coloured 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 colours 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 colours as 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.

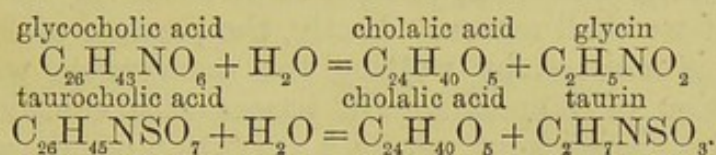
Insoluble in ether but soluble in alcohol and in water, the aqueous solutions having a decided alkaline reaction, both salts may be obtained by crystallisation in fine acicular needles. They are exceedingly deliquescent. The solutions of both acids have a dextro-rotatory action on polarized light.

**Preparation.** Bile, mixed with animal charcoal, is evaporated to dryness and extracted with alcohol. If not colourless, 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



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 colour (Pettenkofer's test) with a characteristic spectrum. A similar colour 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 neutralise 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. More-



over 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 and bile separate 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 of fats through membranes is assisted by wetting the membranes with bile, or with a solution of bile-salts. Oil passes with considerable 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.

### *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 cannula 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 p. c.; but in the thoroughly active secretion from a permanent fistula it is not more than about 2 to 5 p. c., '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 favoured 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 neutralisation. 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 neutralisation 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 alkalis. If the digestive mixture be supplied with sodium carbonate to the extent of 1 p.c., digestion proceeds rapidly, just as does a peptic mixture when acidulated with hydrochloric acid to the extent of .2 p.c. Sodium carbonate of 1 p.c. seems in fact to play in pancreatic digestion a part altogether comparable to that of hydrochloric acid of .2 p.c. in gastric digestion. And just as pepsin is rapidly destroyed by being heated to about 40° with a 1 p.c. solution of sodium carbonate, so trypsin is rapidly destroyed by being similarly heated with dilute hydrochloric acid of .2 p.c. Alkaline bile, which arrests peptic digestion, seems, if anything, favourable 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 alkalis, 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 shewn by the appearance, in the pancreatic digestion of proteids, of two remarkable nitrogenous crystalline bodies, *leucin* and *tyrosin*. 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 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 neutralisation, 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 dilute acids, alkalis, or various oxidising 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 colour with chlorine water (this reaction is often seen in the juice itself), and *indol*, to which apparently the strong and peculiarly faecal odour which makes its appearance during pancreatic digestion is due. Indol, however, unlike the leucin and tyrosin, is not a product of pure pancreatic digestion, but of an accompanying decomposition due to the action of organised 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 odour 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 shews 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 &c. 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 4 to 10 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.

### *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 re-established. 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 24 hours has been roughly calculated at as much as from 1 to 2 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. 48) 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. 48, stimulation of the tongue produces, under ordinary circumstances, no flow. This shews 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 ganglion (represented diagrammatically in Fig. 48 *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 shewn.

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

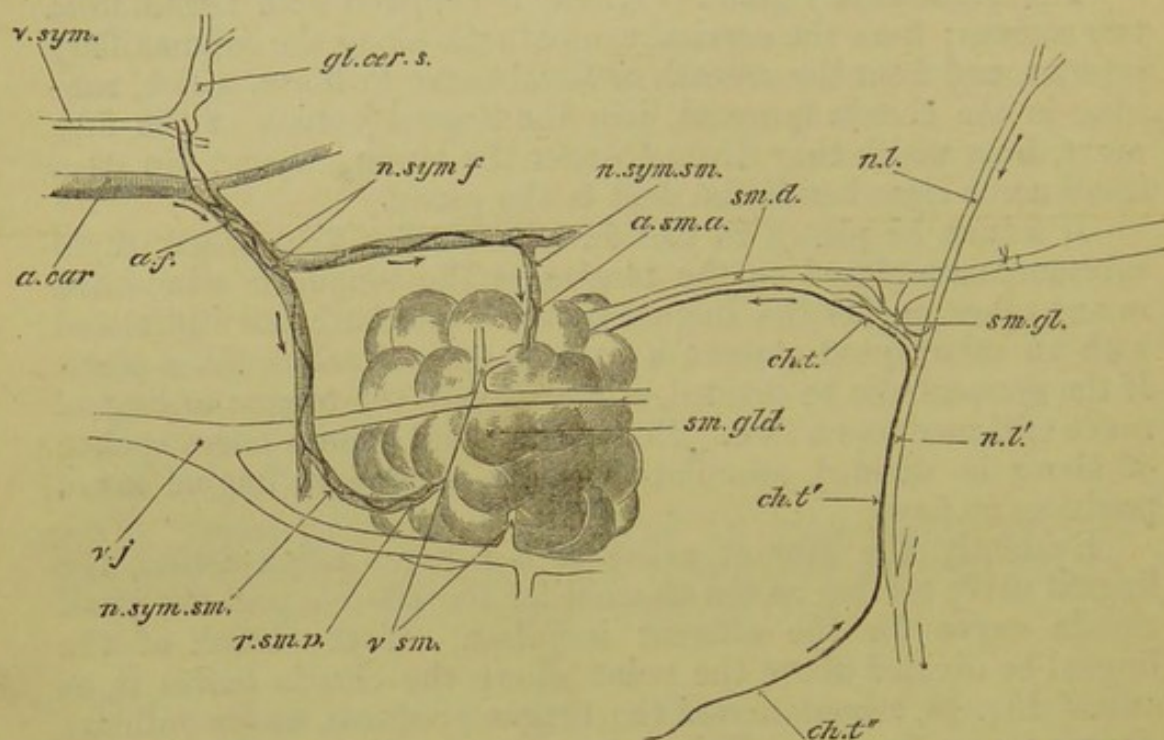


FIG. 48. DIAGRAMMATIC REPRESENTATION OF THE SUBMAXILLARY GLAND OF THE DOG WITH ITS NERVES AND BLOOD-VESSELS.

(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 cannula has been tied. The sublingual gland and duct are not shewn.

*n. 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 super-cervical 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.

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 roused, 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 blood-vessels 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 favourable to active secretion, need not necessarily bring it about. Moreover, the following facts are distinctly opposed to such a view. When a cannula is tied into the duct and the chorda is energetically stimulated, the pressure acquired by the saliva accumulated in the cannula 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 blood-vessels is greater than that of the blood inside the blood-vessels. 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 blood-vessels 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 blood-vessels only, and further that atropin, while it has no effect on



the latter, paralyses the former just as it paralyses 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 blood-vessels 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 blood-vessels 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 latter 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 blood-vessels, 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 cerebro-spinal 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, as 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 alkalis 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 grey colour, 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 is 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 neighbourhood 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 neighbourhood 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 is further shewn 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 oesophagus 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 shew 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. 255), 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 nuchae, 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. 49. 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

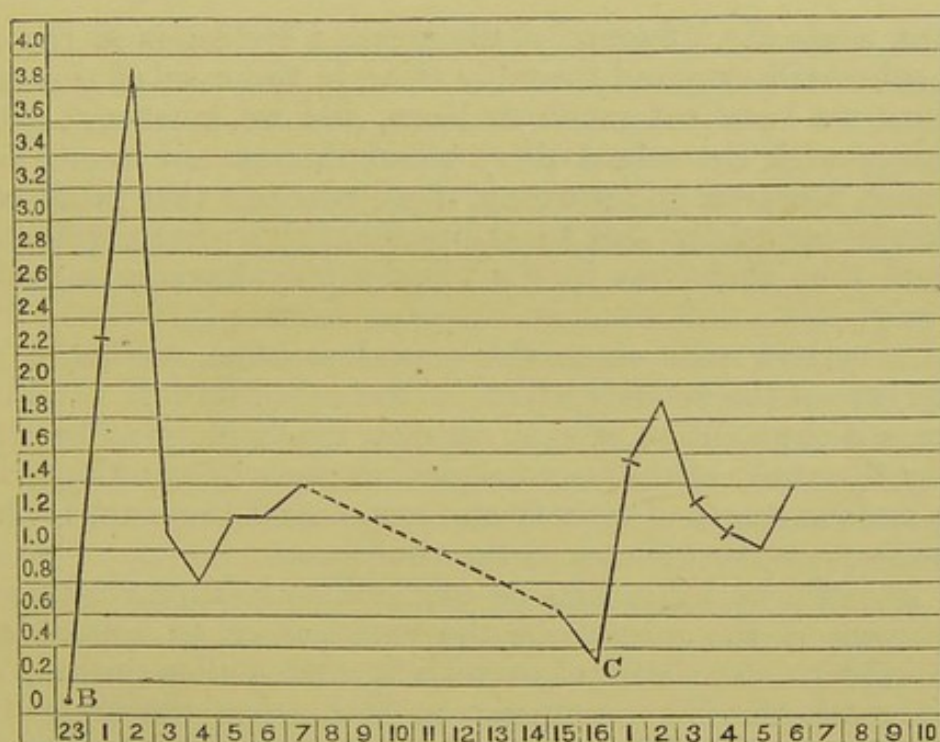


FIG. 49. DIAGRAM ILLUSTRATING THE INFLUENCE OF FOOD ON THE SECRETION OF PANCREATIC JUICE. (N. O. Bernstein.)

The abscissæ represent hours after taking food; the ordinates represent in c.c. the amount of secretion in 10 min. 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 observation was 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.



secretion. The quantity secreted in 24 hours by man has been calculated at 300 c.c. Like the salivary glands, the pancreas while secreting is flushed, through dilation of its blood-vessels.

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 shew 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 shewn 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 recognised. The outlines of the individual cells forming an alveolus (Fig. 50 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 on the lumen of the alveolus, leaving the outer part of the cell next to the basement membrane

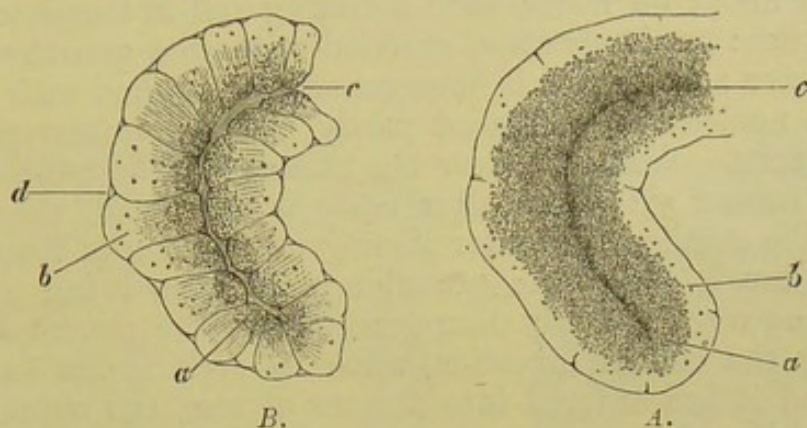


FIG. 50. A PORTION OF THE PANCREAS OF THE RABBIT (KÜHNE AND SHERIDAN LEA), *A* at rest, *B* in a state of activity.

*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 *B*, but not occurring in *A*.

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 zone thickly studded with granules. At the same time it may be remarked that the lumen of the alveolus is narrow and 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. 50 *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 and 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 blood-vessels 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 30 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 viscosity 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 reagents (Fig. 51 A) appears to consist of two parts: of a small quantity of what we may speak of as ordinary protoplasm, readily staining with carmine, &c. and gathered round the nucleus, which is placed towards the outside of the cell, generally close to the base-



ment membrane; and of another different substance which occupies the greater part of the cell. 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

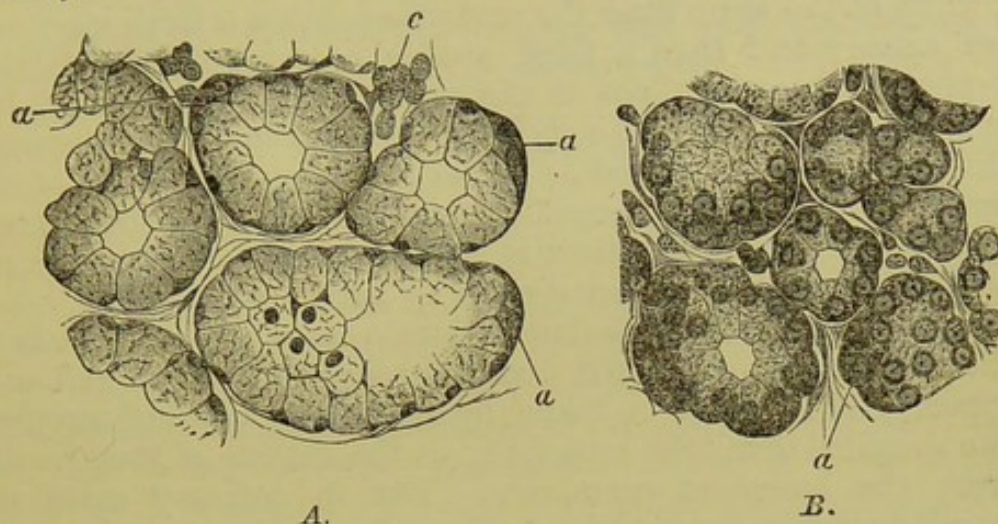


FIG. 51. SECTION OF A 'MUCOUS' GLAND, *A* in a state of rest, *B* after it has been for some time actively secreting. (After Lavdowsky.)

*a* demilune cells. *c* leucocytes lying in the inter-alveolar spaces. The darker shading in both figures is intended to indicate the amount of staining.

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 subjected 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. 51 *B*) almost wholly formed of protoplasmic substance readily staining with carmine. In extreme 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 made on p. 255, 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 24 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 shew 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 favoured 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 afford 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 vigour, 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, where-



by 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. 52). In some mammals

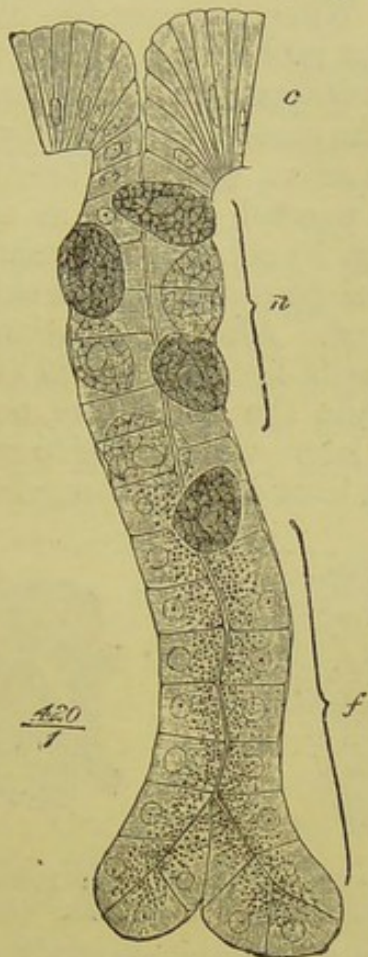


FIG. 52. GASTRIC GLAND OF MAMMAL (Mole) DURING ACTIVITY (Langley).

*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, the round nucleus of which is conspicuous.

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 copious secretion has been called forth by stimulation of the auriculo-temporal nerve, alcohol specimens shew 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. 53 *A*) are pale, transparent, staining with difficulty, and the nuclei possess irregular outlines as if shrunk by the reagents employed. After stimulation of the sympathetic, the protoplasm of the cells becomes turbid (Fig. 53 *B*), and stains much more 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



FIG. 53. SECTION OF A 'SEROUS' GLAND: THE PAROTID OF THE RABBIT. *A* at rest, *B* after stimulation of the cervical sympathetic. (After Heidenhain.)

distinctly smaller. When however we study the gland in a living state, we find that the changes which take place during activity are quite comparable to those of the pancreas. During rest (Fig. 54 *A*), the cells are large, their outlines very indistinct, in fact almost invisible and the protoplasm of the cell is studded with granules.

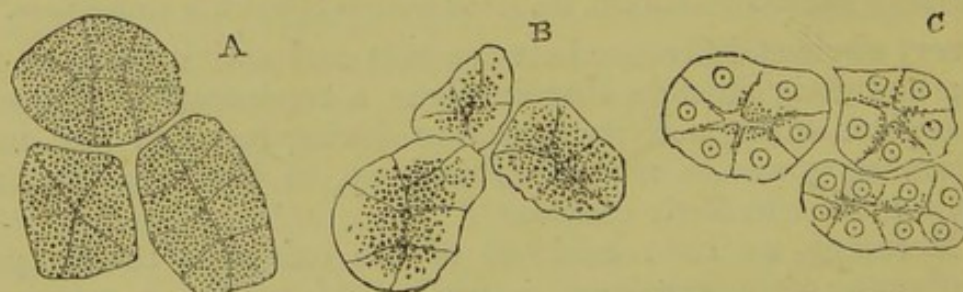


FIG. 54. CHANGES IN THE PAROTID DURING SECRETION (Langley).

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 shew 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 shew their appearance and position.



During activity (Fig. 54 *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. 54 *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 protoplasm 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 discussion 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 secretion 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 inevitably 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 a while 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 only 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 gives rise to certain constituents, while the former, so to speak, washes 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 one 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* (*ὀξύναι* 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 shewn 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 actinozoön or hydrozoön 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, leads 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 constituents 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 ligature 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 labours, 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 cholesterol 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 re-absorbed, 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 shews 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 labour 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 shewn 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 shewn 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 con-



tractions 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 shew 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 ensure that nothing has been left behind. Deglutition in this fashion still remains possible after the constrictors have become paralysed 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. 101, 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 move-



ments, 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 shewn 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 ileo-cæcal valve. The contractions of the longitudinal coat appear to be chiefly of use in producing peculiar oscillating movements of the pendent 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 favouring 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 distension 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 apnoea (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 pylorus. 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 ileo-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 fæces 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.

**Defæcation.** 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 connexion 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, shewing 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 defæcation 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 at the anus. Since however, as we have seen, the pressure of the abdominal walls is warded off the sigmoid flexure, such a mode of defæcation 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, defæcation 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 fæces 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 defæcation, 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 faeces 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 descends 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 defæcation, 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 coeliac 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 shewn 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.



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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 fæces.

**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 emulsified, 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 imbedded, 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 discs, 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 greyish 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 the 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 12 to 24 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. 265), the pancreatic juice, which flowed freely into the intestine at the taking of the meal, is secreted again with renewed vigour, 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 fæces.

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 favours 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 emulsified in this way than others. Now the bile and pancreatic juice supply just such conditions as the above for emulsifying fats: they both together afford an alkaline medium, 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 greyish 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 favours the transference of neutral fats from the intestine into the lacteals, is shewn 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 shewn 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 .02 p.c.) by the ligature and fistula, obviously point to the same conclusion. That in man the succus entericus possesses a wholly insufficient emulsifying power is shewn by the observation of Busch, in a 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 coloured 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 indicated 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 blood-vessels, so that the contents of the small intestine, by the time they reach the ileo-cæcal 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 shewn 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 shew 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 fæces, and the colour shifts from the bright orange, which the grey chyme gradually assumes after admixture with bile, into a darker and dirtier brown.

**In the fæces** 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 fæces 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), colouring 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. 280), the less stable taurocholic acid (of the dog) disappearing more readily than the glycocholic acid (of the cow). The fact that the fæces become 'clay-coloured' when the bile is cut off from the intestine shews that the bile-pigment is at least the mother of the fæcal 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<sup>1</sup>. We have already seen that during artificial pancreatic digestion, a distinctly fæcal odour 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 fæcal odour, formed after prolonged putrefaction of the pancreas and present in human excrement) being the chief cause of the natural odour of fæces, 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.

<sup>1</sup> See Appendix.



## 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 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 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 cannula 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 colour 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, p498 an abundance of oil-globules of various sizes but all small, and a quantity of fatty granules, too minute to be recognised 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 alkalis, 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 shewn.

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 shewing 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 24 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 amoeba. 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 inter-epithelial processes of the peculiar epitheloid-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 move-



ments 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 cannula be inserted in one of the larger lymphatic trunks of the limb of a dog, the discharge of lymph from the cannula 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 blood-vessels, 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 shewn 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 (.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 shews the influence of the nervous system in maintaining the tonicity of the blood-vessels 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. 108) 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. 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 ~~portal~~ <sup>thoracic</sup> ~~vein~~ <sup>duct</sup> 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 cannula 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 20 hours from the swallowing of the food, differ materially whether the fat has been during the whole time shut off from the blood by being allowed to flow out of a cannula 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 condition 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 proteids 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 alimentary 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 labours 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 shewn for instance by an observation made on a dog, in which such fairly soluble and diffusible salts as sodium taurocholate 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 be 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 cannula 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 shew 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 conversion 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 favour 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 behaviour 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 dialyser, 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 dialyser to water, about 200 parts of water pass through the membrane of the dialyser 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, produces diarrhoea, 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.

WE have already seen (Introduction, p. 3) 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 carbonic acid in the contrary direction, are affected, if at all, in a wholly subordinate manner, by the behaviour 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.



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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 blood-vessels 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 about 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 laboured 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 laboured 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 distension. 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 distension 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 3—4000 c.c. (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

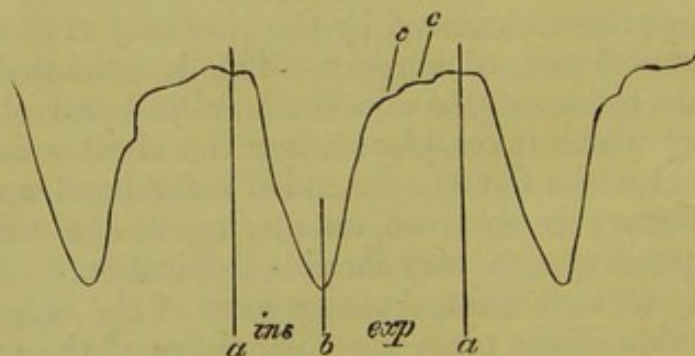


FIG. 55. TRACING OF THORACIC RESPIRATORY MOVEMENTS OBTAINED BY MEANS OF MAREY'S PNEUMATOGRAPH. (To be read from left to right.)

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.



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 shewn in Fig. 55.

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 connected with a Marey's tambour or with a receiver which in turn is connected with a tambour, Fig. 22, p. 140, and Fig. 56. The movements of the column of air in the trachea are transmitted to the tambour, the consequent 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 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. 22 and 56, *m'*), a small ivory button (in place of the lever shewn in Figs. 22 and 56). 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 callipers, 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 immobile, give rise to variations of pressure within the tambour. These variations 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 shewn in Figs. 22 and 56, the lever of which records the variations 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 depressed: 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.

As is shewn in Fig. 55, 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.



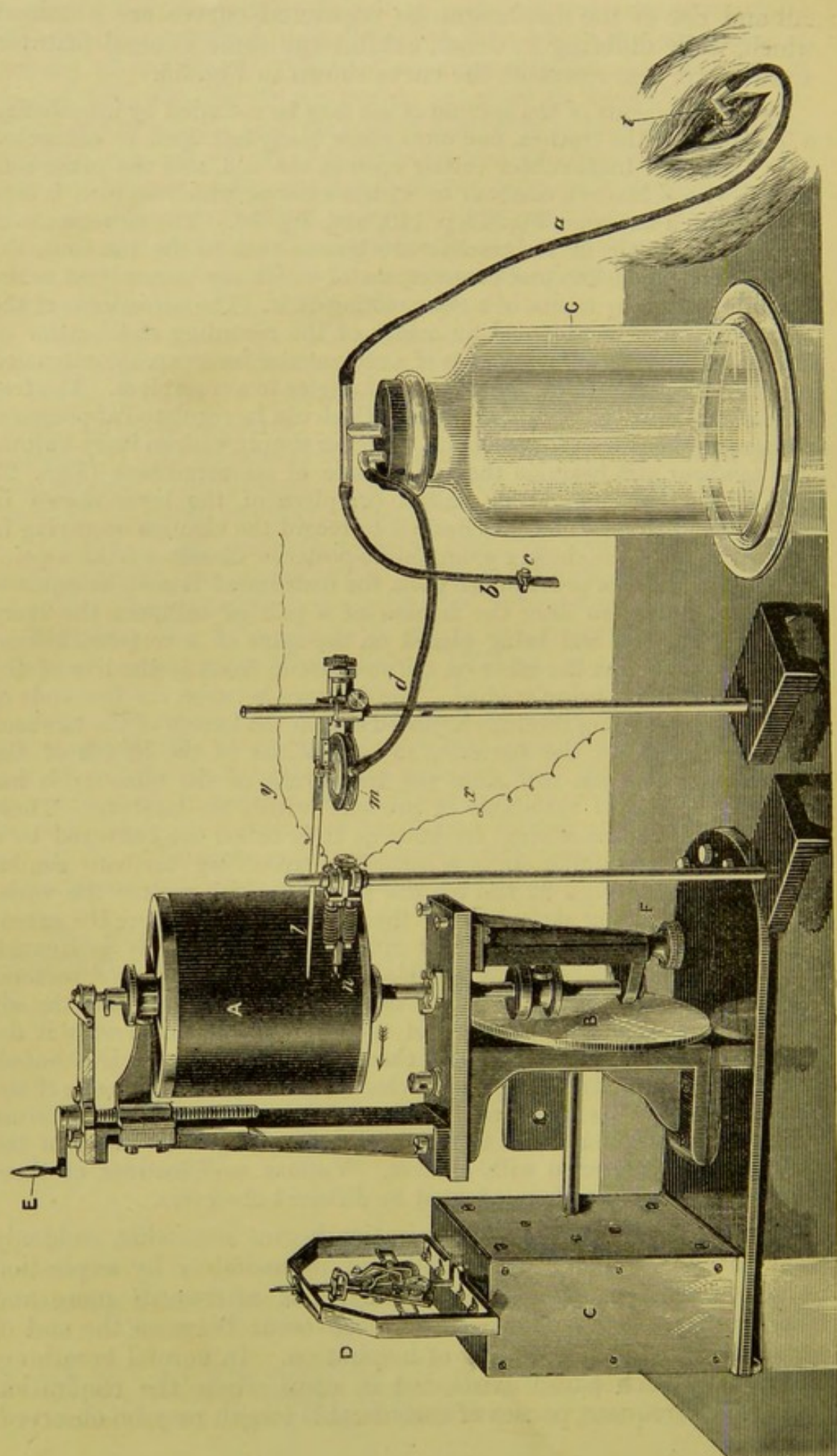




FIG. 56. APPARATUS FOR TAKING TRACINGS OF THE MOVEMENTS OF THE COLUMN OF AIR IN RESPIRATION.

The recording apparatus shewn 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 clock-work 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. 22, p. 140), 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 a battery by the wires *x* and *y* is made and broken by a clock-work or metronome.

In what may be considered as normal breathing, the respiratory act is repeated about 17 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 20 to 13 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 laboured respiration, and this in turn to dyspnoea, 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 laboured 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. The rib 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 farther 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, permit 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 favoured by the fact that the first rib is less moveable 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 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 moreover 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 complex, 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 shew that in these animals the contraction of the internal intercostals, along their whole length, takes place, in point of time, alternately with that of the diaphragm, and thus afford an argument in favour of these muscles being expiratory in function.

Next in importance to the external intercostals come the levatores 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.

**Laboured Inspiration.** When respiration becomes laboured, 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 laboured breath-



ing 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 laboured. 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 cartilages 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 laboured, 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 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 laboured 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 laboured than in tranquil breathing. Indeed in the latter case it is frequently absent. The manner in which this rhythmic opening and narrowing is 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  $20^{\circ}\text{C}$ ., the temperature of expired air is, in the mouth  $33.9^{\circ}$ , in the nose  $35.3^{\circ}$ . When the external temperature is low, that of the expired air sinks somewhat, but not to any great extent, thus at  $-6.3^{\circ}\text{C}$ . it is  $29.8^{\circ}\text{C}$ . When the external temperature is high, the expired air may become cooler than the inspired, thus at  $41.9^{\circ}$  it was found by Valentin to be  $38.1^{\circ}$ . 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 vapour. 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 vapour, varies with the temperature, being higher with the higher temperature. For its own temperature expired air is according to most observers saturated with aqueous vapour.

3. When the total quantity of tidal air given out at any expiration is compared with that taken in at the corresponding inspiration



ration, 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 4 or 5 p.c. less oxygen, and about 4 p.c. 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	·04
Expired „ „	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 shewn to be present in the expired air are the cause in part of the odour of breath. It is probable that many of them are of a poisonous nature; for an atmosphere containing simply 1 p.c. 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 1 p.c. by breathing, is highly injurious. In fact, air rendered so far impure by breathing that the carbonic acid amounts to .08 p.c. 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 measure 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 4 p.c. He will accordingly at each breath load 2 litres to the extent of 1 p.c.; and in one hour, if he breathe 17 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 below .1 p.c., he should have 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 colour; 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 colour, 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.

The vacuum produced by the ordinary mechanical air-pump is insufficient 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. 57) case two large globes of glass, one fixed and the other moveable, 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 moveable 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 moveable globe is then depressed thirty inches below the fixed one, in which the consequent fall of the mercury produces an almost complete vacuum. By turning the proper cock this vacuum is put into connection with the receiver containing the blood, which thereupon becomes proportionately exhausted. By again adjusting the cocks and once more elevating the moveable 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 100 vols.	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 8 to 12 p.c. less oxygen and 6 p.c. 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.



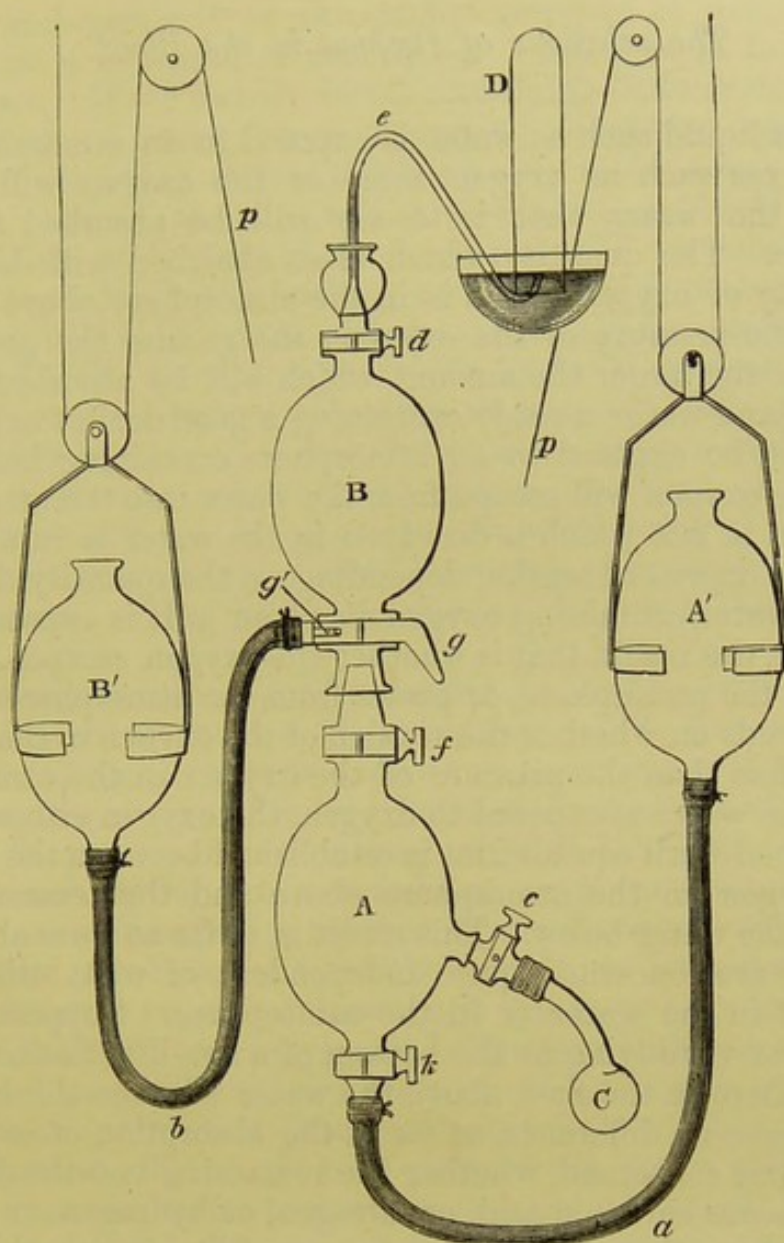


FIG. 57. DIAGRAMMATIC ILLUSTRATION OF LUDWIG'S MERCURIAL GAS PUMP.

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 analysed, and B by means of the stopcock *d* and the 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 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 suggest 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 absorbed 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 exceedingly 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. 26) 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 the 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 crystalline, 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 shews 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 hæmoglobin must, in natural blood, keep the latter from being dissolved by the serum. Hence in preparing hæmoglobin it is necessary first of



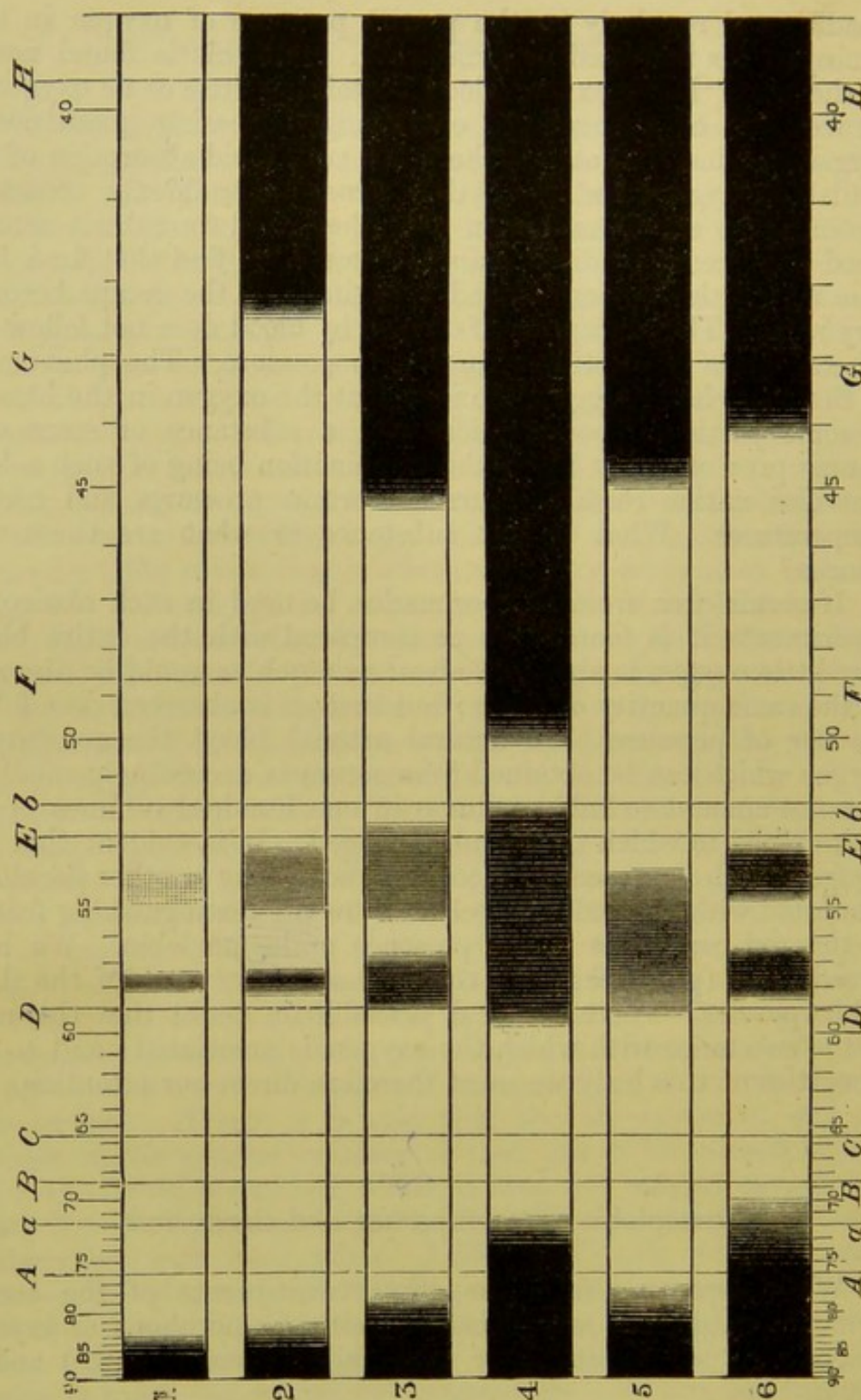


FIG. 58. (After Preyer and Gamgee). THE SPECTRA OF OXY-HÆMOGLOBIN IN DIFFERENT GRADES OF CONCENTRATION, OF (REDUCED) HÆMOGLOBIN AND OF CARBONIC-OXIDE-HÆMOGLOBIN.

1. Solution of Oxy-Hæmoglobin containing less than .01 p.c.
2. " " " containing .09 p.c.
3. " " " " .37 p.c.
4. " " " " .8 p.c.
5. " (reduced) Hæmoglobin containing about .2 p.c.
6. " carbonic oxide Hæmoglobin.



In each of the six cases the layer brought before the spectroscope was 1 c.m. in thickness.

The Letters (*A, a* &c.) indicate Fraunhofer's lines, and the figures wave-lengths expressed in 100,000th of a millimètre.

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 thawing. 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 corpuscles 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, &c. 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 cool place; the mixture soon becomes a mass of crystals. The crystals may be separated by filtration, redissolved in water and re-crystallized.

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. Why these differences exist is not known; but the composition, 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. ·43, with 3 to 4 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 colour as arterial blood has to the naked eye; when seen in a mass they naturally appear darker. An aqueous solution of hæmoglobin, obtained by dissolving purified crystals in distilled water, has also the same bright arterial colour. A tolerably dilute solution placed before the spectroscope is found to absorb certain rays of light in a 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

C =  
H =  
N =  
O  
S  
Fe  
36



strongly marked absorption bands, lying between the solar lines D and E. (See Fig. 58.) Of these the one towards the red side, sometimes spoken of as the band  $\alpha$ , is the thinnest, but the most intense, and in extremely dilute solutions (Fig. 58 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 Fraunhofer'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  $\alpha$  of hæmoglobin corresponds to the wave-length 578; as may be seen in Fig. 58, where however the numbers of the divisions of the scale indicate only 100,000 of a millimetre. The other, sometimes called  $\beta$ , much broader, lies a little to the red side of E, its blue-ward edge, even in moderately dilute solutions (Fig. 58 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. 58 3). This may go on until the two absorption bands become fused together into one broad band (Fig. 58 4). The only rays of light which then pass through the hæmoglobin solution are those in the green between the blueward 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 colour 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.



When crystals of hæmoglobin, prepared in the way described above, 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 colour. 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. 335), 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 colour 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 recognised at once, by the characteristic change of colour; from a bright scarlet the solution becomes of a purplish claret colour, when seen in any thickness, but green when sufficiently thin: the colour 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. 58. 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 farther 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 colour between hæmoglobin which retains the loosely combined oxygen<sup>1</sup>, 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 crystal), as it takes up the oxygen, regains its bright scarlet colour, 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 shewing the purple colour and the single band, be shaken up with air, the bright scarlet colour at once returns, and when the fluid is placed before the spectroscope, it is seen 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 colour shifts from scarlet to purple, and from purple to scarlet, while the two bands exchange for the one, and the one for the two.

**Colour of venous and arterial Blood.** Evidently we have in these properties of hæmoglobin an explanation of at least one-half

<sup>1</sup> 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.



of the great respiratory process, and they teach us the meaning of the change of colour 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 colour 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 colour forthwith shifts into scarlet.

The hæmoglobin of arterial blood is saturated or nearly saturated 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 colour between venous and



arterial blood depends almost entirely on the fact that the reduced hæmoglobin of the former is of purple colour, while the oxy-hæmoglobin of the latter is of a scarlet colour.

There may be other causes of the change of colour, 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 colour 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. 58.6); 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 colour, 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 colour 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 colour. As Bernard phrased it, the corpuscles are paralysed.

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 colourless proteid, associated with a coloured 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 colour, 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 colours 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 alkalis split up hæmoglobin 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 hæmoglobin), but though belonging to the globulin family, has characters 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 composition of  $C_{82}, H_{84}, N_4, Fe, O_5$ . 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 exclusively 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 colour, 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 hydrochloric 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 colours of venous and arterial blood are in the main due to the fact that the colour 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.*

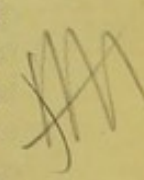
We have already seen that the blood in passing through the lungs takes up a certain variable quantity (from 8 to 12 vols. p. c.) of oxygen. We have further seen that the quantity so taken up, putting aside the insignificant fraction simply absorbed, enters into direct but loose combination with the hæmoglobin. 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 as 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 dis-



sociation is further especially dependent on temperature, a high temperature favouring 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 p.c. 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 p.c. of oxygen take up sufficient oxygen (from 8 to 12 vols. p.c.) 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 behaviour at the temperature of the body or at ordinary temperatures 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 shew 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. p.c. 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 in as much 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 shewing 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 p.c., 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 favour 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 oxy-hæmoglobin 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, shewing the presence of a large quantity of reduced hæmoglobin; when the gland is active, the venous blood in its colour, 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 only when at rest go on producing and discharging a certain 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 blood-vessels 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 developes 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 intra-molecular 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 intra-molecular oxygen, leaving the oxygen tension of the muscular substance once more nil. Con-



versely, 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 intra-molecular 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 intra-molecular 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 shew 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 blood-vessels and tissue-spaces of the animal.

We may add, that the oxidative power which the blood itself removed from the body is able to exert on substances which are 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 pyrogallie 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 shewed long ago that animals might continue to breathe out carbonic acid in an atmosphere of nitrogen or hydrogen; and more recently Pflüger has shewn, 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 blood-vessel 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 coordinated 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 coordinated muscular contractions should be brought about in any other way than by coordinate nervous impulses descending along efferent nerves from a coordinating 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 laboured.

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 vigour. 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 coordinated 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 coordinate nervous impulses of inspiration followed in due sequence by a smaller but still coordinate group of expiratory impulses, in laboured respiration fresh and larger impulses are generated, though still in coordination with the normal ones, the expiratory events being especially augmented; and in the cases of more extreme dyspnoea and asphyxia impulses overflow, so to speak, from it in all directions, though only gradually losing their co-ordination, 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 coordinated 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 shew 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 shew 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 medulla, 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 shewn 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 co-ordinated 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 dyspnoea, 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 effect 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 apsychnical 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 influence 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 oxy-hæmoglobin and more heavily laden with carbonic acid, the respiration from being normal becomes laboured. We may speak of normal breathing as *eupnæa*, and say that this, when the blood is insufficiently arterialized, passes into *dyspnæa*, an intermediate stage in which the respiratory movements are simply exaggerated being known as *hyperpnæa*. 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 latter 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