ON THE INNERVATION OF THE HEART, WITH ESPECIAL REFERENCE TO THE HEART OF THE TORTOISE.

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[Plates II—V.]

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THE views held by physiologists upon many points connected with the innervation of the heart have been too exclusively based upon observations upon a single type of heart, viz. that of the frog. It is therefore very advisable wherever possible to control these experiments by a corresponding elaborate series of observations upon the hearts of a large number of other animal types, and in this way to trace the evolution of function in the same way as the morphologist tracks that of structure. With this object in view I propose in this paper to discuss as fully as I can the series of experiments which I have made during this last year upon the innervation of the tortoise heart, comparing them at the same time with corresponding observations upon the hearts of other animals. I shall therefore embody in this paper the substance of three separate preliminary papers which I have already published, viz.:

1. Preliminary observations on the innervation of the heart of the tortoise[1]. 2. On the sequence of the contractions of the separate parts of the heart[2]. 3. On certain points in the function of the cardiac muscle[3].

I propose to divide the paper into four parts, viz.:

1. On the *spontaneous* rhythm of the different parts of the heart and of the heart as a whole;

2. On the sequence of the contractions of the different heart cavities;

3. On the action of the cardiac nerves;

4. On the action of atropin and muscarin;

and in each part to strictly confine myself to the subject matter of that part.

In a concluding section a general discussion on the four previous sections will be given.

[1] *Journ. of Physiology*, Vol. III. Nos. 5 and 6.

[2] *Brit. Med. Journ.* 1882, p. 572.

[3] *Proc. Camb. Phil. Soc.*, Vol. IV., Pt. V.

PART I.

On the spontaneous rhythm of the different parts of the heart and of the heart as a whole.

In the early days of physiology before the nerves of the heart were known or ganglion cells thought of, the beat of the heart was attributed to the direct stimulating action of the blood upon the cardiac muscle. The discovery of the cardiac ganglia and especially their situation in that part of the heart—the sinus—from which it had been long recognized that the rhythmical beat took its origin, led instantly to the hypothesis that they played the chief part in the causation of the beat, although at the same time they were recognized as appendages to the nerves and not as separate independent structures. The fact that upon section certain portions of the frog's heart continued to beat while other portions remained quiescent and that ganglion cells were always found in the former seemed proof positive of their preponderating influence in the causation of rhythm. Further, the knowledge that the respiratory muscles responded to rhythmical discharges sent out from the nerve cells of the respiratory centre naturally led to the conclusion that the supposed motor nerve cells of the sinus of the heart caused the heart's beat by a series of separate single discharges, each of which brought about a contraction of the cardiac muscle. When however from the experiments of Eckhard, Foster, Merunowicz and others it was known that a constant stimulus whether electrical, chemical or mechanical applied to the muscular tissue of the apex was able to cause that muscle to beat rhythmically even although no nerve cells were to be found in it, the question arose—Are really these motor centres similar to those of the respiratory centre, or is it not more likely that they supply a constant stimulus to the muscle and that it is the property of the cardiac muscle to produce a rhythmical result from that continually acting stimulation? Whichever view be accepted we still see that certain ganglia are supposed to possess motor functions upon which the heart-beat ultimately depends, and the cardiac muscle itself is not supposed to possess any power of automatic rhythm but merely contracts rhythmically upon the application of a suitable external stimulus.

Further the experiments of Stannius have given rise to many investigations and much discussion upon the question, whether the automatic rhythmical power is confined to the region of the sinus or is

inherent in other portions of the heart of the frog; whether, therefore, the rhythm which is observed after removal of the sinus and other parts is in reality automatic, i. e. produced by internal causes in the rhythm-producing tissue itself, apart from external stimuli, or whether it is due to some stimulus caused by the operation itself. We may briefly sum up the main facts which have been accumulated on this question as follows:—

1. Removal of the sinus by section or ligature causes a temporary standstill of the auricles and ventricle followed by an auriculo-ventricular rhythm, which is at first slow and though gradually quickening, never or seldom reaches the rate of the sinus rhythm.

2. The duration of this standstill depends upon the situation of the section, being very slight or even absent when the section is made exactly at the junction of the sinus and auricles, and much greater when a portion of the auricles is cut away as well as the sinus.

3. During the standstill removal of sinus and auricles by section or ligature in the auriculo-ventricular groove causes a rhythm in the ventricle, which is quickest immediately after section and then gradually becomes slower and slower up to complete and permanent standstill of the ventricle.

The rhythm of the ventricle described in § 3 is clearly from the nature of it a rhythm of excitation and not automatic; the fact that the greatest rhythmical effect is produced immediately after the operation and gradually dies away shows clearly its dependence upon the method of procedure, as well as the difference between its causation and such a rhythm as is seen after the first Stannius ligature, where the contractions commence with long intervals between them and gradually quicken in rate. In addition, as I have shown in my paper read before the Royal Society[1] Dec. 1881, it is possible, by properly applying a micrometer screw clamp to the auriculo-ventricular groove, to separate the ventricle from the sinus and auricles without producing any independent ventricular rhythm whatever. I found that if the clamp be tightened suddenly and forcibly, an independent ventricular rhythm was set up, often lasting a long time, but always becoming slower and slower and finally ceasing; but that if the clamp be tightened gradually a short series of independent ventricular beats might occur with each movement of the screw exactly similar to those often seen in the auricle and ventricle, before the standstill takes place, when the sinus is removed by

[1] *Phil. Trans.*, Part III., 1882.

section, ligature or clamping at or near the sino-auricular groove. In other cases I have succeeded in isolating the ventricle without causing any independent ventricular contractions.

We may then leave out of consideration the contractions which are evidently due to the stimulus caused by the operation and shall therefore arrive at the following law:—

"The power of independent rhythmical contraction decreases regularly as we pass from the sinus to the ventricle."

We can however go further; for although the ventricle remains permanently still after separation and therefore does not appear to possess automatic rhythmical power, yet a very slight amount of assistance is required to set it in rhythmical action; the presence of a blood solution in its cavity, together with a slight amount of internal pressure is sufficient to bring to view its latent rhythmical power, to produce in it a permanent rhythm which is not at its maximum rate when the blood first passes through, but on the contrary does not commence for some little time and then beginning at a slow rate quickens to a more or less regular rhythm. So too the apex itself can be set in rhythmical action with however greater difficulty than the whole ventricle; the standstill after the blood begins to pass in is here much longer, the production of any rhythm at all is much less certain and the rhythm itself is slower and less regular.

We see then that the part of the ventricle which is nearest the sinus, viz. the base, is nearer the condition requisite for the manifestation of automatism, than the part further removed, viz. the apex; and in accordance with this, we know that a slight stimulus applied to the base of the ventricle will cause a series of ventricular contractions, while the same stimulus applied to the apex will cause only a single contraction.

If therefore we use the term "rhythmical power" to represent the capability of rhythmical contraction in any heart segment, whether that rhythm be strictly automatic or requires external assistance for its production, we can say that—

"The rhythmical power of each segment of the heart varies inversely as its distance from the sinus."

It may be urged from experiments upon the frog alone, that the rhythm of the isolated ventricle or apex is fundamentally different from that of the isolated auricles, in that the latter is so much more clearly automatic than the former; that therefore these two kinds of rhythm have in all probability a different origin, the former being essentially due to the properties of the muscular tissue and constituting a

purely muscular rhythm, while the latter resembles that of the heart as a whole and depends for its production upon the rhythmical qualities of some nervous mechanism presumably of the nature of motor ganglia. Whether there is any fundamental difference in the rhythmical properties exhibited by the sinus, by the auricles, the ventricle, and the apex of such a character as to necessitate the hypothesis of two distinct modes of origin, the one nervous and the other muscular, can be better decided when we have compared the behaviour of the heart of the tortoise in this respect with that of the frog.

All experiments involving the removal of the different ganglionic masses or section of the large intra-cardiac nerve trunks can be performed on the tortoise with much greater ease and certainty than on the frog; for, in the former the nerve trunks with their accompanying ganglia are situated externally lying in or just under the visceral pericardium, the septum between the auricles containing neither nerves nor blood-vessels; while in the latter as is well known the nerves run internally along the septum between the auricles. The septum then in the tortoise has no such importance as in the frog. Its place is taken by a flat band of tissue which connects the sinus and ventricle, from which on each side the two auricles spring. This band is plainly visible if the heart be turned over by seizing the apex of the ventricle as is represented in the accompanying woodcut (Fig. 20). It is seen as a

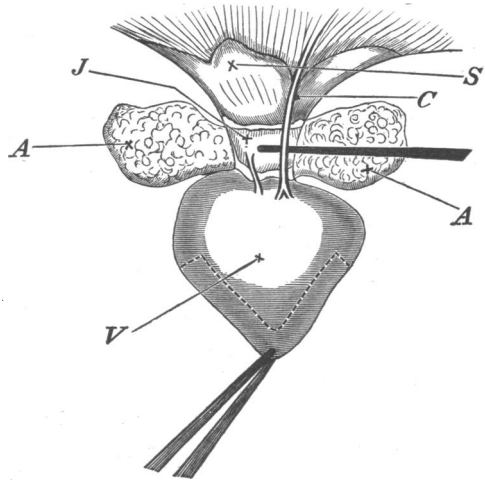


FIG. 20. Ventricle turned over, to show the connection of the sinus (*S*) by means of the junction wall (*J*) with the ventricle (*V*) and the auricles (*A*). The point of a seeker is placed under the free coronary vein and nerve (*C*).

band of tissue joining together the two auricles but differing in appearance from the rest of the auricles. This junction wall (J) of the auricles is flat and smooth, not bulged out like the rest of the auricular tissue, and the two auricles (A) spring from it as from a flat base, like fungi growing on a flat strip of wood. The septum between the auricles arises from the central line of this junction wall. The two vagus nerves pass to the sinus with the sup. venæ cavæ and their main trunks pass from the sinus to the auriculo-ventricular junction just under the pericardium covering this junction wall, so that this band of tissue which not only joins together the two auricles (A), but connects the sinus (S) with the ventricle (V) is of the same physiological importance that the septum is in the frog.

In my former paper[1] I have described fully the method used by me in investigating the nature of the rhythm of the heart and the action of the cardiac nerves in the frog and toad. This method enables slight variations in the force of the contractions of both auricles and ventricle to be simultaneously registered as accurately as has hitherto been accomplished for the rhythm alone. Its principle consists in the fixing of a point of the heart and registering the contractions of any two parts which are separated by that fixed point, the recording being effected by means of two levers attached by silk threads to the two parts of the heart thus separated. Such a method can be applied to the hearts of all animals whether in the body or out of the body; and as soon as the first experiments made on the heart of the frog in January and February 1881[2] convinced me of the great value of the method, I determined to examine in the same manner the nature of the heart beat and the action of the cardiac nerves in the first instance in the case of all available cold-blooded animals and finally to pass on to the heart of the warm-blooded animals; being convinced that the study of the evolution of function as we pass up higher in the scale of animal development is the true method by which the complex problems of the mammalian heart will receive their final solution. Such a task necessarily demands a large amount of time, especially when, as I have seen in the course of the last year, the investigation of each new animal introduces new variations, and thus suggests new problems to be solved. It is therefore with pleasure that I find that Dr Roy has undertaken the investigation of the action of the vagus and accelerans nerves upon the

[1] *Phil. Trans.*, Part III., 1882.

[2] *Proc. Camb. Phil. Soc.*, Vol. IV., Pt. II., p. 75; read March 7, 1881.

heart of the dog by a method which is the same as that which I have used for the frog and the tortoise. This method gives results for the mammalian heart which are as striking as those seen in the case of the frog and the tortoise.

In the majority of my experiments on the frog and toad, I made use of a clamp to fix the heart in position. In the tortoise it is more convenient simply to hold the aortic trunk when it is desired to register the contractions of the auricle and ventricle; I have therefore made use of the clamp chiefly in the sino-auricular groove in order to register separately the contractions of the sinus and auricle. My method of experimentation is as follows:—The heart is removed together with the upper portion of the body of the tortoise, the pericardium slit open and the liver carefully cut away; the aortic trunk is cut across and held by a pair of Kronecker's forceps, a silk ligature with a hook at one end is tied to the very apex of the ventricle and another to the top of the right auricle, and the vagus nerves are exposed in the neck, ligatured and cut. The whole of the upper portion of the body is now placed on a stand and fixed in a suitable position between the two levers. The small forceps attached to the aorta is tightly held by an ordinary holder and the two hooks are attached to the upper and lower levers respectively. The appearance of the heart is given in the accompanying woodcut (Fig. 21), which shows at a glance the position of the sinus, auricle and

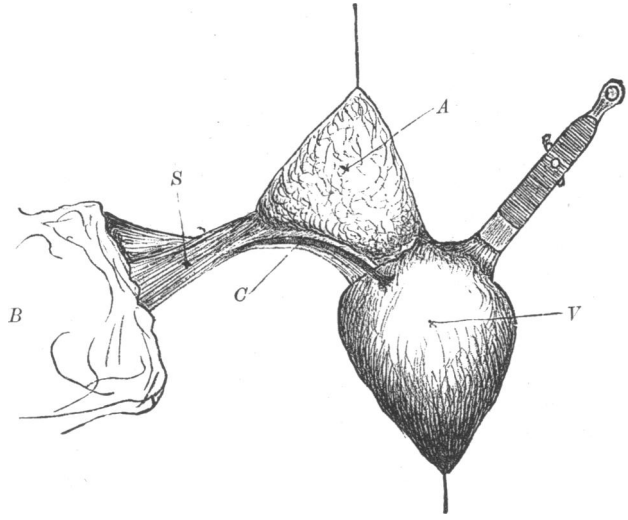


FIG. 21. Appearance of heart when suspended. *B* signifies the upper part of the body; other letters as in Fig. 20.

ventricle without further description. In most of the experiments which I have made on the tortoise heart I have not used a clamp in order to hold the heart firm but have simply held the aorta in a suitable holder, so that in these cases any separation of the different parts of the heart is made by section and not by clamping.

The consideration of the large number of experiments at my disposal brings out certain differences between the frog and the tortoise. In the first place, the ventricle of the tortoise when isolated beats automatically with as great a certainty as the isolated auricle. The extra assistance in the shape of some constant chemical, mechanical or electrical stimulus which is required by the frog's ventricle to make it beat rhythmically is not needed here; the rhythmical power of the ventricle of the tortoise as a whole is greater than that of the frog and is of identically the same nature as that of the auricle. In the tortoise then we can compare strictly the rhythm obtained from the ventricle with that of the auricles and sinus, and see whether there is the slightest reason for attributing different origins to them, for ascribing the former to the properties of the muscular tissue and the latter to those of the nervous elements.

First then I will compare the resemblances and differences between the resulting rhythms, when the separation has been effected either by clamping or section, at the junctions of the sinus with the auricles, and of the auricles with the ventricle. In both cases the production of the automatic rhythm presents the same characteristics, viz., the beats are at first slow and gradually quicken to a greater and greater extent; in both cases a longer or shorter time may elapse before an independent beat takes place, or a rhythm of excitation may be caused, characterized by contractions which, at first quick, gradually slow down and give place to and merge into the slowly commencing automatic rhythm. The differences are differences of degree not of kind, and can be summed up by saying that the rhythmical properties of the auricles are more easily developed than those of the ventricle; thus, (1) when the independent rhythm starts its rate is much slower in the ventricle than in the auricle; (2) the auricular rate can increase up to or near to that of the sinus more easily than can the ventricular; (3) a perfectly regular rate is reached more quickly by the auricle than the ventricle. The preliminary pause, which after separation often takes place before independent contractions begin, is either absent or very short when the sinus is removed by section or clamping exactly at the junction of the sinus and auricles, and is well marked when the section is made between the sinus and the ventricle or in the auriculo-ventricular groove, pro-

vided that in this latter case a rhythm of excitation is not set up by the clamp or the section sufficient to obscure the standstill. In Figs. 1, 2, Pl. II., I give examples of the development of rhythm when both auricle and ventricle are left and also when the ventricle alone remains. The close relationship between the automatic rhythm of the ventricle and of the auricle is further shown when the section is made between sinus and ventricle; the rhythm which then occurs resembles in its characteristics sometimes that of the ventricle sometimes that of the auricle, though perhaps on the whole, as long as any part of the junction wall between the two auricles is left in connection with the ventricle, the resulting rhythm tends rather towards the auricular than the ventricular type. The evidence then shows strongly that the automatic rhythm of the ventricle is of the same kind as that of the auricle, and therefore as that of the sinus, so that if the latter is due to the presence of motor ganglia so too is the former, and on the other hand, if the former be due to some inherent rhythmical property of the ventricular muscle then the latter is due to a somewhat better development of the same kind of property in the muscular tissue of the sinus. The possibility of deciding between these two views is given by the study of the rhythmical power of the ventricular muscle freed entirely from ganglion cells; in other words, by the comparison of the rhythmical power of the muscular tissue from the apex of the ventricle with that of the whole ventricle.

My method of experimentation is as follows. A strip of muscular tissue is cut from the apex of the ventricle in the direction and of the size represented by the dotted line in Fig. 20, p. 47, and held firmly at one end; a thread of silk is tied to the free end and attached by means of a hook to the lever of an ordinary muscle and nerve moist chamber. A very thin wire, insulated except at the ends, is twisted round each extremity of the strip of muscle and connected by means of a Du Bois Reymond key with the secondary coil of an ordinary induction apparatus. By means of this induction coil an interrupted current can be sent through the whole strip of muscle, and owing to the extreme thinness of the two wire electrodes the muscular strip can register any movements without the slightest impediment. At the fixed end of the muscular strip, so as to touch the muscle on opposite sides, are placed a pair of electrodes connected with another induction coil so arranged as to send single induction shocks[1] into the muscle every ten seconds. The muscular strip is moistened with the blood of the animal or a drop

[1] N.B. Throughout this paper a single induction shock includes both the making and breaking shock.

of salt solution, wet blotting-paper is placed in the moist chamber, the glass cover is put in position, and the experiment can then commence. The experiment consists in causing rhythmical contractions of the muscular strip every ten seconds by means of the single induction shocks applied at one end, and at the same time observing at intervals the effect upon these contractions of sending through the whole strip an interrupted current so weak as not in itself to cause contractions. The single induction shocks are of such a strength as to be certain of causing a contraction each time. The sequence of events is as follows—When the artificial rhythm is first induced the contractions are small, irregular in size, and somewhat flat-topped. Upon inspection it can be seen that a number of blocks exist in the strip of muscle (see p. 66, and Fig. 3, Pl. II.), so that the contraction started at the fixed end passes a short distance only along one region, while at another part the contraction though delayed eventually passes on, and at still another part it is perhaps only every second contraction which passes; and so on. It is in this way that the weak irregular contractions are caused, and the first effect of the application of the interrupted current is to remove these blocks. Each time the interrupted current is sent through, the contraction due to the single shock is enabled to pass a little further; gradually and surely all the blocks are removed, the contractions become more regular in force, stronger, the passage of the contraction becomes more rapid until at last the strip contracts evenly and vigorously from end to end; every obstruction is gone, the conduction power and contraction force is fully restored. The excitability of the tissue gradually increases hand in hand with the restoration of contraction power; the single induction shocks do not require to be so strong in order to cause an invariable contraction, the interrupted current must be made weaker in order not of itself to cause contractions; in fact the functional activity of the tissue has been in every respect repaired and increased. Further, when this process of repair has reached its maximum, when every induction shock produces equally strong vigorous contractions which pass rapidly and without hindrance from one end of the strip to the other, then spontaneous contractions begin to appear: the artificial stimulation can be removed and the automatic contractions of the strip of muscle be observed. These independent contractions are as strong as those caused by the single induction shocks; they, like the automatic contractions of the ventricle or of the auricle, commence with a slow rate of rhythm which gradually and steadily quickens, becoming more and more regular and approaching nearer and nearer to the rate of the sinus rhythm.

Hour after hour the strip of tissue continues beating with unimpaired vigour with the same rapid regular rhythm; kept in the moist chamber through the night it is found to be still beating strongly and regularly though more slowly on the next morning. How long this rhythmical power remains, how long these vigorous contractions will continue I cannot say; I have seen the strip beating with great vigour and regularity as long as 30 hours after suspension, i.e. between 28 and 29 hours after the commencement of the spontaneous independent contractions.

These contractions are clearly both myogonic and automatic.

They are myogonic because no special nerve structures are to be found here, and when the rhythm is once well established the strip can be cut into small pieces, each of which will still continue its rhythm for a long time; the rhythmical power then is not specialized in any portion of the strip, but is distributed over the whole of it. Its origin must therefore be in the muscle or in the nerve fibres supplying the muscle, as is suggested by Schiff[1] in his discussion on the mode of the movements of the heart. That the rhythm is not only muscular in origin, but also due to some quality inherent in the muscle itself, i.e. is automatic, is clearly shown by the method of its development. It is evidently not a "rhythm of excitation" due to the direct stimulation of the muscle by the single induction shocks or the interrupted current, for it continues at least 30 hours after the discontinuance of all stimulation; it begins, like the automatic rhythm of the ventricle and auricle, and unlike the excitation rhythm caused by the second Stannius ligature, with contractions at long intervals from each other, and then gradually and regularly quickens up to its maximum rate. Further, nothing can be more striking than the nature of its development; the gradual recovery of the conduction power throughout the strip, the steady improvement in the force and rapidity of the contractions, the increase of excitability, all show a gradual improvement and development in the activity of the processes upon which the various properties of the muscle depend, a development which when it reaches its culminating point is manifested by the outburst of automatic rhythmical contractions. In fact under the guidance of the interrupted current and the single induction shocks the rhythmical power inherent in the muscular strip has been developed and made manifest, the muscle has been taught to beat.

[1] *Modus der Herzbewegung*, Roser's *Archiv*, 1850, Vol. IX., p. 22 and 220.

The action of the interrupted current is not absolutely necessary for the manifestation of this rhythmical power, it simply hastens on the development of the automatic rhythm but does not produce any new property in the tissue. Thus if two strips of muscle be cut from the apex of exactly the same length and in every respect as similar to each other as possible, and the one strip be taught to beat in the manner described, while the other is simply left suspended in a moist chamber, without the application of any stimulus or any foreign fluid, then it is found that after a time this latter strip is beating of its own accord, and beating with contractions which in most cases become eventually nearly if not quite as strong and vigorous as those of the former strip. The difference then between the behaviour of the two strips is in no way essential, the same processes are taking place in the one as in the other, but not at the same rate. Not only is the rapidity of the genesis of the automatic rhythm markedly quickened, but also the rhythm itself is more regular and quicker in the strip which has been taught than in the one which has been left alone. Thus in the former case I have generally noticed the occurrence of independent contractions between one and two hours after the suspension of the strip; in the latter I have never seen any sign of a beat under three hours, and seldom before four hours after suspension. In the latter case as well as in the former the strip continues to beat all night and is beating strongly and well next morning, and indeed may be beating more regularly than during the previous afternoon. Thus in one case where the rhythm of the control strip was during the afternoon of Nov. 8th irregular, with a strong tendency to the formation of groups, separated by single contractions at long intervals or by long pauses of 3, 7 or even 18 minutes duration, the rhythm when seen next morning ($24\frac{1}{2}$ hours after suspension) was perfectly regular at the rate of one beat every 25 seconds; in addition the contractions were nearly as strong as on the previous day[1]. In order to show the manner in which the rhythmical power of the tissue is gradually developed I will endeavour to describe fully a typical case.

Nov. 7, 1882. Plate II. Fig. 3. Curves I—VI.

A strip of muscle, cut from the apex of the tortoise ventricle, was suspended at 3.30 p.m., and moistened, the electrodes being arranged as above

[1] I have never yet been able to obtain similar automatic contractions from a strip of muscle cut from the apex of the ventricle of the frog. In order to obtain success with the strip from the tortoise ventricle it is advisable that the animal be well fed, in a lively vigorous condition, and therefore that the experiment be made during or at the end of the warm months of the year.

described. Single induction shocks sent in at the fixed end every 10 seconds. Weak interrupted current sent through the strip at intervals as marked in the figures on the upper line. The first two curves represented in Fig. 3, Pl. II. show the original weak partial contractions of the strip in response to each induction shock, the gradual improvement of the contractions, the removal of blocks in the strip so that at first every second contraction was enabled to pass a block, and then on again stimulating every contraction passed[1] (see curve II), until at last each contraction was of the same strength and had nearly reached its full vigour. The same process continued, the contractions became stronger and stronger, passed more and more rapidly along the strip until at last about one hour after suspension a spontaneous contraction appeared occasionally, in addition to the contractions caused by the single induction shocks. These spontaneous contractions became more and more frequent and upon then removing the single induction shocks the strip was found to be beating of its own accord somewhat irregularly and with considerable rapidity. The contractions quickly improved in regularity and rapidity and the two curves (IV, V.) were taken between 5.30 and 6 o'clock. The rhythm was then, as is seen, very regular and as rapid as the sinus rhythm. All wires and electrodes were then removed and the preparation placed under a bell-jar with plenty of moisture and left through the night. At 9.15 p.m. when the laboratory assistant left, i.e. nearly six hours after suspension and five hours after the commencement of the spontaneous contractions the strip was still beating strongly and regularly at the rate of ten beats per minute. On the next morning, Nov. 8, I found the rhythmical contractions still continuing, and at 11 a.m. i.e. 18 hours after the commencement of spontaneous contractions the tracing Fig. 3, curve VI. was taken. The strip was then cut into three pieces which were placed on a glass slide and kept moist. Each of these pieces continued to contract rhythmically and were observed to be still rhythmically contracting up to 1 p.m. i.e. 22 hours after removal of the strip from the ventricle. Further observation was then discontinued.

We see then that just as the whole ventricle of the tortoise when isolated remains quiescent for a short time and then begins to beat, so too any strip of the ventricular muscle begins to beat spontaneously after a longer standstill; just as the rhythm of the whole ventricle commences with a slow rate and gradually increases to its maximum, so does the commencing slow rhythm of the apex strip gradually increase in rate. No fundamental difference therefore exists between the rhythmical phenomena in the two cases, no extra factor is required for the production of the one rhythm rather than of the other; the differ-

[1] These alternately weak and strong contractions are probably the same as noticed in my previous paper in the case of the frog's ventricle.

ence is one of degree not of kind, being mainly, that the length of time required before the rhythm is manifested is, as might be expected from the greater severity of the section, greater in the one case than in the other. A strip from the apex of the auricle behaves in a manner very similar to that from the ventricle apex. Since therefore the purely myogonic rhythm of the apex is closely related to that of the ventricle, and therefore as has already been argued to that of the auricle, and since no line of demarcation can be drawn between the rhythm of the auricle and that of the sinus, the logical conclusion is that the rhythm of the sinus and therefore of the whole heart depends upon the rhythmical properties of the muscular tissue of the sinus, and not upon any special rhythmical nervous apparatus.

According to Engelmann[1] the myogonic origin of the automatic pulsations of the bulbus of the frog's heart, as well as of the contractions of the apex under the influence of a supply of blood, &c., is demonstrated by the fact that in both cases the rhythm never reaches the rate of those parts of the heart which contain motor nerve centres; a difference which is in accordance with the law that the specific irritability of muscle is much less than that of nerves or nerve centres. According to this view then we may hope to decide between the nature of the origin of two spontaneous rhythms by an examination of the rates of such rhythms, especially when as in the case of all my experiments, the portions of cardiac tissue, whether ventricle, auricle, whole heart or apex, were all suspended in the same manner, and all under the same conditions. Before however a comparison can be made of the rates of the different portions of the heart, it is necessary to know the rate at which the whole heart beats when taken out of the body and suspended in the manner already described. The heart of the tortoise beats in almost every case with the most perfect regularity, varying in rate, apparently according to the time of year, from 10 to 20 beats per minute. Thus the average rate of the beat of the whole heart when first suspended was as follows: February nearly 10 per min., March 10·4 per min., April 12 per min., May 16 per min., June and July nearly 20 per min., Oct. and Nov. 13·5 per min. In this series the averages for the first four months are taken from a much larger number of experiments than for the last four; moreover the animals were kept under cover during November. We have already seen that the rate of rhythm of the isolated auricle or ventricle increases progressively

[1] Pflüger's *Archiv*, Vol. xxix., p. 425.

from a very slow rate to a very much quicker one; hence we have no right to assert that that rhythm cannot attain the rate of the sinus unless the experiment has lasted so long that the maximum rate has been attained. When the clamp is tightened in the sino-auricular groove the decision is easy; the rate of the independent auricular rhythm is fairly quick at the very commencement, and in a comparatively short time may quicken so as to reach the original sinus rhythm. Thus the following examples show that there is no essential difference between the sinus and whole auricle as far as rapidity of rate is concerned.

Feb. 8, 1882. The clamp had been placed in the auriculo-ventricular groove, tightened, and the development of the independent ventricular rhythm observed; the ventricle was then cut away, the auricle attached to the lower lever, the sinus to the upper, and the clamp placed in the sino-auricular groove. This clamp was then tightened and the auricle immediately began to beat independently of the sinus, slowing down in the first ten beats until the length of the pause between two consecutive beats reached 14 secs. and then gradually quickening until in between 9 and 10 minutes after the separation the auricular contractions were as rapid and regular as the original sinus contractions (the rate in each case being 1 in 4·6 secs.), though absolutely independent of them and indeed the rate of these had by this time quickened up to 1 in 3·8 secs.

Dec. 20, 1882. In this case the sinus was cut away at the sino-auricular groove and auricles and ventricle left suspended; no standstill occurred but the slow auricular beats improved in rapidity in a somewhat irregular manner until in between 20 and 30 minutes after isolation the auricle and ventricle were beating at a rate slightly less than 12 beats per minute, the original sinus rate being slightly over 12 beats per minute.

When however the section is made or the clamp tightened between the sinus and ventricle or in the auriculo-ventricular groove, then it is not so evident that the ventricle has the power of initiating a rhythm equal in rate to that of the sinus; for the pauses between the beats are at first so long and the increase in rate becomes soon so gradual that the observation has to be discontinued before the maximum rate has been attained. In the following example I give a typical case of the behaviour of the isolated ventricle during six hours' continuous observation, to show the manner in which the rate of the ventricle and the rate of the sinus gradually approach each other, the one becoming slower and slower, the other quicker and quicker.

Feb. 9, 1882. Plate II. Fig. 2, curves I—VII. The heart was at 12 o'clock suspended with the auricle attached to the upper and the ventricle to the lower lever, and was held by means of a clamp in the auriculo-ventricular groove. This clamp was tightened to its uttermost so as to separate the ventricle absolutely from the auricle and sinus; the preparation was moistened at intervals and a series of tracings were taken up to 6.40 p.m. When the clamp was tightened, a rhythm of excitation was set up in the ventricle which gradually became slower and slower until it reached its minimum as seen in curve I. No absolute standstill took place, but from this minimum point the rate of the ventricular beats steadily improved as is shown in curves II. and III. which were taken immediately in succession to curve I. Curves IV., V., VI., VII. were taken at 2.45, 4.0, 5.15, and 6.40 p.m. respectively, and are selected out of the whole number taken in this experiment as fairly illustrative of the rate at which the rhythms of the ventricle and of the sinus tended to approximate by the quickening of the one and the slowing of the other.

This experiment shows that the establishment of the full rhythmical power of the isolated ventricle takes place very slowly when the ventricle is simply kept moist but is otherwise not interfered with. If however it be supplied with suitable food material then the full rhythmical power is manifested much more quickly, then the rate of rhythm easily reaches that of the sinus.

The heart of the tortoise differs from that of the frog in the manner of its blood supply; for whereas in the frog a special system of blood vessels does not exist for either ventricle or auricle, in the tortoise the ventricle is supplied with a well developed coronary system which, commencing as two fine arteries in the systemic aorta a little above the aortic valves, ends in a number of coronary veins which pass from the auriculo-ventricular groove to the venous sinus along the junction wall of the two auricles. This coronary system is confined to the ventricle, the auricular tissue like both auricle and ventricle in the frog being entirely devoid of blood-vessels. If a cannula be tied into the systemic aorta above the origin of the coronary arteries and a blood solution be sent through it under a sufficient pressure, this pressure will close the aortic valves and so prevent the blood passing into the ventricle, while at the same time it sends the blood through the coronary system and so into the venous sinus. If further the junction wall between the auricles and therefore the coronary veins be cut across, the blood which has passed through the thickness of the ventricular tissue will drop from the cut ends of the veins instead of passing

into the venous sinus, and so any distension of the heart cavities with blood will be prevented. In this way then the muscular and nervous elements of the ventricle can be supplied with blood while the heart still remains empty and the sinus remains under the same conditions as before; in other words we can feed the ventricle without feeding the sinus and without distending the heart. Among the numerous problems to the solution of which we may hope that this method may give some insight I will confine myself in this place to one, viz. the effect upon the automaticity of the ventricle of a supply of blood through its coronary system.

After the cannula had been inserted into the aorta a small portion of defibrinated blood solution (1 sheep's blood to 2 normal saline) or of normal salt solution was sent through the coronary system in order to remove the coagulable blood in the vessels; the heart was suspended and the junction wall cut across; the blood solution was then again allowed to run through the coronary system at a constant pressure varying from 50 to 70 mm. Hg. The blood solution dropped from the cut ends of the coronary veins, the heart remained undistended as before, and the ventricle responded to the contractions of the sinus and auricles. The influence of the sinus was then removed either by a section through the auricles intermediate between the sinus and the ventricle or by the removal of the whole auricle. In no case have I seen any sign of stand-still following upon the isolation of the ventricle under these circumstances; an immediate regular ventricular rhythm was always observed.

Thus:—

March 7. Rate of the ventricular beat immediately after separation was regular at 1 in 18 secs. and in 35 min. it had increased to 1 in 12 secs.

„ 8. Rate immediately after separation 1 in 15 secs. and in 45 min. still 1 in 15 secs.

„ 14. Rate varied with blood pressure, quickest when the pressure was highest, was perfectly regular at 1 in 6 secs., i.e. the sinus rate.

„ 15. Rate immediately after separation 1 in 8 secs. perfectly regular, blood running through at the time, varied according to pressure, quickest rate being 1 in 5 secs., i.e. same rate as sinus.

„ 16. Rate immediately after separation 1 in 20 secs., no blood through at the time, varied with blood pressure up to maximum rate of 1 in 5 secs., i.e. rate of sinus.

March 17. Rate immediately after separation 1 in 12 secs., no blood through at the time, varied with blood pressure up to the maximum rate of 1 in 6 secs., i.e. about the same as the sinus rate.

Every experiment shows that the flow of blood through the coronary system not only causes the independent rhythm of the ventricle to be developed much more rapidly, but also that the rhythm of the isolated ventricle when so developed may be as regular and as rapid as that of the sinus, provided that the pressure of blood in the coronary arteries is sufficiently great.

Again, not only is the whole ventricle capable of initiating and sustaining a rate of rhythm as great as the normal sinus rate, but also the suspended strip from the apex can be taught to beat as quickly and as regularly as the sinus itself. Thus in the example already mentioned (Fig. 3, Pl. II., see p. 54) the whole heart had been previously suspended in order to show Prof. Horvath the action of the vagus, and its rate was then found to be perfectly regular at ten beats per minute. The apex strip in between 2 to 2½ hours after preparation and suspension was beating spontaneously, as shown in Fig. 3, curves IV., V., at the rate varying from 9·5 to 10 beats per min., and at 9·15 p.m., i.e. six hours after suspension and nearly five hours after the commencement of automatic contractions, at the rate of 10 beats per min. Since then, the whole auricle is able of itself to beat as fast as the sinus, while the rate of the automatic rhythm of the ventricle or of a strip of ventricular muscle can be developed up to the same extent by the trophic action of nutrient material or of the interrupted current respectively, it is impossible on the ground of differences in the rate of rhythm to make such a vital distinction between the origin of the rhythms of the sinus and apex strip as is implied in the terms nervous and myogonic applied to them respectively.

To sum up then: Between the rhythm of the sinus and the rhythm of the muscular strip from the apex no hard and fast line can be drawn; between these two extremes a distinct gradation of rhythmical power is manifested, and wherever such automatic rhythm is developed the laws of its development are the same. What differences there are, are differences of degree not of kind. In all cases the development of the automatic rhythm to its fullest extent is a gradual one, commencing with beats at a slower rate than that subsequently attained, and the preliminary standstill which so often occurs is simply a sign of this gradual development.

PART II.

On the sequence of the contractions of the different heart cavities.

Just as Haller and the physiologists of his time looked upon the rhythm of the heart as due to the action of the blood upon the muscular tissue of the heart, so also they spoke of the type of the heart's movements as a peristaltic contraction which started in the venæ cavæ and spread in regular order over the whole heart. In those days the continuity of the cardiac muscular fibres was not fully appreciated and in consequence arguments were given and experiments made to show that the contraction of each muscle fibre caused a contraction of the next muscle fibre because the act of contraction pinched compressed and stimulated nerve fibres which supplied the muscle fibre next in order. The peristaltic contraction then was looked upon as due rather to a progressive nervous action than to the passage of a wave of contraction over a hollow muscle. It was soon felt however that the type of a peristaltic contraction was unsatisfactory, since the different parts of the heart were able, especially when the heart was dying, to contract singly and separately. Schiff[1] therefore came to the conclusion that the sequence is regulated from the starting point of the rhythm, and that the ventricle contracts after the auricle because, although the motor nerves of the auricle and ventricle are stimulated at the same moment in the venous sinus, the nervous arrangements are of such a character that the stimulus does not reach the ventricle so soon as the auricle. Of late years the conception of a peristaltic wave of contraction passing from one end of the heart to the other seems entirely to have dropped out of sight, and the sequence of the contractions as well as their origin is attributed to the action of motor nerve cells. Thus Eckhard[2] and Marchand[3] both assert that the sequence of ventricular upon auricular contraction is lost when the two auriculo-ventricular ganglia are extirpated in the frog, and from the experiments of Marchand—which show that the time between the excitation of the auricle and the resulting contraction of the ventricle is too long to be explained by a wave of contraction passing along such a muscular tissue as that of the frog's ventricle,—it has been generally argued, that the path of the excitation from the auricle to the

[1] *Op. cit.* [2] *Beiträge*, Vol. VII., p. 191.
[3] Pflüger's *Archiv*, Vol. XVII., p. 137.

ventricle passes through the auriculo-ventricular ganglia. At the same time, Eckhard[1] and others have observed that section of the inter-auricular septum and therefore of the large nerve trunks between the sinus and the ventricle does not in any way affect the sequence of ventricular upon auricular beat. Here again, as in the investigation of rhythm, the heart of the tortoise offers great advantages over that of the frog from the fact that the intra-cardiac nerves and ganglia as they pass from the sinus to the ventricle are situated externally and not internally. In all cases the ganglia are rather to be considered as appendages to the nerves than as separate organs to which nerve fibres pass; the largest accumulations of them are found at the bifurcation of large nerve trunks in the sinus, in the junction wall between the two auricles, and in the termination of this wall in the auriculo-ventricular ring. In all these places the ganglion cells are also found on the smaller branches of the nerves which ramify over the sinus and form a rich plexus in the junction wall between the two auricles and at the junction between auricles and ventricle. The nerves with their accompanying ganglia are distributed around the whole junction of the sinus and the auricles, and from this ring as well as laterally from both sides of the junction wall between the two auricles nerve fibres with ganglia are plainly seen passing into the auricular tissue; as the nerves pass further into the tissue the ganglia become more and more scarce and soon disappear. If then we call the junction wall between the two auricles the flattened part and the rest of the auricles the bulged part of the auricles, we find that the larger nerve trunks and ganglia of the auricles are found only in those parts of the bulged portion which are in the immediate vicinity of the flattened portion, of the sino-auricular junction and of the auriculo-ventricular junction. Again at the junction of the auricles and ventricle the nerve trunks passing from the junction wall of the two auricles anastomose and form a rich plexus containing large groups of ganglion cells along the line where this junction wall passes into the auriculo-ventricular ring, along that is the side of the ring furthest removed from the aorta,—this I will in future call the "base" of the auriculo-ventricular ring. From thence a plexus of nerve fibres, also containing ganglia though much more sparingly than the basal portion, passes round the auriculo-ventricular ring. From this ganglionic nervous ring, fibres ramify over both the ventricle and the auricles, in each case accompanied by ganglion cells for a short

[1] *Op. cit.*

distance. Similarly the junction between the sinus and the auricles contains a ganglionic nerve plexus ring, and over the whole surface of the sinus nerve fibres anastomose and carry ganglion cells with them. In some cases the two vagi nerves join together in the sinus to form a perfect chiasma as is also often the case in the frog, in others they run slightly apart and join simply by anastomosing branches, as according to Ranvier is the usual method in the frog. When they form a chiasma the junction is filled up with a very large group of ganglion cells. The nerve trunks passing from the sinus to the ventricle along the junction wall are accompanied by the coronary veins in their passage from the auriculo-ventricular groove to the sinus. One of these coronary veins runs free from the surrounding tissue so as to form a separate and distinct connection between the sinus and the auriculo-ventricular groove (C in the Figs. 20, 21); this vein can therefore be cut and either end stimulated without any injury to the heart itself. A branch of the right vagus nerve in the majority of cases accompanies this vein and is usually large and well defined but sometimes small and insignificant. This inter-cardiac nerve I propose to call the "coronary nerve". It branches off from the right vagus directly after the nerve has left the large group of ganglia in the sinus and is well supplied with ganglia until it is entirely free from the heart; during its free course it contains very few if any ganglion cells and just before it enters the auriculo-ventricular groove ganglia again become abundant. In the auriculo-ventricular groove it is in connection with a large group of ganglion cells, anastomoses freely with the ganglionated nerve plexus of the groove, and is distributed over the auricles as well as the ventricle. Its auricular fibres as well as its ventricular are supplied with ganglia for a short distance. The cardiac nerves then after they leave the sinus form two ganglionated nerve rings at the junctions of the sinus and auricles and of auricles and ventricle respectively, connected by a ganglionated nerve plexus band in the junction wall between the two auricles. In Fig. 21, p. 49, the appearance of the heart when suspended is represented; the curved line C represents the free coronary vein and nerve, and the line directly joining the sinus S with the ventricle V the position of the junction wall between the two auricles. A vertical cut therefore between S and V will divide this junction wall and with it all the nerves which pass directly from the sinus to the ventricle.

In endeavouring therefore to find out the reason of the sequence of the heart contractions, we can at the outset eliminate the hypothesis that stimuli pass from the sinus to the auricles and ventricle through

the cardiac nerves and attached ganglia, and that the function of the latter is to regulate the time of arrival of the stimulus at the ventricle, so that the ventricle may always contract in due sequence to the auricle. For, section of all the nerve trunks between the sinus and ventricle or even absolute removal of them with their accompanying ganglia does not in the very slightest degree affect the due sequence of ventricular upon auricular beat. Again, on the other hand, if the auricles be cut away from the ventricle leaving only the coronary nerve as the link of communication between the sinus and the auriculo-ventricular groove, there is never the slightest sign on the part of the ventricle and the auricle in connection with it of any ability to beat in response to the rhythm of the sinus and that part of the auricle in connection with it. Since then the sequence of ventricular upon auricular beat does not depend upon the transmission of stimuli along nerve fibres from the starting point of the rhythm to the auricle and ventricle respectively, what does it depend upon? The answer to this question is simple and perfectly certain, viz.

The ventricle contracts in due sequence with the auricle because a wave of contraction passes along the auricular muscle and induces a ventricular contraction when it reaches the auriculo-ventricular groove.

We have seen that a slit can be made through the junction wall and that part of the auricle in connection with it without at all interfering with the sequence of the beats. We can further carry this slit much nearer to the point of attachment of the ligature at the apex of the auricle so that, the other auricle being cut away, the connection between the sinus and the ventricle is maintained by two bands of auricular tissue joined at their apex by a narrow bridge of tissue as shown in the accompanying woodcut Fig. 22; and yet the due sequence of the ventricular upon the auricular beats is not disturbed. That part of the slit-up auricle which is in connection with the sinus will be called in future "sinus-auricle" or A_s, and the part in connection with the ventricle, ventricle-auricle or A_v.

When the auricle is slit up for only a short distance so that the bridge of tissue at the apex is broad, then the auricle contracts as a whole and the ventricle follows just as though no section had been made. The section can be continued further and further without much difference in the result; at last however, when the bridge is quite thin, it is apparent that a wave of contraction passes from the sinus up A_s and then after a slight pause down A_v to the sulcus where another pause

occurs and then the ventricle contracts. In Fig. 4 A, Pl. III. the graphic representation of these pauses is shown together with the due sequence

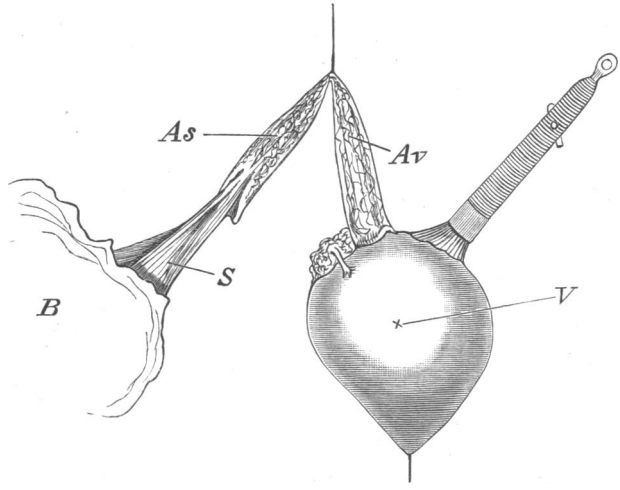


FIG. 22. Junction wall and auricle slit up so as to separate auricle into 2 parts *As*, *Av*.

of the ventricular upon *every* auricular beat. When the section is still nearer the apex then it is seen that *every* contraction wave is unable to pass the narrow bridge of tissue, but that *every second* contraction passes over and when it reaches the ventricle induces a ventricular contraction. The ventricle *never* contracts in response to those alternate contractions of A_s which do not pass the narrow bridge of tissue at the apex, but only when the contraction wave passes down A_v and reaches the auriculo-ventricular sulcus. By the right amount of auricular section then we can make the ventricle beat perfectly regularly after every second beat of the sinus. The nature of the curves obtained is seen in Figs. 4, 10, 11, 12, 13, Pl. III., IV. Fig. 4 B is taken from the same experiment as Fig. 4 A, in order to show graphically the effect of slightly increasing the severity of the section. As the section is continued nearer the attachment of the ligature so that the bridge of tissue is still further reduced the contractions pass with greater and greater difficulty, so that a contraction wave passes along A_v after perhaps 5, 6 or more beats of A_s and then and then only the ventricular contraction follows. Finally when the tissue is so thin that it often appears impossible to cut further without cutting the ligature itself, then the contraction wave is absolutely unable to pass, then

the "block[1]" is complete and any contractions of the ventricle which may occur are absolutely independent of those of the sinus and sinus-auricle. Even when the block is complete so that no contractions have been able to pass for many minutes and the independent ventricular contractions have commenced, it is still possible as will be shown later on for a more or less complete recovery to take place, so that again every or every second contraction may pass the blocking point.

These experiments show definitely that the ventricle contracts after the auricle only when a contraction wave passes to the auriculo-ventricular groove, and I have never seen any evidence that anything of the nature of a nervous influence such as a wave of excitation can pass the block and set the ventricle in action when the contraction wave cannot pass. It is certain that no nervous influence passing along nerve fibres in the visceral pericardium apart from the muscle fibres is concerned in the production of the ventricular beat, for, after having slit up the auricle slightly so as not to cause any block, I have then thinned down a small ring of tissue in A_v midway between the attachment of the ligature and the ventricle in such a manner as to remove all the pericardial surface, and therefore to leave at this spot a connecting bridge of muscular tissue alone; through this the contraction wave passed and a ventricular contraction followed. By thinning it sufficiently a partial block, so that every second contraction passed, or a complete block could be caused. When the contraction wave reached the ventricle it responded, when no contraction passed the ventricle remained quiescent; in fact, no doubt can possibly remain that the ventricle beats after the auricle because it does not contract until the auricular contraction reaches it.

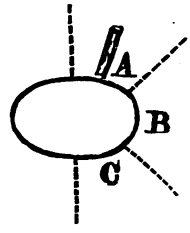
In precisely the same way the due sequence of the contractions in the frog's heart does not depend upon the integrity of the nerves in the auricular septum but upon the contraction of the auricle, and here also as I have elsewhere[2] shown a blocking of the auricular contraction wave can be caused by compression of the muscular fibres as they pass into the auriculo-ventricular groove, a block which may be partial or complete in precisely the same way as already described for the tortoise.

[1] In his experiments upon the passage of contraction waves along the muscular tissue of the swimming bell of the Medusæ, Romanes (*Phil. Trans.* Vol. CLXVI. Pt. I.) has throughout made use of the term "block" to express any artificial hindrance to the passage of the contraction. I therefore make use of the same term in speaking of the results of experiments on the cardiac muscle which are very similar to those which he performed on the muscle of the Medusa.

[2] *Phil. Trans.* 1882, Pt. III.

Since then the ventricle does not contract after the auricle because separate stimuli pass from the sinus to the ventricle along nerve fibres, but does contract because a contraction wave passes along the muscular tissue of the auricle to the junction of the auricles and ventricle, the question arises; How is it that a contraction of an auricular muscle fibre is able to cause a contraction of a ventricular muscle fibre? and especially, what is the reason of the pause which ensues before the ventricle contracts after the auricular contraction has reached the auriculo-ventricular groove?

An answer to these questions is most likely to be found by examining whether any particular portion of the junction of the auricles and ventricle is especially concerned with the maintenance of the sequence of ventricular upon auricular beats, and at the same time investigating the structure of the auriculo-ventricular groove. For the purposes of description it is convenient to divide the auriculo-ventricular ring into sections, and therefore in accordance with its position in all my experiments I will call the portion of the ring or rather of the half ring nearest the aorta, the upper, or A in the accompanying diagram, the lateral portion the middle or B, and the lowermost portion the basal segment or C.



In the first place the integrity of the whole ring is unnecessary for the due sequence of the contractions; the whole of one auricle can be removed together with the corresponding half of the base of the ventricle, and yet the contractions of the remaining auricle will be followed regularly by contractions of the ventricle. I commence therefore by cutting away the left auricle and that part of the ring to which it is attached, and then remove the auricular attachments and the ring on the right side bit by bit until the sequence is lost, beginning in the one case with the removal of the basal portion C and cutting round towards the aorta and in the other with the removal of the upper section

A and gradually passing towards the base. The following example shows the difference in effect of the two operations.

July 5, 1882. Upper portion of tortoise removed from the body with the heart in position, and placed on a plate. The left auricle and the base of the ventricle to which it was attached was cut away. The ventricle still contracted after every contraction of the right auricle.

The base C of the right part of the auriculo-ventricular ring was then removed, together with that part of the right auricle which was attached to it. The ventricle still beat absolutely synchronously with the auricle.

The middle B of the right side of the ring and the auricular attachments were cut away. Still every contraction of the auricle induced a ventricular contraction.

The section was then carried close to the aorta, so that the only part of the auriculo-ventricular ring which was left intact was that part of the upper portion A of the ring on the right side between the middle line and the whole attachment of the aorta.

After this last section at 1.9 p.m. the ventricle remained quiescent for a while, then contractions began to pass from auricle to ventricle and in ten minutes, at 1.19 p.m., the ventricle was contracting regularly after every second auricular contraction.

1.30 Ventricle still misses every second auricular beat.
1.40 do. do.
1.52 Ventricle misses only every third beat.
1.59 Ventricle misses only every fourth beat.

At 2 p.m. I cut away a small piece of the ring at the middle line of the upper part of the ring where the right and left auricles meet.

2.5 Ventricle beats after every contraction of the auricle.
2.9 do. do.
2.12 do. do.

At 2.13 I cut from the middle line towards the aorta up to the middle of the attachment of the aorta, so that the auricle was now attached to only a narrow strip of the auriculo-ventricular ring comprising the middle of the attachment of the aortic trunk. After this last section the ventricle was quiescent but again

at 2.17 was beating after every second auricular beat,
and at 2.19 was again synchronous with the auricle.

A small piece of tissue was again removed underneath the aorta. Ventricle immediately quiescent.

At 2.25 the sequence had again recovered to the extent that the ventricle was able to respond to every second auricular beat.

The strip of auricular tissue was then cut away, and the ventricle was

found to be beating spontaneously at a rate somewhat slower than 1 to 3 auricular beats.

The last small piece of the auriculo-ventricular ring was now cut away at 2.28. The ventricle immediately became quiescent and remained without a single contraction as long as observed, i.e. up to 3.30 p.m.

A second tortoise was now taken and the reverse operation performed, the left auricle and auriculo-ventricular ring being cut away at 2.44 p.m. The ventricle responded regularly after every contraction of the right auricle.

The upper portion of the right ring and the attachments of the right auricle were now cut away from the upper middle line to the end of the attachment of the aorta at 2.49. The ventricle immediately remained quiescent.

2.57 Still quiescent.
3.4 do.
3.45 First ventricular beat.
3.12 Ventricle beats alternately after every second and every third auricular beat.
3.15 Still alternately after every third and every second beat.
3.22 Ventricle beats regularly after every second auricular contraction.
3.25 do. do.

The middle portion B of ring was now removed, leaving the whole of the broad base C with its nerves, ganglia and auricular attachments still intact.

The ventricle was immediately quiescent; observed up to 4 p.m.; the ventricle never responded with a single contraction although the auricles continued to beat regularly and well.

This experiment shows clearly that the basal part of the auriculo-ventricular groove has the least share in the maintenance of the sequence of ventricular and auricular beat, and yet this is precisely the part where the nerve fibres enter, where the ganglion cells are to be found in greatest profusion. From this fact alone the assumption that ganglion cells play an important part in the transmission of the contraction from the auricle to the ventricle is rendered very doubtful; and microscopical evidence shows that such an assumption is not only improbable but unnecessary.

The heart of the tortoise consists of three muscular cavities, the sinus cavity, the auricular cavity and the ventricular cavity, separated from each other by two more or less well defined constrictions, the auriculo-ventricular and sino-auricular grooves. The arrangement of the muscular fibres is somewhat as follows. In the sinus the muscular fibres are closely set together, largely parallel to each other, with a tendency to

form a circularly arranged continuous muscular sheet, and from these arise and branch in various directions other fibres which form separate bundles, passing from point to point and constituting a rudimentary reticulated structure similar to what is seen in perfection in the auricles. At the sino-auricular junction both sets of fibres join to form a regular band of parallel closely-set muscle fibres which form a circular muscular ring, from which the fibres of the auricle take their origin. On both sides of this ring, whether in the sinus or the auricle, those fibre bundles which pass towards it at right angles to the direction of its fibres split into two parts, which curving in opposite directions are continuous with the ring fibres. From this sino-auricular muscular ring a network of loose reticulated fibres connected in all directions springs to form the bulged portions of the auricles. In the flattened portion of the two auricles—in, that is, the band of tissue forming the junction wall between the auricles, the muscle fibres are arranged in a closely-set sheet of fibres which are continuous with and largely parallel to the circularly-arranged fibres of the sino-auricular ring. This portion of the auricles then resembles in the arrangement of its muscular structure the ground-work of the sinus and the sino-auricular ring, and not the reticulated mesh-work of the rest of the auricles. From the sino-auricular ring and from the junction wall, the reticulated fibres of the auricle ramify in all directions until they approach to their attachments in the upper and middle parts of the auriculo-ventricular groove. Here again as in the sinus the arrangement gradually changes from a network into a continuous sheet, the fibres become more and more parallel, and at last form another well defined circularly arranged ring of parallel muscular fibres. From this ring the muscular fibres of the ventricle in part take their origin. The base of this ring is continuous with and its fibres are parallel to the non-reticulated muscular fibres of the inter-auricular junction wall. We see then that the arrangement of the muscle fibres in the heart of the tortoise, the two rings of circularly arranged muscle fibres joined at their base by a band of similarly circularly arranged fibres is very suggestive of the primitive origin of the heart from a tube like that of an artery or of the ureter, where the fibres are throughout arranged in a circular manner. The existence of these two muscular rings connecting the three muscular cavities of the heart is amply sufficient to account for the passage of the contraction from the sinus to the auricle, and from the auricle to the ventricle, without the necessity of invoking the presence of ganglion cells, and leads directly to the view originally

held by physiologists that the cavities of the heart contract in regular sequence, because a peristaltic wave of contraction commencing at the sinus passes from one end of the heart to the other.

Before this view can be accepted some explanation must be given of the natural pauses which occur between the contractions of the sinus and auricles and of the auricles and ventricle respectively. Also attention must be paid to Marchand's[1] assertion that the time which elapses before the ventricle responds when a stimulus is applied to the auricle is too long to be explained on the assumption that the stimulus reaches the ventricle along simple nerve or muscle fibres, as well as to the assertion that the ventricle of the frog does not contract after the auricle, when the two auriculo-ventricular ganglia have been removed.

We have already seen that an additional pause as well marked as either of the natural pauses can be artificially produced in a purely muscular part of the auricles by a simple hindrance of the passage of a wave of contraction. Such a commencing block is caused when the path of the contraction wave is narrowed to a thin bridge of muscle, the conduction power of which has moreover been in all probability lowered by the previous operation. It is therefore possible to interpolate a pause in the course of a wave of contraction by artificially altering the conduction power of the muscle at any one point. If then such an alteration of conduction power occurred naturally at any point owing to the normal arrangement or structure of the muscle fibres at that point, a pause or rather an alteration of rate in the progress of the contraction wave would take place here of the same character as the pause between the contractions of the auricle and ventricle.

Further, such an alteration in conduction power in the course of the passage of the contraction wave from the auricle to the ventricle would explain all the objections which have hitherto been raised against the hypothesis that the beat of the heart is a peristaltic wave of contraction passing from one end of the heart to the other. Thus in the first place such an assumption will explain Marchand's experiment mentioned above; for the whole point of that experiment is based on the supposition that the rate of conduction along a supposed muscular path from the auricle to the ventricle must be equal to the rate along the muscles of the body of the ventricle as determined by the experiments of Engelmann. In the second place the facts—that under certain conditions, especially when the heart is near to death, a contraction of the ventricle

[1] *Loc. cit.*

alone can be caused which does not induce an auricular contraction and *vice versâ*; and also that in the same circumstances of lowered excitability whether caused by impaired nutrition or by the action of poisons, &c. the ventricle is often found to be beating after every second, every third or more auricular beats, and finally to cease beating while the auricle continues to contract—which were in the eyes of Schiff, Volkmann, Budge, &c. insuperable objections to the acceptance of a peristaltic wave passing from auricle to ventricle, have now I venture to say become the strongest arguments for the existence of such a peristaltic wave, which at the auriculo-ventricular junction passes through a region of diminished conductivity. Just as in the passage of the contraction from the sinus-auricle to the ventricle-auricle a successively increasing severity of section, that is, an increasing impairment of the tissue, produces first a commencing block, i.e. a simple delay in the rate of the passage of each contraction wave, then a partial block, so that only every second contraction passes, and finally a complete block, in which no contractions pass; so too any impairment of the whole heart of such a character as to lower the excitability and the conduction power of the cardiac muscle will necessarily convert the slight block which exists naturally at the auriculo-ventricular junction into first a partial block during which the ventricle will respond to every second, third, or more beats of the auricle, and finally into a complete block when the auricles will continue beating but the ventricle will remain quiescent. The special tendency for the contraction wave to be blocked at both the sino-auricular and auriculo-ventricular junctions will be further considered when we come to deal with the action of the cardiac nerves.

Further, we have every reason to believe that the contraction wave is not likely to pass so easily from the auricle to the ventricle as over the surface of the auricle or ventricle themselves, not only because the auriculo-ventricular muscular ring is narrow and a somewhat abrupt change occurs in the direction of the muscular fibres along which the contraction wave passes, when it reaches and leaves this ring, but essentially because the structure of the muscular fibres here is different from those of the auricle or ventricle. This difference of structure can be best discussed in connection with a description of the structure of the muscle fibres in all the different parts of the heart of the tortoise.

The muscle fibres throughout the heart are of the same type, any differences which are seen are differences in the prominence of the various structural peculiarities of the cardiac type of muscle, and are not so great as the differences between unstriated and striated muscle

fibres. Thus all the muscle fibres are to a greater or less extent transversely striated; but the prominence of this striation varies considerably. Similarly the thickness of the fibre, the extent of parallelism of its edges, the size of the nucleus in relation to the size of the fibre, and therefore the extent of crowding of the nuclei in any strip, all present differences in different parts of the heart. The greatest contrast is seen when the muscular fibres of the ground layer in the sinus are teazed out and compared with the muscle fibres of the spongy tissue of the ventricle. The sinus muscle fibre is thin and delicate, tapering somewhat at both ends, with a large central oval nucleus which causes a distinct bulging of the fibre; the substance of the fibre shows a striation which is decidedly indistinct, presenting often a granular rather than a distinct banded appearance. On the other hand the ventricular muscle fibre is boldly and strongly striated, it is much thicker than that of the sinus, its edges are parallel and the thin elongated nucleus is small in comparison to the size of the fibre. The muscle fibres of the reticulated tissue of the auricle are not so large or so coarsely striated as those of the ventricle, though larger and much more distinctly striated than the sinus muscle fibres. Their edges also are more parallel than in the fibres of the sinus. The muscular ring forming the junction of the auricles and ventricle, and to a certain extent the whole junction wall joining the two auricles are composed of muscle fibres with a structure intermediate between the sinus and the auricle muscles. The nuclei are large, conspicuous on section both in size and number, the striation is not so well marked as in the bulged portion of the auricles, and the fibres are thin and delicate with somewhat parallel edges.

Such a structure as above described is very suggestive not only as an explanation of the pauses which occur naturally in the course of the peristaltic wave of contraction, but also of the differences of rhythmical power exhibited by different parts of the heart. We see that the sinus, the sino-auricular ring, the junction wall between the two auricles and the auriculo-ventricular ring are all composed of muscular fibres which differ from those of the ventricle and the bulged portions of the auricles not only in arrangement but also in structure, and that this difference is exactly what we should expect to see, if these latter parts had reached a higher stage of development than the former. The more developed tissue would not only possess a more marked striation, a less conspicuous nucleus and a contour with parallel edges rather than spindle-shaped, but would be characterised by a greater rapidity both of contraction and

conduction than the less developed. If then a wave of contraction were started at the sinus end it would pass most rapidly along the reticulated fibres of the sinus, auricles, and ventricle, and more slowly at the junctions of the sinus with the auricle, and of the auricle with the ventricle; if further these more rapidly contracting parts were bulged out so as to conceal the junctions, then the true nature of a wave of contraction would be completely masked, and the contractions of the three cavities of the sinus, auricles and ventricle would appear to take place independently with pauses between them.

The difference in the conduction power of the muscular tissue of the inter-auricular junction wall from that of the auricle proper, is evident from a number of experiments which I have made for the purpose of comparing the effect upon the sequence of the ventricular and auricular contraction of removal of the junction wall alone, leaving the bulged portion of the auricles as the means of communication between the sinus and the ventricle, and conversely of removal of the bulged portions, leaving only the junction wall between the two auricles. The following example is typical of the opposite effects of these two operations.

March 10, 1882. Two small tortoises were taken and their hearts removed and pinned out with the junction wall uppermost. In each case the free coronary vein and the flattened portion of the auricles was well defined. The line of junction of the bulged and flattened portions was cut through on each side in both cases, without affecting the sequence, and then in the one case the whole of the junction wall was cut away leaving the bulged portion intact, and in the other the bulged portions were separated from the ventricle leaving the junction wall intact. In the first case the sequence was absolutely unaffected by the operation, in the other the ventricle remained still for a long time and then began to beat slowly and independently of the auricular contractions. In the first case the auricular tissue was then cut through to a greater and greater extent, until at last only a narrow bridge of the reticulated muscle of the auricle remained, and yet the sequence was maintained. In fact, the sequence of ventricular upon auricular beat is able to continue when the contraction wave is obliged to pass over an exceedingly narrow bridge of the muscular tissue of the bulged portion of the auricle, but is absolutely lost, when the only path for the contraction wave is the flattened junction wall between the two auricles, although in the latter case the strip of muscle is much broader than in the former and although in both cases the auriculo-ventricular ring is intact.

The difference between these two cases is most striking and is

always the same, although the band of tissue which was left intact in the first case along which the contractions might travel to reach the ventricle, was many times broader than the final bridge of the reticulated muscular tissue in the second case; although, in addition to the greater breadth of the strip, the nerve communications ganglia and all, between the sinus and the ventricle were intact in the first experiment while in the second nothing was left but a narrow muscular bridge as the means of communication between sinus and ventricle; yet the sequence was absolutely prevented in the former case, absolutely unaffected in the latter. We see then without doubt not only that the sequence depends on the passage of a contraction over the bulged portion of the auricles to the upper portion of the auriculo-ventricular junction ring, but also the conduction of the contraction is less easy along the muscular tissue of the junction wall between the two auricles than along the reticulated muscular network of the bulged portion of the auricles. I do not desire to assert that a contraction wave can never pass along the inter-auricular junction wall and so to the ventricle, for I have seen in one or two cases a slight and partial repair of the sequence some time after the operation when the junction wall alone was left; I only assert that in all cases the sequence is maintained with immensely greater ease when only a small bridge of the reticulated muscular tissue is left, over which the contraction wave can travel, than when the whole of the junction wall is left intact.

Finally, the assertion based upon the experiments of Eckhard and Marchand, that the auriculo-ventricular ganglia are essential for the due sequence of the ventricular upon the auricular contractions in the frog, must be examined into and its truth or falsity proved.

The fibres of the auricles in the frog pass into a well defined ring of circularly arranged muscle fibres at the junction between the auricles and ventricle of the same nature as already described for the tortoise. The diameter of this ring is naturally as small as the orifice between the auricles and the ventricle, so that in such an operation as the removal of the auriculo-ventricular ganglia it is easy to cut away or damage this muscular ring, even while apparently leaving the connections between auricles and ventricle intact. I have however succeeded in removing the two ganglia without injury to this ring as follows. I first opened and removed a portion of the apex of one auricle, washed out and at the same time slightly distended the heart with a jet of normal saline solution, so as to bring the septum into view: I then seized the septum with a pair of fine forceps and gently drew it forward, until the two white

masses of the auriculo-ventricular ganglia could be plainly seen. With a fine pair of scissors the septum and the two white masses were now carefully cut away, great care being taken not to injure the auriculo-ventricular ring itself. After the operation the sequence continued just as well as before, every auricular contraction was followed by a ventricular contraction without any preliminary standstill or alteration of any kind. The parts that had been cut away were placed in osmic acid, and the two nerves of the septum terminating in the two well-known bulbous ganglionic masses together with portions of the auriculo-ventricular valves were well shown.

From what has been already said, it is evident that if this muscular ring be either much injured or cut away, a more or less complete block in the passage of the contraction from auricle to ventricle must take place, just as a block can be always caused in the passage of the contraction wave from any one to any other part of the heart of the tortoise. Eckhard's[1] description of the result of his experiments shows to my mind clearly that he had produced, by his method of procedure, such a block, which at first was complete, so that the ventricle remained still, then was partial, so that a certain number of contractions of the ventricle took place, and finally had almost though not quite disappeared. The dependence of these ventricular contractions, which he observed after extirpation of the two ganglia, upon the contractions of the auricle, and therefore the independence of the sequence upon the integrity of these ganglia, could not require a better proof than he himself gives[2], viz. that stimulation of the vagus outside the heart brings these ventricular contractions to rest at the same time as the contractions of the auricle. In other words, stimulation of the nerve is able to influence in the same manner, at the same moment and to the same degree, the contractions of the auricle and these supposed independent contractions of the ventricle, although the nerves of the septum and the two auriculo-ventricular ganglia had been removed. If, then, the ventricular contractions in this case were really independent of the auricular, the influence of the vagus must have passed to the ventricle over the tissue of the auricles, apart from the direct route by the large nerve trunks from the sinus to the ventricle; a mode of action which is not only extremely unlikely, but is also contrary to all experimental evidence afforded by the heart of the tortoise. If, on the

[1] *Op. cit.* [2] *Op. cit.*, p. 193.

other hand, these contractions were not really independent of those of the auricle, but only appeared to be so owing to a blocking of the contraction wave in its passage from the auricle to the ventricle, then naturally when all auricular contractions were stopped by the stimulation of the nerve the ventricular contractions ceased also. Similarly the experiments of Marchand[1] do not in the smallest degree prove that the sequence of the contractions depends on the integrity of the auriculo-ventricular ganglia; they simply show that if a sufficient amount of the muscular ring at the auriculo-ventricular junction be cut away, the block so caused may be permanent, and that in some of the pieces so cut away ganglion cells may be found.

Again, from what has already been said in Part I., those very parts which possess a less developed muscular structure possess also greater rhythmical power than those which have attained a higher development. As we pass from the sinus along the junction wall of the auricles to the auriculo-ventricular ring, and from thence to the muscular tissue of the bulged portion of the auricles and ventricle, we find evidences of successive grades of rhythmical power in fair correspondence with the grades of development of the tissue. The study of the development of the heart shows that it is originally a simple tube with muscular walls from end to end of which waves of contraction pass; a portion of this tube expands to form the auricles and another portion to form the ventricle; these two being connected by an unexpanded part called the *canalis auricularis*, which gradually disappears as the auricles and ventricle bulge more and more, until the original tubular heart becomes converted into a series of cavities with constrictions between them. If in this process those parts which expand take on a higher development for the purpose of executing more rapid contractions, and if this expansion did not include quite the whole circumference of the auricular portion of the tube, we should have in the adult heart the remnant of the original tube represented both in the arrangement of its fibres and in function by the ground fibres of the sinus, the sino-auricular ring, the junction wall between the auricles, and the auriculo-ventricular ring. According to this view, then, we can conceive that the variations in rhythmical power and in conductivity which are characteristic of the different parts of the adult heart of the tortoise may all be accounted for on the supposition, that the development of the muscular tissue of the originally tubular heart has not proceeded at the same rate through-

[1] *Op. cit.*

out the tube; so that in the adult heart greater variations in rhythmical power are apparent in the different sections of it than in the original tubular heart; the peristaltic wave of contraction which originally passed smoothly from end to end, passes finally along a tube of irregular calibre, the muscular walls of which have become so modified in their rates of contraction and conduction, as well as in the arrangement of their fibres, as to form out of a simple peristaltically contracting tube such an efficient muscular pump as is represented by the adult heart.

Such a conception is entirely in accordance with all experiments which I have had an opportunity of making on the hearts of animals lower than the tortoise. In the skate especially, which possesses a large strong muscular conus arteriosus, the passage of the peristaltic wave of contraction can be easily observed. I have not yet had an opportunity of studying the action of the skate's heart to any extent; the following observations being the results of an examination of two large skates, weighing respectively about 60 and 40 pounds, which I had the opportunity of making this last summer during a yachting trip along the west coast of Scotland. The hearts were examined on the deck of the yacht almost immediately after the skates were taken out of the water, and were found to be beating vigorously and regularly, with a good supply of blood in them. The muscular fibres of the large fleshy conus arteriosus are arranged circularly, and merge imperceptibly into the muscular structure of the ventricle. The heart beats somewhat slowly, with great regularity, in the order auricle, ventricle, conus, and it is plainly evident that the contraction passes along the conus in the form of a peristaltic wave. Again, if the auricle is slit up in the same way as described for the tortoise, a very long strip of auricular tissue is obtained, along which each beat travels most plainly to the ventricle in the form of a peristaltic wave, which again reappears as soon as the contraction reaches the conus arteriosus. The peristaltic nature of the beat of the whole heart could not be demonstrated more clearly than in the simple heart of the skate. Further, the rhythmical powers of the conus are nearly as great as those of the sinus; when isolated it continues to beat with great regularity, waves of contraction following one another as readily as in the case of the isolated sinus; this rhythm does not depend on any particular part, one piece continues to beat as well as another.

What, however, is most striking of all, and shows the near relationship between the rhythm of the conus arteriosus and of the sinus, and is the strongest argument in favour of the development of the heart from an

original muscular tube, of which the rhythmical properties are nearly the same throughout, is the ease with which in the skate's heart a reversal in the order of the contractions can be brought about, i.e. the rhythmical preponderance of the sinus end of the tube be transferred to the conus end, and *vice versâ*. If, when the heart is beating normally, the conus arteriosus be touched with the sharp point of a knife, a contraction wave is immediately started in it which when it reaches the ventricle causes a contraction of the ventricle, and then in due sequence of the auricle. After this interpolated contraction wave, due directly to the stimulus, a slight pause takes place, and then for some minutes the heart beats with regular contractions in the order conus, ventricle, auricle, each beat commencing with a distinct peristaltic wave running along the conus into the ventricle. Another slight pause then occurs, and the heart resumes the normal order of its contractions. In both the instances observed by me, the rate of the contractions started from the conus end was somewhat quicker than the normal rate from the sinus end. Further, if the sinus or junction of the sinus with the auricles be gently stimulated, when in consequence of a previous stimulation of the conus the order of the peristaltic contraction has been reversed, then immediately a second reversal takes place, and the contractions recommence at the sinus end. In this way I was able, by alternate slight momentary stimulations of the conus arteriosus and of the sinus, to make the heart of the skate beat in a way similar to the Ascidian heart, in which the normal beat consists of a series of waves of contraction passing alternately in opposite directions. In fact, we see that in the Ascidian the rhythmical power of the two ends of the heart is so nearly equal, that the contractions start with equal, or nearly equal facility from either end, and the alternation of the direction of the contractions is in all probability due to some slight stimulus alternately affecting first one and then the other end, such as an increased blood pressure due to the flow of blood in one direction, which would act as a stimulus chiefly upon that end towards which the contraction waves had been previously travelling[1]. In the skate we reach a higher stage than this, the difference between the aortic and venous pressures alone does not constitute a stimulus sufficient to overcome the greater rhythmical power of the sinus, and therefore to reverse the order of the con-

[1] In the paper by Foster and Dew-Smith upon the effects of electricity applied to the hearts of Mollusks (*Proc. Roy. Soc.* No. 160, 1875) an observation of Dew-Smith is mentioned, which showed that the interrupted current when applied to the heart of the Salpa caused that heart to beat for two minutes entirely in one direction.

tractions; a slight mechanical stimulus is required in addition in order to give such a preponderance to the rhythmical power of the conus arteriosus as is necessary for the production of a rhythmically contracting heart, in which the direction of the contractions is reversed at regular intervals. Again, the cardiac nerves of the skate, like those of all vertebrata, enter the heart at the venous end, and from thence are distributed over the heart; ganglia therefore are found plentifully in the sinus, and disappear before the conus arteriosus is reached; in the conus, as in the bulbus[1] of the frog, ganglia are not to be found. Not only then does the skate's heart afford a good example of the peristaltic nature of the heart's beat, but it also gives a new proof that the starting point of these peristaltic contractions is determined by the nature of the muscular substance rather than by the presence or absence of ganglion cells.

In the frog, as well as in the skate, there is evidence to show that the rhythmical powers of the muscular tissue of the bulbus are more nearly allied to those of the sinus than of the bulged portions of the ventricle. Thus Engelmann has shown not only that the bulbus is free from ganglion cells, but also that its rhythmical power is much greater than that of the muscular tissue of the ventricle. The length of the standstill after isolation, the rapidity of development of its full rate of rhythm when distended with serum, and the regularity of that rhythm, all point to a rhythmical power inherent in the muscular tissue of the bulbus, which is greater than that of the muscular tissue of the apex of the ventricle.

The conception advanced above, that the rhythmical beating of the heart is due to a series of peristaltic contractions which start from that particular portion of the muscular tissue of the heart in which the property of automatic rhythm has been most largely developed, brings the heart's action into harmony with the rest of the vascular system and with the rhythmical properties which are so often manifested by the less specialized forms of muscular tissue. The experiments of Luchsinger[2] have shown not only that the regular well-marked rhythm of the veins of the bat's wing is due undoubtedly to peripheral and not to central causes, but also that the rhythm resembles that of the apex of the frog's heart in its dependence upon a certain amount of pressure within the veins themselves. In this case then, as well as in the strictly analogous case

[1] See Engelmann, *Op. cit.*

[2] Pflüger's *Archiv*, Vol. xxvi. p. 445.

of the middle third of the ureter[1], we have in all probability an instance of a rhythm dependent upon the special development of a particular function of the muscular tissue, and not upon the hypothetical existence of ganglion cells.

PART III.

On the action of the cardiac nerves.

Stimulation of the vagus nerve in the frog is able to produce two opposite effects upon the rate of rhythm of the heart, either slowing and standstill or else acceleration. In my former paper, read before the Royal Society in Dec. 1881[2], I have shown clearly that these two effects are so far independent of each other that the acceleration may occur without any previous slowing. Again, the experiments of Nuël[3] have shown that the vagus can produce a diminution of the force of the auricular contractions independently of any action upon the rate of rhythm. In my paper I have shown that this diminution of the force of the contractions occurs both in the auricle and ventricle and is followed by a most remarkable increase in the force of the contractions, and that these two effects are so far independent of each other that the augmentation of force may occur without any previous diminution. I have also drawn attention to the fact that the vagus can produce an apparent standstill by the reduction of the contractions of the auricle to the point of invisibility. Further, it was pointed out that the vagus caused the ventricle to beat for a time synchronously with every contraction of the auricles when in consequence of the tightness of the clamp in the auriculo-ventricular groove, or by heating the auricles and sinus without heating the ventricle, it was beating after every second auricular contraction or else was absolutely quiescent while the auricle still continued beating. The reverse effect to this was also seen, the ventricle responded to fewer auricular contractions, or in other cases the apex of the ventricle responded to fewer base contractions during the stimulation than before. So too when the ventricle was beating with alternately weak and strong contractions, the vagus removed this alternation during the time when it augmented the force of the contractions, and when it was previously not present caused it to appear

[1] Sokoloff and Luchsinger. Pflüger's *Archiv*, Vol. xxvi. p. 464.

[2] See abstract in *Proc. Roy. Soc.* Vol. xxxiii. p. 199. Full paper in *Phil. Trans.* 1882, Pt. iii.

[3] Pflüger's *Archiv*, Vol. ix. p. 83.

during the time of stimulation coincidently with the diminution of the force of the contractions. Assuming, as I did in that paper, that the auricular and ventricular contractions were due to impulses proceeding from certain motor nerve centres I imagined that these experiments proved that the vagus had the power of both diminishing and increasing the excitability of the ventricular muscle. Subsequently however[1] my experiments on the tortoise convinced me that such an interpretation was erroneous, and that in reality both sets of phenomena were proofs that the vagus was able to diminish and to restore the conduction power of the auricular as well as of the ventricular muscular tissue. Finally it was shown that the vagus was able to diminish the tonicity of the cardiac muscle even when the rate of rhythm was unaltered, but that any evidence of an increase of tone was doubtful.

For the investigation of the action of the cardiac nerves, as well as for the study of the rhythm of the heart, the tortoise offers special facilities over the frog. Not only is the heart more adapted for manipulation owing to its greater size and the external position of its intracardiac nerves, but it is specially suitable for the examination of the vagus action owing to the presence of the coronary nerve. I propose, therefore, to examine in order, the effect of the stimulation of the cardiac nerves upon the rhythm, the force of the contractions, the conduction power, and the sequence of the contractions, and afterwards to combine the results of my experiments on the frog with those on the tortoise, and see to what conclusions they lead.

On the action of the vagus nerves on the rhythm of the tortoise heart, whether that rhythm originates in the sinus or in other parts of the heart.

The results of stimulation of the vagus nerves upon the suspended tortoise heart are very much more constant than in the case of the frog or toad. Standstill can always be obtained, whatever may be the time of year, when the right vagus is stimulated. And though the standstill is frequently followed by acceleration, in no case have I seen any evidence of primary acceleration. The left vagus is much less effective on the rhythm than the right. As a rule the same strength of stimulation which when applied to the right nerve produces marked slowing or absolute standstill, is without effect on the left nerve as far as the rhythm is concerned. With a stronger stimulation the left nerve very

[1] This Journal, Vol. III. p. 369.

often causes a distinct slowing which seldom if ever reaches absolute standstill; in many cases even when the stimulation is very strong the rate remains absolutely unaltered. This distinction between the right and left nerves of the common tortoise, obtainable in England (*Testudo Græca*), is evidently of the same nature as that observed by A. B. Meyer[1] in another species (*Emys Lutaria*), in which the left vagus was entirely unable to affect the rate of rhythm, and shows distinctly that only a certain number of the nerve fibres which are contained in the two vagi nerves have any direct influence upon the rhythm, or according to the view already put forward, the nerve fibres supplying those muscular fibres of the sinus which by their automatic contractions originate the rhythmical beats of the heart run almost exclusively in the right vagus nerve.

When the heart is slowed or reduced to standstill by stimulation of the vagus this slowing is often followed by distinct acceleration. The maximum increase of rate during this after-acceleration is as a rule much less marked than in the case of the frog, but on the other hand the quicker rate lasts a much longer time. The maximum of this rate cannot be increased by repeated stimulations of the nerve, so that it frequently happens that the first stimulation alone produces any after-acceleration, the subsequent stimulations serving only to make that quicker rate more permanent, and not being able therefore to produce any after-acceleration themselves. The after-acceleration is most evident when the heart is beating slowly, and indeed in most cases where the heart is beating fairly rapidly when first suspended, the augmentative effects due to the stimulation of the nerve are manifested not so much by any distinct acceleration as by the maintenance of the original rate of rhythm. When the heart is left to itself the rate of rhythm very slowly and gradually diminishes as is seen in Plate II., Fig. 2.

Further, the existence of the coronary nerve in the tortoise gives us an excellent opportunity of determining whether the intra-cardiac nerve trunks between the sinus and the ventricle are able to influence the rate of rhythm or not. As has been already mentioned no effect whatever is produced by its section. If it be cut close to the sinus and its peripheral end[2] stimulated, the rate of beat continues absolutely the same, it is impossible by any strength of stimulus to alter the rate of

[1] *Hemmungsnerven System des Herzens.* Berlin, 1869.

[2] By the peripheral end I mean the end in connection with the ventricle; by the central end, the end connected with the sinus.

the sinus rhythm by stimulating nerve fibres which are no longer in direct connection with the sinus but only with the auricles and ventricle through the auriculo-ventricular ganglia. In Fig. 5, Pl. IV., I give a typical example of the effect of stimulation of the right vagus, the left vagus and the peripheral end of the coronary nerve; in all three cases both the strength and the length of the stimulation was the same.

On the other hand, if the coronary nerve be cut close to its entrance into the auriculo-ventricular groove and the central end stimulated, then in most cases a decided slowing of the rate takes place. In Fig. 6, Pl. III., I give two consecutive stimulations of the central end of the coronary nerve. As is seen the stronger stimulation slowed the rhythm most decidedly, while the weaker one produced no effect on the rate of the contractions, but only upon their force. In all cases in which I have obtained decided slowing upon stimulation of the central end of the coronary nerve, the effect has only been produced with a fairly strong stimulus, so that doubts arise in my mind whether such slowing was not in reality due to escape of current, owing to the shortness of the nerve. I am however inclined on the whole, for the following reasons, to think that the effect was truly due to nervous influence. If the auricles be cut away from the ventricle without cutting the coronary nerve and vein, then the ventricle and the end of the coronary nerve which is in connection with the auriculo-ventricular groove will in a large tortoise be some distance away from the sinus, so that if one electrode be placed on the ventricle, and the other on the coronary nerve just at its entrance into the ventricle, the electrodes will be well removed from the sinus, and yet in this case the stimulation of the nerve is still able to cause slowing. Also it happens occasionally that the free coronary vein is not accompanied by any nerve, or at all events only a very insignificant branch; stimulation of the vein in these circumstances whether of the central or the peripheral end does not produce the slightest effect either upon the rate of rhythm or the force of the auricular contractions, even with a much stronger current than is necessary to produce slowing when a well defined nerve is present. Finally, as will be proved in the next section, it is clear that impulses can pass from the ventricle to the sinus, which are able to influence the contractions of the auricular muscle, and therefore it is highly probable that similar nervous arrangements should exist for the regulation of the rhythmical contractions of the sinus muscle.

Combining the results of these experiments with the conclusions of

Part I. of this paper, we see that the rate of the automatic rhythmical contractions of the muscular tissue of the sinus are regulated by nervous impulses which pass centrifugally to the sinus from the central nervous system, or centripetally from the other parts of the heart. The muscular tissue of the sinus however is not the only rhythmical tissue of the heart; when the sinus is removed regular contraction waves still pass over the heart which originate from that part of the remaining muscular tissue which possesses the greatest rhythmical power. It is then of great interest to see whether the vagus possesses the same power of inhibiting the rhythm when that rhythm is no longer associated with the sinus, but originates in the muscular tissue of the junction wall between the auricles or in the auriculo-ventricular ring. Such an investigation is rendered possible in the tortoise by the presence of the coronary nerve. If the auricle be attached to the upper lever, the ventricle to the lower, and the sinus be separated from the auricle by a section which does not include the coronary nerve, then the auricle and ventricle are connected with the body of the animal by the coronary nerve alone, and stimulation of the right vagus in the neck can affect their contractions only by nervous action through the coronary nerve. As has been already explained the isolated auricle and ventricle will after a longer or shorter pause commence to beat entirely independently of the sinus, slowly at first, and finally more quickly and with great regularity. When this independent auriculo-ventricular rhythm has become regular the right vagus can be stimulated and any alteration of rhythm observed as easily as in the whole heart. In Pl. III., Fig. 7, I give an example of the commonest effect produced, the whole action of the nerve is upon the force of the auricular contractions, the rhythm remains unaltered, although at the same time the sinus rate was absolutely inhibited. In the preliminary communication to this paper[1] I have stated that the rate of this independent rhythm is never affected by stimulation of the right vagus in the neck. At that time I had only made very few experiments of this kind, and in none of them had I seen any alteration of rhythm. Since then however I have again repeated this experiment, and in one case obtained most marked evidence of complete inhibition of this independent auriculo-ventricular rhythm with every stimulation of the right vagus nerve in the neck. During the whole time of the stimulation of the nerve the rhythm ceased entirely, and that this was no chance occurrence was

[1] *Loc. cit.*

seen from the fact that it occurred with certainty with every stimulation of the nerve, and never at other times. I had previously noticed that direct stimulation of the coronary nerve was apparently sometimes able to slow, sometimes to quicken this independent rhythm to a slight extent, but as it was possible that this effect might be due to escape of current owing to the shortness of the nerve, I was unwilling to accept it as evidence of nervous action upon this rhythm, unless it were confirmed by similar results following upon the stimulation of the right vagus in the neck, when the coronary nerve was the only means of communication left between the vagus and the auricle and ventricle. Although up to the present time I have only seen one manifest instance of inhibition of this rhythm upon stimulation of the vagus nerve in the neck, yet in my opinion that one instance of positive action outweighs all the simply negative experiments; for it is not easy to explain this particular marked case of inhibition if it were not due to nervous action, while it is easy to see how the rhythm might remain unaffected, even though the stimulation of the nerve was effective in other ways such as in influencing the force of the auricular contractions. In all probability the explanation is simply as follows: When the coronary nerve happens to contain fibres which supply the particular muscles which originate the independent rhythm, then stimulation of the vagus can inhibit that rhythm; in the opposite case the rhythm is unaffected just as Meyer found for the sinus when the left nerve of certain tortoises was stimulated. When therefore we consider that the coronary nerve is only one of various nerve trunks which pass from the sinus to the ventricle, and that the auriculo-ventricular rhythm which arises after removal of the sinus starts from different places in the junction wall between the two auricles or in the auriculo-ventricular muscular ring, according to the situation of the section by which the sinus is removed, the probability is great that the automatic rhythm of all parts of the heart can be inhibited by the vagus nerves, when those nerve fibres are stimulated which supply directly the muscular fibres upon which the automatic rhythm in question depends.

Further, experiment proves that the vagus possesses no power indirectly over this rhythm. If the auricle be slit up as described in Part II., so that all the nerve trunks between sinus and ventricle are cut, and yet the slit has not been carried far enough to cause a block in the auricular contraction wave; and if from any cause, such as the flow of blood through the coronary vessels, an independent ventricular rhythm has been set up, that rhythm remains latent, and cannot make itself

apparent, because the ventricle is compelled to contract in due sequence with the more rapid contractions emanating from the sinus. When however the right vagus is stimulated and a standstill of the sinus is thus produced, then during this standstill the independent ventricular contractions are able to appear, and are sometimes followed, sometimes preceded, by an auricular contraction. The effect of the nerve stimulation is therefore to bring to light the hidden independent ventricular rhythm which it is unable to inhibit, although it is able to affect the force of the auricular contractions which accompany it. That these beats are clearly due to the unmasking of a concealed rhythm which has been developed at the auriculo-ventricular junction by the action of the pressure of blood in the coronary vessels is made very evident by the simple device of slitting the auricle still more until a complete block is caused, or by cutting away the ventricle with its part of the auricle from the sinus. It is then found that the ventricle is beating at the rate which was disclosed during the last stimulation of the vagus, and that stimulation of the nerve causes now an absolute standstill of the sinus and of the part of the auricle in connection with it. Occasionally I have noticed the same manifestation of a ventricular rhythm during vagus standstill, when the main nerves passing from the sinus to the ventricle have not been previously cut. In these cases there has always been some external cause for the development of this ventricular rhythm, such as the presence of the clamp in the auriculo-ventricular groove, which may have been sufficient to prevent any inhibitory action of the cardiac nerves upon this rhythm. In the following case, each successive stimulation of the right vagus brought to view the successive stages of the development of this hidden ventricular rhythm in the neatest manner.

Feb. 13, 1882. Plate IV., Fig. 8, curves I.—V. The heart was suspended and held by a clamp placed in the auriculo-ventricular groove and screwed tight enough to hold the tissue without preventing the due sequence of the ventricular upon the auricular beats. The right vagus was then stimulated at different intervals throughout the experiment. Curves I.—V. represent the effects of the several stimulations. As is seen the nerve in no case caused complete standstill and with each successive stimulus a greater number of regular contractions occurred during the stimulation. *In every case these contractions passed in the reverse direction, the ventricle contracted first and the auricle followed.* In the figures the arrow with the letters V. A indicates where this reversal began and the arrow with the letters A. V indicates the point of return to the normal direction of the sequence. The gradual and

regular increase in the rate of these V. A contractions thus brought to light is exactly similar to the development of the rhythm in the isolated ventricle or auricle and shows that such a development was going on during the whole time of the experiment. When the ventricle was isolated by clamping and section it was found to be beating with great regularity at the same rate as during the last vagus stimulation in curve v.

In these cases the independent rhythm of the ventricle was at no time quicker than the rhythm of the sinus, and therefore was entirely concealed until the sinus rhythm was brought to a standstill by the action of the vagus nerve. If however after section of the coronary veins the rhythm of the sinus be artificially slowed by the application of cold salt solution, while that of the ventricle is at the same time developed and quickened by sending a warm blood solution through its coronary vessels, then as soon as the ventricular rhythm reaches a rate quicker than that of the sinus, the latter is concealed by the quicker ventricular rhythm, and we have the phenomenon of a regularly beating heart, in which every contraction starts from the ventricle and passes through the auricle to the sinus. Upon then cutting away the ventricle, the slow sinus rhythm is immediately manifested. Thus the automatic sinus rhythm can be obscured by a quicker ventricular rhythm just as the automatic ventricular rhythm can be obscured by a quicker sinus rhythm.

On the action of the cardiac nerves upon the force of the contractions of the auricle, ventricle, and sinus.

According to the principles previously laid down, we have already examined the action of the cardiac nerves upon one of the properties of the cardiac muscular tissue, viz. the property of rhythm, and have therefore confined our attention exclusively to the relation of the cardiac nerves with those particular portions of the cardiac muscle in which the rhythmical power has been preeminently developed. We have now to consider *seriatim* the action of the nerves upon the other properties of the cardiac muscular tissues, and in the first place their action upon the contraction force. The movements of the upper and lower levers register the contractions of the whole auricle and ventricle, i.e. the contractions of the reticulated fibres of these two cavities which form by far the largest mass of muscular fibres. In considering, then, the variations of contraction force produced by nervous action, we are essentially considering the relations of the cardiac nerves, in one respect at all events, to a group of muscle fibres different in arrangement and charac-

ter to those which were treated of when the action of the nerves upon rhythm was discussed.

In the course of the last year I have accumulated a large number of curves illustrating different experiments on the heart of the tortoise, and as the greater number of experiments commenced with the stimulation of the right and left vagus nerves, and in many cases of the coronary nerve as well, I am enabled to compare the action of the three nerves in a large number of cases. In all cases the result of stimulation is wonderfully constant, and is well represented in Fig. 5, Pl. III.

a. In all cases the auricular contractions only are affected by the stimulation, the ventricular contractions are never directly influenced in the slightest degree.

b. The contractions of the auricle are always markedly diminished in strength during the stimulation of the nerves.

c. The contractions of the auricle are increased in strength after the end of the stimulation.

a. The strength of the ventricular contractions is uninfluenced by the stimulation of the nerves. The contractions of the ventricle are affected simply by the alteration of rhythm produced by the stimulation of the nerve. It must always be borne in mind that the force of the contraction of the cardiac muscle, whether of the ventricle or of the auricle, varies inversely as the rate of the contractions up to of course a certain limit. The normal rate of heart beat, whether in the frog or the tortoise, is quicker than the rate at which the maximum contractions would be produced. In consequence, any slowing of the rhythm will necessarily of itself produce contractions of greater strength than the normal, and any increase of rate will diminish the force of the contractions in due proportion. Such an alteration in force is the sole variation which the ventricle exhibits when the cardiac nerves are stimulated. Thus the contractions are greater when the right vagus is stimulated in strict accordance with the extent of the slowing produced by that stimulation; they are absolutely unaltered when the coronary nerve is stimulated because that nerve does not affect the rate; they are either unaltered or increased in force when the left vagus is excited according as the nerve is without effect upon or somewhat slows the rhythm. During the after-acceleration, which is sometimes fairly well marked, they are diminished in size in proportion to the extent of the acceleration. In no case have I seen any evidence that the cardiac nerves have the slightest power over the force of the contractions of the ventricular muscle.

When we compare the curves illustrating the action of the nerves on the contractions of the frog's ventricle[1] with those obtained from the tortoise, the absolute indifference displayed by the ventricle of the latter to all nervous action becomes most puzzling and most astounding. That the vagus should have the same action upon the strength of the contractions of the frog's auricle, the frog's ventricle, and the tortoise auricle, and yet be powerless to affect the contractions of the tortoise ventricle, leads instantly to the examination of the differences between the ventricle of the frog and of the tortoise, which are likely to be the cause of the marked contrast in the behaviour of the two hearts. My attention was naturally directed in the first place to the coronary system possessed by the ventricle of the tortoise. Brown-Sequard long ago suggested that the vagus was the vaso-motor nerve of the heart, and it was therefore possible that the force of the contractions of the ventricle of the tortoise might be regulated by the dilating or constricting action of the vagus nerves upon the coronary vessels; this seemed especially probable when, as already mentioned, it was found that the force of the contractions of the ventricle, as well as the rate of its automatic rhythm, varied directly with the pressure of the blood in the coronary arteries. Naturally such an influence if present would not be manifested in the bloodless heart cut out of the body and suspended according to my usual method. I therefore examined the action of the vagi nerves when the circulation was intact, and also when an artificial circulation was passing through the coronary system of the ventricle. The contractions of the ventricle and auricle can be registered by my method just as easily when the heart is left in situ within the body as when it is cut out and suspended. A thread is attached to the apex of the ventricle and to the extremity of a thin rod fixed firmly at right angles to the lever near its fulcrum. When the lever is horizontal and placed over the body of the animal, this rod projects vertically downwards so that the thread between the apex and the extremity of the rod is horizontal, and the ventricle therefore is not pulled out of its normal position. By this means the contractions of the ventricle are registered by the movements of the lever in a vertical plane in precisely the same way as in the suspended heart. In the suspended heart the fixed point between the auricles and ventricle necessary for the registration of their separate contractions is obtained by the use of the clamp or by holding the aortic trunk firmly. In the heart with the blood flowing through it in the body I hold the

[1] *Phil. Trans.* 1882, Pt. III.

aorta firm by passing a thread partly through the thickness of its walls and then tying it tightly to the extremity of a fixed rod which touches the aorta at that point. Under these circumstances stimulation of the vagus produced precisely the same curves as in the suspended heart; the force of the ventricular contractions varied with the rate only and was entirely uninfluenced by the action of the nerve. Fig. 9, Pl. III. The same negative result followed when in the suspended heart an artificial blood solution was allowed to flow through the coronary system of the ventricle under a constant pressure. In this series of experiments either a slit was made in the bulged portion of the auricle in order to prevent the distension of the heart cavities with blood, or the auricles were entirely removed with the exception of the junction wall along which the nerve trunks pass to the ventricle; or the coronary nerve alone was left as the means of communication between the ventricle and the sinus. In none of the curves, however, whether the pressure in the coronary system was small or great, whether the ventricle was beating in response to the auricles or with its own independent rhythm, was there any evidence that the vagus nerves are able to influence the force of the ventricular contractions. We must then seek for some other cause than the presence of a coronary system in order to account for the indifference of the muscular tissue of the tortoise ventricle to vagus stimulation.

b. The contractions of the auricle are diminished in strength during the stimulation of the nerves. All three nerves act in the same manner upon the contractions of the auricle, as is shown in Fig. 5, Pl. III. During the stimulation the contractions are most markedly diminished in force quite independently of the action of the nerves upon the rate of rhythm, and in fact in this respect the left vagus often appears to possess greater power than the right. Occasionally, as mentioned in my preliminary paper[1], the right nerve loses this power to a greater or less extent after section of the coronary nerve, although naturally its effect upon the rate of rhythm is as powerful as ever. It is evident, then, that those nerve fibres which supply the bulged portion of the auricles run in both vagus nerves and pass to the auricles not only from the nerve trunks in the sinus but also from those in the junction wall of the auricles, even after they have reached the auriculo-ventricular groove. These nerve fibres are in no way dependent for their action upon those which supply the rhythmical tissue of the sinus, as is shown plainly

[1] *Loc. cit.* p. 372.

enough by the similar effect produced by the right, left, and coronary nerves, and still further by the action of the right vagus when the coronary nerve is the only channel left by which nerve impulses can reach the auricle. As has been already described, a regular independent auriculo-ventricular rhythm is ultimately set up after separation of the auricle and ventricle from the sinus. The force of these auricular contractions can be diminished by stimulation of the right vagus in the neck (the coronary nerve being left intact) without any alteration of this rhythm, as is shown in Fig. 7, Pl. III. At the same time the sinus may be reduced to standstill. Similarly, when the auricle is slit up so that a complete block occurs, and in consequence the sinus and that part of the auricle which is connected with it are beating at one rate while the ventricle and its part of the auricle are contracting independently at another rate, then naturally stimulation of the vagi nerves in the neck reduces only the contractions of the sinus-auricle, while stimulation of the peripheral end of the coronary nerve reduces only those of the ventricle-auricle.

Again, stimulation of the central end of the coronary nerve may not only slow the rhythm but also diminish the force of the auricular contractions; that this result is not due to escape of current is shown by the effect of stimulating the surface of the ventricle when the coronary nerve is the only channel of communication between the ventricle and the sinus. In this case the auricle is left in connection with the sinus and the electrodes placed on the surface of the ventricle at different distances from the auriculo-ventricular groove and the entrance of the coronary nerve into that groove. At distances from one to two centimetres from the point of entrance to the nerve in the neighbourhood of the base of the ventricle, a decided diminution in the force of the auricular contractions without any alteration of rhythm may be produced when an interrupted current is sent through the small portion of the surface of the ventricle between the electrodes; and indeed I have seen this effect plainly manifested when the current was so weak that no contraction of the ventricle was caused by it. It would seem therefore that in the tortoise the cardiac nerves have no power over the force of the ventricular contractions, but that nervous arrangements exist by means of which the ventricle is able to regulate the force of the auricular contractions as well as in all probability the rate of rhythm. It is then conceivable that the function of many of the nerve fibres which pass into the ventricle is, by their action upon the force of the auricular contractions, to regulate the amount of blood thrown into

the ventricle and therefore the amount of work done by the heart. The nervous arrangements of the tortoise heart seem thus to bear out the view put forward by Roy[1] that the work of the heart is governed chiefly by the contraction of the auricle.

In speaking of the action of the vagus upon the contractions of the frog's heart[2] I have proved that a typical inhibition is often brought about without any alteration of rhythm by the diminution of the auricular contractions to the point of invisibility, a form of standstill described subsequently by Heidenhain[3]. In the tortoise I have never yet seen such a complete obliteration of the contractions of the auricle; although they may be very greatly reduced in force yet they are always visibly registered. Again, another point of some interest is noticeable in all those curves where the stimulation of the nerve has produced standstill. The first auricular contraction after the standstill is somewhat larger than the contractions immediately following it, although considerably smaller than the contractions before the commencement of the stimulation. This is well shown in Fig. 14, Pl. IV., and is clearly due to the antagonism between the augmenting effect of a longer pause and the diminishing effect of the action of the nerve.

Finally the contractions of the sinus are diminished in force similarly to those of the auricle, when the vagus nerves are stimulated.

c. *After the end of the stimulation the contractions of the auricle are increased in strength.* Here again, just as in the case of the rhythm, the augmentation effects consequent upon nerve stimulation are much less marked than in the frog's heart. In the latter the maximum increase in the strength of the contractions is rapidly attained and its extent is often very great; in the tortoise the increase of the auricular contractions after each stimulation is very slight but lasts over a long period of time, so that in the course of each experiment, when the vagus nerves have been stimulated many times, the net result upon the auricular contractions is a very marked increase in their strength. That such an increase is truly due to the action of the nerves and would not have occurred otherwise, is shown by experiments similar to that described on p. 57, where the contractions of auricle and ventricle were registered for many hours without any stimulation of nerves, and it was seen that the auricular contractions did not increase in strength from

[1] This Journal, Vol. I. p. 495.

[2] *Op. cit.* See also *Trans. of the Internat. Med. Congress*, London, 1881. Vol. I. p. 257.

[3] Pflüger's *Archiv*, Vol. XXVII. p. 383.

the time of suspension onwards, but on the contrary, gradually steadily and persistently became smaller and smaller.

This slow, gradual, and permanent improvement in the force of the auricular contractions is manifest after the stimulation of either the right vagus, the left vagus, or the coronary nerve; in fact, just as all three nerves are able to diminish the strength of the contractions, so also are they able afterwards to increase that strength. Fig. 5, Pl. III. Here also as in the frog, toad, and rabbit the augmentation effects produced by the vagus are most manifest when the heart is beating weakly. The following example illustrates both the extent and the permanence of the augmentative effects of the nerve stimulation upon both the rate of rhythm and the strength of the contractions.

Feb. 7, 1882. The heart was held by the clamp in the auriculo-ventricular groove so slightly that the ventricle was able to respond to every auricular contraction. The auricle was fixed to the upper, the ventricle to the lower lever. The tracings were made upon the blackened paper of a drum which completed one revolution in 12 minutes. The first five tracings were taken without any alteration in the conditions of the experiment, so that allowing for the time of changing drums, pauses purposely made during the experiment, &c., the fifth tracing was made at least $1\frac{1}{2}$ hours after the commencement of the first.

	Rate per min.	Height in mm.	
At the commencement of curve I.	7·75	22·5	R. vagus was stimulated once during this curve.
At the end of curve I.	8·15	25·5	
At the commencement of curve II.	?	26·5	L. nerve twice stimulated during this curve.
At the end of curve II.	8	30	
At the commencement of curve III.	7·75	33	R. vagus twice stimulated.
At the end of curve III.	9·25	36·5	
At the commencement of curve IV.	8·5	38	R. vagus twice stimulated.
At the end of curve IV.	9·5	38·5	
At the commencement of curve V.	8·25	38·5	

As is seen the strength of the contractions increased steadily after every stimulation whether of the right or left nerve, so that in less than $1\frac{1}{2}$ hours the height of contraction had increased to the extent of $\frac{3}{4}$ of the original height.

On the action of the cardiac nerves upon the conduction power of the auricular muscle.

The reticulated fibres of the auricle not only contract with a certain degree of force, but their contraction takes place in the shape of a wave

which passes from the sinus end over the whole network of fibres to their termination in the auriculo-ventricular muscular ring. The power of the muscular tissue to conduct this wave of contraction is clearly as likely to be influenced by the cardiac nerves as the force of the contraction itself; and in fact, experiment proves that the right vagus, the left vagus, and the coronary nerve, all possess an influence over the conduction power, just as we have already seen that they are all able to influence the force of the contractions. In all probability then, the nerve fibres which supply the reticulated muscle fibres of the auricle produce changes which affect both the force of the contractions and the power of conduction.

When the auricle is slit up to a sufficient extent a partial block is always produced, such that only every second contraction which is started from the sinus end passes over the block and produces a ventricular contraction. This is the condition which is most favourable for determining the action of the cardiac nerves upon the conduction power, because it represents a condition intermediate between the two extremes of a complete block and no block at all; we can therefore study the variations in both directions. Evidently such a partial block may be increased by the action of the nerves and therefore only every third, fourth, &c. contraction be able to pass, or on the other hand the conduction power may be improved and then every contraction will be able to pass. By careful manipulation the right amount of section necessary for the production of such a partial block is always attainable, and indeed this condition can be reproduced at will again and again in the course of a single experiment. I have already shown how, in the case of the frog, tightening of the clamp in the auriculo-ventricular groove produces a partial block, permitting only every second contraction to pass, and that this may last a considerable time or may give way to a complete synchronism of the auricular and ventricular contractions. In exactly the same way such a partial block of the auricular contraction wave in the tortoise lasts sometimes a long time without alteration, at other times lasts only a short time and then every contraction passes over. The application of 0·75 p.c. solution of salt to the blocking point is very efficacious in removing this partial block and causing every contraction wave to pass over, and then by simply drying with a piece of blotting paper the block can be brought back and again only every second contraction will pass. In this way by alternately moistening and drying the blocking point I have been enabled to see again and again in the course of an experiment the formation and disappearance of such

a partial block. Hence it is necessary to be careful that any apparent removal of such a block by nervous action is not in reality due to a chance removal of the block coinciding with the time of the nerve stimulation. As a matter of fact such an explanation is out of the question; the large number of curves which I possess show that the coronary nerve as well as the right and left vagus possess the power of removing a partial block as conclusively as my former curves show the same power in the vagus nerves of the frog. Again and again by careful section I have caused a partial block and watched for a long time the regular passage of every second contraction, and then after stimulation of one of the three nerves seen every contraction pass (see Figs. 10, 11, Pl. IV.). This improvement of conduction power is, like the improvement in the force of the contractions or the after-acceleration, spread over a long period of time, so that in most cases stimulation of the nerve removes the partial block altogether, and every contraction continues to pass with absolute regularity until by drying or further section the partial block is brought back. In the frog, on the other hand, as has been shown in my former paper, the restoration of the conduction power in consequence of nerve stimulation is not so lasting. Occasionally (see Fig. 10, Pl. IV.) stimulation of the vagus or the coronary nerve in the tortoise improves the conduction power for only a limited time after the stimulation, so that in these cases there can be no question as to the influence of the nerve; every second contraction passes before the stimulation, then during and after the nerve stimulation every contraction passes, and then again in a very short time only every second contraction is able to pass. It does not seem to make any difference whether the nerve influence reaches the blocking point from the ventricular side or from the sinus side, whether therefore the coronary nerve or the right or left vagus nerves be stimulated. Sometimes the conduction power is most easily restored by the coronary nerve, sometimes by the right or left vagus, and as a rule one nerve may be more efficient than the other two. Doubtless such differences are due to differences in the arrangement of the nerve fibres in each particular case, as well as to the exact position of the section by which the partial block was caused.

In the frog experimental evidence showed that nerve stimulation much oftener removed than increased a block in the contraction wave; so too with the tortoise, I possess but few curves which show unmistakeably any diminution of conduction power in consequence of nerve stimulation. Still, as Figs. 12, 13, Pl. IV. show, such an increase in the

extent of the block does undoubtedly sometimes occur. In these cases every second contraction was passing before stimulation of the right vagus and coronary nerves respectively, and during the stimulation every contraction failed to pass.

We may then say that both in the tortoise and in the frog the cardiac nerves are able both to depress and exalt the conduction power of the muscular tissue of the auricle. The nature of this nerve action can only be examined after an answer has been given to the question, Under what conditions can a partial block be caused of such a character that only every second contraction wave passes the block? If the sinus and its connections with the auricle be removed and single induction shocks be sent through the sinus end of A_s at regular intervals, so as to cause a regular series of artificial contraction waves, it is found that—

1. Variations in the strength of the stimulus have no effect upon the passage of the contraction wave over the block. If a contraction wave can pass at all, it will pass as well when caused by a weak as by a strong stimulus; if it cannot pass with a weak stimulus, it will not with a stronger one.

2. Two consecutive contractions cannot pass the block unless a sufficient time elapse between the contractions. Thus with single induction shocks every ten seconds all the contractions will pass or will not pass according to the extent of the section; but with the same severity of section when all contractions at ten seconds intervals are able to pass, it is possible that with single induction shocks every five seconds only every second contraction will pass. So too with a section such that all contractions at five seconds intervals can pass, it is possible that with three seconds intervals only every second contraction will pass.

Now we know from the experiments of Marey that a certain time must elapse after a contraction before the cardiac muscle is in a condition to contract again; in other words, the muscle takes time to recover its full excitability after a contraction. The same law applies to every portion of a cardiac muscle along which a wave of contraction travels, and we may therefore say that a certain time must elapse after a wave of contraction has passed over the muscle before the conduction power is sufficiently re-established to allow the passage of a second contraction wave. The effect then of the injury caused by the section together with the narrowing of the path of conduction is to retard this process of re-establishment of the conducting power; in consequence

a still longer time must elapse after a contraction wave has passed, before the tissue at the blocking point has recovered sufficiently to allow a second contraction to pass.

Nervous action therefore removes a partial block, and enables every contraction to pass the blocking point because it expedites the recovery of the conduction power of the muscle at that point: a recovery which without the stimulation of the nerve would take place more slowly after the passage of each contraction wave.

This repair of conduction power due to nerve action is apparently independent of the action of the nerves upon the force of the auricular contractions. When a partial block has been caused, so that every second contraction passes, and the right vagus nerve is stimulated, it frequently happens that from the commencement of the stimulation every contraction passes the block, although during the stimulation the force of the contractions of the sinus-auricle at all events is very markedly reduced. Since, however, this diminution is always accompanied with considerable slowing, it is possible that in this case every contraction passes the block, even when the force of the contractions is reduced, because a sufficient length of time elapses between consecutive contractions; and indeed, in those cases in which nerve stimulation has caused a distinct increase in the block, whether the nerve in question be the right vagus, left vagus, or coronary, the rate of the contractions has never been appreciably slowed. Such an explanation however will not hold good in those cases, where by stimulation of the coronary nerve or the left vagus the force of the contractions is markedly reduced while the rate is left unaltered. In both these cases the force of the contractions may be markedly diminished and at the same time the conduction power as markedly increased, so that during the stimulation every contraction is able to pass, although before the beginning of the stimulation only every second contraction was passing. The evidence then goes to show that the same nerve may produce both an increase or a diminution of the conduction power of the auricular muscle simultaneously with a diminution of the force of its contractions.

Finally, I have shown that in the frog and toad the stimulation of the vagus is able to make the ventricle respond for a time to every contraction of the auricles, even when in consequence of the tightening of the clamp in the auriculo-ventricular groove or of the application of heat to the auricles and sinus alone, it was unable to respond to

any single auricular contraction before the stimulation of the nerve. In other words, the vagus was able temporarily to remove a complete block in the passage of the contraction wave from auricle to ventricle. In the tortoise also it is possible to restore the conduction power by nerve stimulation even when the block is apparently complete. Naturally it is not easy to make sure of success in such an experiment every time, for, if the section of the auricle be carried slightly too far, the block will be complete enough but the vagus will be unable to repair it. It is however possible to cut the auricle just sufficiently to prevent the passage of any contractions to the ventricle; if the nerve then be stimulated contractions immediately begin to pass the block, and increase rapidly in number, until a short time after the stimulation the conduction power is so fully restored that every contraction passes the blocking point, and a new cut must be made in order again to block the passage of the contraction wave.

On the action of the cardiac nerves upon the sequence of the contractions of the different heart cavities.

It has already been argued that the natural pauses between the contractions of the different heart cavities, and therefore the normal sequence of those contractions, is a consequence of an alteration of conduction power which occurs normally as the contraction wave passes from the sinus to the auricles, or from the auricles to the ventricle respectively. It is extremely likely then, that the cardiac nerves should be able to influence the passage of the contraction wave at these natural blocking points, in the same manner as has just been described in the case of an impairment of conduction produced by an artificial block. We may therefore expect to find, that the vagus can either increase or diminish the natural block in the same manner as it is able to affect the artificial block. When an artificial partial block is produced, the most striking effect of nerve stimulation is the removal of that block and therefore the complete repair of the conduction power; on the other hand, the most striking alteration of the normal sequence of the contractions would result not from any improvement but from an impairment of the conduction power. Thus, any alteration of conduction power at the sino-auricular and auriculo-ventricular junctions is made evident simply by a corresponding alteration in the natural pause, which occurs between the contractions of the sinus and the auricles and of the auricles and ventricle respectively;

any increase therefore of the conduction power at these junctions can only be manifested by the contractions of the auricles and ventricle following upon those of the sinus and auricles respectively with greater rapidity than before, while any diminution in the conduction power may cause either a diminution of the rapidity of the sequence or an absolute cessation of sequence according to its extent. For this reason it is clear that any marked increase in the natural block at these junctions will be much more striking and apparent than an equally marked diminution of that block. Such is the case; when the vagus nerves are stimulated, the cessation of the sequence in consequence of the stimulation is manifest enough, the recovery of the sequence is only well marked when the natural block has been artificially increased by the pressure of the clamp in the sino-auricular or auriculo-ventricular grooves.

When the heart is suspended and the aorta fixed, no clamp being used to the heart itself, the contractions of sinus, auricle and ventricle follow one another with perfect regularity and the beats of the sinus are often registered on the auricular curve. In many cases stimulation of the right vagus stops the contractions of the auricles and ventricle absolutely, while the sinus still continues beating; see Figs. 14, 12, Pl. IV. This standstill of the auricles is not due to a diminution of the force of the auricular contractions sufficient to render them invisible, as was previously noticed in the case of the frog and toad; for the sinus contractions are well marked and can be plainly seen to stop short when they reach the sino-auricular junction; in addition it frequently happens that the block caused by the vagus stimulation is not a complete one, so that some of the sinus contractions are followed by contractions of the auricle; these auricular contractions are no smaller than is usually seen when the right vagus is stimulated. Clearly then the passage of the contraction from sinus to auricle may be completely or partially blocked during the stimulation of the right vagus nerve. Such a block is entirely independent of the effect of the nerve upon the rhythm or the contraction force of the sinus muscle. In many cases the sinus continues to beat during the whole of the stimulation at absolutely the same rate as before the stimulation, in other cases the sinus rate is markedly slowed; and yet in both cases not a single contraction passes into the auricle. Sometimes the sinus contractions are diminished so as to be barely visible, at other times their force is scarcely if at all affected, and yet the block is complete in both cases. A similar complete cessation

of the sequence of the auricular upon the sinus contractions during stimulation of the vagus nerve is often seen in the snake, and to a less extent in the frog and toad, so that a third method of producing standstill must be ascribed to the vagus. We may have therefore standstill of the auricles and ventricle produced in the three following ways:

1. Cessation of rhythm.
2. Cessation of contraction.
3. Cessation of conduction.

In many cases the diminution of the conduction at the sino-auricular junction during vagus stimulation is not sufficient to produce a complete block, but only to lengthen the pause between the contractions of the sinus and auricles. Such an increase in the natural pause is often well marked even with the drum revolving very slowly (once in 13 minutes), as is seen in Fig. 15, Pl. V. The want of relation between the contraction force and the conduction power, which was noticed in the case of the artificial block, is equally noticeable when the natural sequence of the contractions is the subject of examination. Even when stimulation of the vagus reduces the force of the contractions of the auricle very greatly no sign of a block can be seen at the auriculo-ventricular junction. The ventricle may respond with strong vigorous contractions to each of these diminished auricular contractions just as well as to the previous strong auricular contractions. This fact not only suggests that the conduction of the contraction wave from auricle to ventricle is not necessarily impaired at the same time that the force of the auricular contractions is diminished, but it also shows that even with a great diminution of the force of the contractions, a contraction wave still passes from end to end of the auricular muscle and induces a ventricular contraction, and therefore that the diminution in force due to the vagus stimulation is not brought about by the cutting short of the contraction wave when it had passed only a short way along the auricle.

The improvement in conduction power at the sino-auricular and auriculo-ventricular junctions caused by the stimulation of the vagus is evident enough when the natural sequence is in any way hindered, so that the ventricle is beating after every second contraction of the auricle or the auricle is made to respond to every second sinus contraction. At both junctions such an increased block can easily be produced by the action of the clamp; in both cases stimulation of the nerve is able to remove that block and to restore the sequence in the manner described already. In the tortoise and the frog the action of the clamp is necessary so as to

increase the natural block, in order to demonstrate the recovery of sequence after vagus stimulation. In the heart of the common ringed snake however no such extra assistance is required. The heart of the snake is apparently much more susceptible to any interference than any other heart which I have as yet examined. It is the rule rather than the exception to find that its mere suspension between the two levers, when the aorta is held and no clamp is used, is sufficient to interfere with the due sequence of the contractions. The sinus continues to beat with great regularity but only a certain number of those contractions are followed by auricular contractions, and again of these latter, some only give rise to a contraction of the ventricle. Thus a common form of rhythm which may last unaltered for a long time is as follows; the auricles contract only after every second sinus contraction, and only every second of these auricular contractions is followed by a contraction of the ventricle. Thus in this case the ventricle contracts after every fourth and the auricle after every second sinus contraction.

Stimulation of the vagus acts here in the manner already suggested; during the stimulation the sequence is sometimes still more hindered than before; the sinus alone contracts, auricle and ventricle remain still. After the stimulation a marked improvement of the sequence often takes place, for a time the auricle may respond to every sinus contraction, and in other cases the ventricle contracts after every auricular contraction. In fact the action of the vagus upon the sequence is very similar to what is seen in a frog when a clamp is placed in the auriculo-ventricular groove. The snake's heart not only affords a good instance of the recovery of sequence in consequence of nerve stimulation, when the sequence has been previously irregular, but also shows the increase in the rapidity with which the contraction of the auricle may be made to follow that of the sinus, in a much more striking manner than I have as yet seen in the tortoise. In Fig. 16, Pl. V., the rotation of the drum was quick and one auricle was attached to the upper lever, the ventricle having been previously cut away. The heart therefore remained in the body and the contractions of both sinus and auricle were registered by the same lever. As is seen, the pause between the contractions of the sinus (S in the Fig.) and of the auricle (A) was remarkably long before the stimulation, so that the contraction of the sinus was over before that of the auricle began. During the stimulation the two contractions were so close as to fuse together in the curve and then gradually the pause became longer and longer until the original length of pause was again reached. It may also be noticed that the nerve stimulation

diminished the force of the auricular contractions to a greater extent than those of the sinus, so that during the maximum effect the beats of the latter were actually stronger than those of the former.

The power of the vagus nerve to hinder the sequence of ventricular upon auricular beat has only been noticed by me, when a hindrance to the conduction has already been caused by the presence of the clamp in the auriculo-ventricular groove. Eckhard's[1] experiments however seem to show clearly that the nerves of the septum in the frog are able on stimulation to block the passage of the contraction from the auricle to the ventricle, for he found that their stimulation caused the ventricle to stand still while the sinus and auricles continued beating. These nerves therefore acted upon the conduction power of the auriculo-ventricular muscular ring in the same way as the right vagus acts on the conduction power of the sino-auricular muscular ring in the tortoise.

On the nature of the action of the vagus nerves and its resemblance to the action of a weak interrupted current.

A comparison of the results obtained from the tortoise with those described in my former paper on the frog, confirms the view put forward there that the vagus is the trophic nerve of the heart. Its action is of the same kind throughout, and the different effects produced are not due to the action of different nerve fibres possessing different properties, but rather to the action of the same kind of nerve fibre upon the different attributes of the cardiac muscular tissues. Thus the nerves supplying the red and white muscles of rabbits are not supposed to be different to other motor nerves, yet their stimulation produces very different results owing to the differences which exist in the red and white muscles themselves. In precisely the same way the same kind of nerve fibre will produce different results in the heart according as the muscle fibres upon which it acts are specially engaged in the initiation of rhythmical contractions, in the conduction of a contraction wave, or in the production of strong and rapid contraction. Thus, to give an example, we have seen that as long as the attention is confined to the movements of the auricle and ventricle it is possible to obtain by stimulation of the vagus nerve a typical inhibition which may be caused in three different ways.

1. The standstill may be due to the cessation of the rhythm, i.e. to the depressing action of the nerve upon the rhythmical power of the muscle fibres of the sinus (Frog, Tortoise, Snake).

[1] *Op. cit.* p. 193.

2. It may be due to the diminution of the auricular contractions to the point of invisibility, i.e. to the depressing action of the nerve upon the contraction power of the rapidly contracting reticulated muscle fibres of the auricle (Frog).

3. It may be due to a blocking of the contraction at the sino-auricular junction, i.e. to the depressing action of the nerve upon the conduction power of the muscular fibres connecting the sinus and auricle (Snake, Tortoise, Frog).

In these three cases the same practical result is brought about by in all probability the same kind of nerve fibre influencing three of the different attributes of cardiac muscle, viz. rhythm, contraction, and conduction. Again, we see that both in the frog and the tortoise the vagus possesses the power of exalting as well as of depressing all the different functions exhibited by the cardiac muscles; and it is noticeable that the difference between the frog and the tortoise is in this respect the same throughout. Thus:—

In the frog the augmentation of the contractions is very marked, the maximum is quickly reached and the contractions return again to their original size.

In the tortoise the augmentation is slight but its effect is spread over a much longer time.

In the frog the exaltation of conduction power follows the same limits as the augmentation of the contractions.

In the tortoise the repair of conduction power is much more permanent.

In the frog the acceleration is marked and does not last long.

In the tortoise it is slight but long enduring.

The exalting action of the vagus then runs a more rapid course in the frog than in the tortoise with a corresponding greater maximum. This is in strict accordance with the greater slowness of all the normal functions of the tortoise heart; thus, the normal rate of rhythm is much less than that of the frog, the contraction of the frog's ventricle is more rapid, the refractory period in the tortoise is longer than in the frog. In other words the augmentation of function produced by vagus stimulation varies in the rate of its production and in the maximum of its effect according to the rapidity of the normal metabolism of the tissue. If then we combine the present observations on the tortoise with the arguments at the end of my paper on the frog we arrive at the following conclusion:

Although the initial effect of the vagus is to depress some

function, its final and most enduring power is to exalt, intensify and repair that function.

Thus, although it slows rhythm, yet its stimulation makes the rhythmical power last longer than it otherwise would and makes the heart beat with regularity when it was previously irregular; although it reduces the force of the contractions, yet its ultimate effect is to improve and sustain the contraction force; although it may diminish the conduction power yet in the end it completely repairs that power. For these reasons I look upon the vagus as essentially the trophic nerve of the heart.

It is possible to gain some insight into the nature of this trophic action by the examination of the behaviour of the cardiac muscle to direct stimulation. Hitherto almost all the experiments upon the effect of single induction shocks on the functions of the cardiac muscle have been conducted in the manner introduced by Ludwig and are extensions and modifications of the original experiments of Bowditch[1]. His experiments combined with those of Kronecker[2] and v. Basch[3] show that—

1. The strength of the contraction of the muscular tissue of the apex of the frog's ventricle does not vary with the strength of the stimulus: a minimal stimulus is at the same time maximal.

2. When the apex is made to contract regularly by sending through single induction shocks at definite intervals, each contraction is stronger than the previous one until a certain maximum is reached, i.e. the series of contractions are arranged in the form of a staircase.

3. When the single induction shocks follow at a sufficiently rapid rate, then the ventricular muscle responds, if the stimulus is weak, to every second stimulation only, although it is able to contract with each stimulation upon increasing the strength of the stimulus.

The explanation of § 3 is to be found in the observations of Marey, that the refractory period of the ventricular muscle of the frog is very long, so that the muscle recovers its excitability after a contraction quite slowly, combined with the assertion of v. Basch, that a stimulus which is of itself too weak to cause a contraction increases the muscular excitability and therefore helps the production of a subsequent contraction.

All these laws can be studied on the muscular tissue of the apex of the auricle of the tortoise as well as on that of the ventricle; moreover,

[1] Ludwig's *Arbeiten*, 1871.

[2] *Das charak. Merkmal der Herzmuskel Beweg.* Ludwig's *Festgabe*, 1874.

[3] *Sitzber. d. k. Akad. d. Wiss.* (Wien), Bd. LXXIX. III. Abth.

it is not necessary to make use of the apex cavity or to keep it supplied with an artificial blood solution; a strip of muscular tissue cut from the apex of the ventricle or auricle and suspended as above described enables us to demonstrate all the laws of the stimulation of cardiac muscle mentioned above. Thus in both the strip from the tortoise's auricle and the frog's ventricle a minimal stimulation is at the same time maximal, in both a series of single stimulations produces a "staircase," in both the strip contracts regularly with every second induction shock when the stimuli are sufficiently weak and sufficiently rapid. A comparison of the reaction of the three muscular strips from the apex of the frog's ventricle, tortoise auricle and tortoise ventricle shows that with single induction shocks of the same strength at five seconds intervals the muscle of the frog's ventricle and the tortoise auricle will respond to every stimulus, but that ten seconds intervals are necessary in order to make sure of an infallible response in the case of the strip from the apex of the tortoise ventricle.

Again Bowditch's law of the "Treppe" is not confined to the development of the power of contraction in the muscle, the same kind of improvement is seen in the development of the rhythmical power. The difference between the rhythm caused by external excitation and the rhythm which is brought about by internal changes is that the first is quickest at the time of excitation and dies away as the effects of the stimulus wear off, while the second is slowest at the commencement and steadily gains in rapidity and regularity as the automatic power is developed. If then a series of lines were drawn inversely as the lengths of time between the successive automatic beats, those lines would form an ascending staircase as the rate quickened, just as the contractions form an ascending staircase in Bowditch's experiment. In other words, each automatic contraction quickens the development of the next automatic contraction, just as each artificial contraction increases the force of the next succeeding artificial contraction, up to of course in each case a maximum limit.

I have already described fully how a weak interrupted current applied to a strip of ventricular muscle gradually improves the conduction power and contraction force of that strip until at last automatic contractions result. In that description I purposely said nothing about the action of a weak interrupted current upon the auricular muscle further than mentioning that it also could be taught to beat automatically. The difference however between the behaviour of the strip from the auricle of the tortoise, the ventricle of the frog and the ventricle of the tortoise

in this respect is most striking and suggestive. In each case the weak interrupted current affects the force of the contractions of the several strips in precisely the same manner as the vagus nerve acts upon the whole auricle or ventricle from which the strips are taken. Thus when the strip from the apex of the frog's ventricle is made to contract every five seconds and the contractions are of equal height, they are immediately diminished most markedly in force during the whole time that the weak interrupted current is passing. After the cessation of the stimulation of the interrupted current the induced contractions increase most markedly in size and rapidly attain a maximum much greater than the original contractions. The curves are in every respect precisely similar to those obtained by stimulation of the vagus as given in my previous paper, except of course that each contraction occurs at five seconds intervals. The diminution of force may be so great that the contractions are barely visible.

Also atropin has here the same effect upon the action of the interrupted current as upon vagus action; at first after atropin has been applied to the strip, the interrupted current still diminishes the contraction force but to a less extent than before, afterwards no diminution occurs but a primary increase of force even during the passage of the current, and finally the interrupted current is unable to influence the force of the contractions in either direction.

In a precisely similar manner an interrupted current, which is so weak as not to cause contractions itself, diminishes the force of the contractions of the strip of muscle from the tortoise auricle during the passage of the current and helps on the contraction force, making the beats more and more vigorous by the same slow sort of permanent after-effect which has already been described as characteristic of the action of the vagus nerves upon the contractions of the whole auricle. Again as is shown in Fig. 17, Pl. V., the same effect is produced after the strip has been brought into the condition of automatic rhythm; and indeed the effect may be even more pronounced on the day after the strip was suspended, when as in the instance given the automatic rhythm had continued at least 24 hours. In Fig. 17, curve II., I give the effect of the stimulation applied at 12.30 on the morning of Nov. 22 to the strip of auricular muscle which had supplied curve I. on the afternoon of Nov. 21. The secondary coil was gradually pushed from 8 to 5 cm. and the interrupted current caused as is seen a single contraction with the sec. coil at 5 cm. The regularity of the automatic contractions at least 24 hours

after suspension of the strip is well shown, as well as the diminution and after increase of force caused by the interrupted current. Here too atropin produces the same effect as upon vagus stimulation.

A precisely similar effect, as far as the diminution of the contractions is concerned, was observed by Foster and Dew-Smith[1] during the passage of a constant current through the muscular tissue of the frog's ventricle, when that ventricle was beating. The similarity between the action of the weak interrupted current upon the contractions, whether spontaneous or produced by single induction shocks, with the above-mentioned effect of the constant current, naturally leads to the suggestion that such an effect may depend upon the polarization of the muscle by the weak interrupted current. I have therefore placed the exciting electrodes at the fixed upper end of the strip, at the lower end, and in the middle of the strip, and in each of these three positions have observed the effect upon the contractions of the interrupted current sent through the whole strip from end to end. In each case I have also reversed the direction of the current through the strip and varied it in strength. In all cases the result was the same, the strength of the contractions was markedly diminished during and slightly increased after the stimulation.

Finally, the interrupted current as already mentioned slowly causes an improvement of contraction force and conduction power in the strip from the tortoise ventricle, until the maximum contractions have been reached, until the rhythmical power has been fully developed and automatic contractions result. During this period of development there is no marked sign of any diminution in the force of the contractions during the passage of the interrupted current. When the strip contracts with equal maximal contractions, when the automatic rhythm is regular the interrupted current is still unable to influence the contraction force, at all events to any definite extent. Sometimes the contractions do appear to have been diminished exceedingly slightly during the passage of the current; especially before the force of the contractions has developed to its full extent. Such a slight diminution may truly correspond to the marked diminution which is brought about in the auricular muscle by the passage of the current, but it is so insignificant and so doubtful when the strip of muscle is contracting to its fullest extent as not to prevent the resemblance between the action of the vagus and the interrupted current in this case also. Again then the action of the interrupted current upon the contraction force of the ventricular strip is the same as that of the vagus upon the whole ventricle of the tortoise.

[1] *Op. cit.*

The resemblance between the action of the vagus nerve and the weak interrupted current upon the conduction power and the contraction force of the cardiac muscle is therefore in all cases very striking. Not only are the effects of the stimulation of the nerve precisely similar to the action of the interrupted current applied directly to the different muscular strips, but also atropin produces the same effect in each case. So close a resemblance must have some very definite meaning; we must therefore in the first place decide between the one or the other of the two following propositions, either

An interrupted current applied to the strip of muscle, which is not strong enough to produce contractions of itself, causes the same effects as vagus stimulation because it stimulates the endings of the nerves in the muscle, or else

The action of the vagus nerve upon the muscular fibres is of the same nature as that of a weak interrupted current upon those same fibres.

If the first of these two propositions is true, then every experiment involving the electrical stimulation of the cardiac muscle which has hitherto been performed must be rediscussed on the assumption that the effects observed may to some extent be due to the excitation of the endings of the vagus nerves, for unfortunately in the case of the cardiac muscle we cannot with certainty separate nervous from muscular action by means of curare. Such a conclusion however is hardly warranted, for if the interrupted current when applied directly to the muscle produces its effects by the stimulation of the endings of the vagus nerves, then other kinds of stimulation must also produce similar results when applied to the muscle as when applied to the vagus itself; single induction shocks therefore ought to produce the same effect whether applied to the vagus or the muscle itself. Bowditch's experiments have conclusively shown that a series of single induction shocks applied to the muscle of the frog's ventricle causes a series of contractions in the form of an ascending staircase, and the same effect is seen in the muscular strip from the apex of the auricle or ventricle of the tortoise; on the other hand, a series of single induction shocks applied every three or five seconds to the vagus nerve of the tortoise reduces the force of the auricular contractions in the most marked manner as long as the induction shocks are sent through the nerve, Fig. 18, curve II., Pl. V.; nay more, a single shock applied to the vagus trunk is sufficient to reduce the next five or six auricular contractions as is shown in Fig. 18, curve I. In fact no better stimulus could be required to set the vagus in action than a series of single induction shocks every five seconds. So much can then be

said, single induction shocks affect the cardiac muscle in a manner directly opposite to their effect when applied to the vagus nerve; for this reason it is more probable that the second proposition is true viz. The vagus produces the same effects on the contraction force and conduction power of the cardiac muscle as an interrupted current applied to the muscle directly, which is too weak to cause muscular contractions.

In order to make the resemblance between the action of the vagus and the interrupted current complete, it must be shown that the latter is able to affect the rhythm in a manner similar to the former and that atropin prevents that effect in the same way in both cases. Up to the present such evidence is by no means complete, although I cannot help thinking that a large number of experiments made by former observers are in reality to be explained by the direct action of the stimulation, rather than by the supposition that the stimulus excites inhibitory nerves or inhibitory centres. Again and again it is seen that the direct stimulation of the place from which the rhythm starts causes a slowing or absolute cessation of that rhythm. Thus Foster and Dew-Smith[1] have shown that an interrupted or constant current sent through the rhythmically contracting heart of the snail, or through the ventricle or auricle alone when beating automatically, produces a standstill or slowing during the passage of the current. So too in the Vertebrata, the direct stimulation of that part of the heart from which the rhythmical contractions arise, viz. the sinus venosus, is a most certain method of obtaining standstill of the heart, and here too we have a further remarkable fact, that atropin prevents that standstill from taking place just as it prevents the depressing effects of the stimulation of the strip of cardiac muscle upon the force of the contractions. So too, as Ranvier[2] has pointed out and as I have seen again and again in the case of the tortoise, the direct stimulation of the right place in the isolated auricle inhibits the automatic rhythm of the auricle. In this case as well as in the case of the sinus venosus, it is commonly supposed that such a standstill indicates the existence of special inhibitory centres which are excited by the stimulation. I venture however to submit that in these cases as well as in the snail's heart such inhibition is the result of the direct stimulation of the muscular tissue from which the rhythmical contractions originate, and is therefore strictly comparable to the diminution of contraction force observed in the muscular strips from the apex

[1] *Proc. Roy. Soc.* No. 160, 1872.

[2] *Leçons d'Anatomie Générale.* Paris, 1880, p. 161.

of the frog's ventricle and tortoise auricle as already described. Still I must confess that in the case of the muscular strips when beating automatically with a perfectly regular rhythm (as in Fig. 17, Pl. V.), the stimulation which is sufficient to depress most markedly the force of the contractions may be absolutely without effect upon the rate of the rhythm. It does not however follow that such a rhythm cannot be inhibited by the direct application of the interrupted current; it is possible that a strength of current which is able to depress the contractions may not be strong enough to influence the rhythm; while a stronger current sufficient to inhibit the rhythm might at the same time induce contractions in some part or other of the muscular strip and so hide the inhibition really produced. Such an explanation is plausible to this extent; in all rhythmically contracting portions of the heart any direct stimulation, which is strong enough to cause a series of contractions following each other with greater rapidity than the previous rate of rhythm, is very apt to be followed by a pause which is of longer duration than the previous regular pauses between the consecutive automatic contractions. Such a pause does not necessarily prove that the rhythm has been inhibited by the stimulation and I therefore prefer for the present to leave it doubtful whether the direct stimulation of a rhythmically contracting tissue can in all cases inhibit the rhythm of that tissue.

PART IV.

On the action of atropin and muscarin.

The observations of Bowditch[1] upon the effects of atropin and muscarin on the force of the contractions of the cardiac muscle are typical of the action of these drugs upon every function of the cardiac muscle. His results may be expressed by saying:—Atropin brings the contraction power of the muscle to a maximum straightway, so that the beneficial effects of successive stimuli disappear. Muscarin depresses the power of contraction without removing the effects of successive stimuli, so that the maximum contraction obtained is much less, though the "staircase" still remains. Expanding these two assertions so as to include all the functions of cardiac muscle we should expect to find that atropin improves the rhythmical power and the conduction power in the same way as the contraction force, such an improvement being of a fixed and

[1] *Op. cit.*

stable character, though not necessarily lasting. On the other hand, muscarin ought to depress every function without preventing the possibility of a limited amount of improvement in that function.

All experimental evidence serves to confirm this view. Thus Sokoloff[1] has shown that the application of atropin restores the rhythmical power when it has been depressed by the application of a variety of different drugs. And I shall show later on that atropin quickens the development of an automatic rhythm, and removes the "staircase" of rhythm in the same way as it removes the "staircase" of contraction force. Not only does this drug develope the rhythmical power in the same way as the contraction force, but it produces the same sort of stable effect upon both. In the first stage of its action neither the stimulation of the cardiac nerves nor direct stimulation of the muscle is able to depress the rhythm or the force of the contractions; the augmenting effect alone remains; the beats are simply quickened and increased in force. Later on, this effect also disappears; neither by nervous action nor by direct stimulation can any alteration either in rhythm or force of contraction be effected. The action of atropin then is to bring about a certain maximum of rhythmical power and contraction force of such a stable character that this maximum is with the greatest difficulty displaced in either one direction or the other. It must not however be supposed that the action of atropin is a purely beneficial one, that it is trophic in the same way as the vagus and the interrupted current, which produce permanently beneficial effects; in the unfed heart outside the body its beneficial effects are followed, with a rapidity varying according to the extent of the dose, by a marked depressing action; the force of the contractions steadily diminish, the rhythm becomes slower and slower. In the frog's heart, when removed from the body, this depressing effect on the rhythmical power is manifested very early, so that, as pointed out in my paper, the rhythm may be markedly slowed at the same time that the force of the contractions is as strong or even stronger than before. In precisely the same way the improvement in conduction power which the atropin at first causes is followed by a diminution of that power, so that the ventricle responds to every second contraction only of the auricle or, what is frequently seen in the atropinized heart, responds to every two out of three auricular contractions. No doubt these depressing after-effects are due mainly if not entirely to an overdose of the drug, combined with the absence of nutrient material.

[1] *Physiolog. und toxicolog. Studien am Herzen*, Bern, 1881.

In my former paper I have throughout spoken of the action of atropin and muscarin as affecting the strength of the impulses from the motor ganglia to the ventricle. In all instances where such phraseology occurs it is clear that in reality the phenomena observed were due to an alteration of the conduction power during the passage of the contraction wave from auricle to ventricle. Muscarin acts upon the cardiac muscle in such a way as to depress every one of its functions, but its action is much more labile than that of atropin. For a long time at all events such depression of function can be affected by nervous and direct stimulation in both directions; it can be both increased or diminished up to a certain limited extent. So too the effect of muscarin can be counteracted immediately by the more stable action of atropin.

The depressing effect of muscarin upon both the rhythmical and contraction power has been so often observed as to admit of no doubt. The same effect upon the excitability and conduction power of the muscle has been noticed by me in my former paper, and can be seen in the most excellent manner by observing its action upon the suspended strip from the auricle of the tortoise. As already mentioned the exciting electrodes, by means of which single induction shocks are sent into the strip every five or ten seconds, are placed at the fixed end of the strip, so that the current passing between their poles passes through a small portion only of muscular tissue at that fixed end. When therefore a single induction shock is sent in, that small portion of tissue alone is directly stimulated and the contraction of the whole strip is due to the spreading of the contraction wave from this initially stimulated portion. When the force of the contractions and the conduction power has been sufficiently improved by the combined action of the single induction shocks and the weak interrupted current sent through the whole strip as already described, then each contraction started by the exciting electrodes passes quickly along the strip, and no distinction can be drawn between the contractions of the small piece between those electrodes and the rest of the strip. After the application of muscarin matters are different; not only is the force of the contractions markedly diminished, but a distinct hesitation is seen before the initial contraction spreads over the whole strip. This hesitation may become greater and greater until a partial block is caused of such a character, that every second induction shock causes a contraction which is confined to the piece of muscle between the exciting electrodes, while the rest of the stimuli cause a contraction which travels through the whole strip. Under such circumstances the passage of the weak interrupted current still further reduces

the force of the contractions, and may cause such a blocking of a larger number of contractions, or may diminish the excitability to such an extent that not even the portion between the exciting electrodes contracts when the single induction shock is sent through. If now a drop of a weak atropin solution be applied to the strip, the contractions instantly increase in force in a wonderful manner, every contraction passes easily and quickly from end to end, all sign of an initial contraction of the muscle between the exciting electrodes immediately vanishes, and in a very short time the interrupted current is able to do nothing more than slightly to diminish the force of the contractions during its passage.

Both atropin and muscarin produce the effects above mentioned by directly modifying the various functions of the cardiac muscle, and in proportion to the stability of the effect so produced is the possibility of a modification of that effect by the direct stimulation of the muscle or by the action of the cardiac nerves. It is partly because the atropin acts on the muscular tissues in such a way as to keep the various muscular powers fixed in a relatively high state of activity, that the cardiac nerves are unable any longer to depress those powers. It is because atropin is able to restore the rhythmical power of the muscle, that stimulation of the vagus and of the sinus is no longer able to produce inhibition; it is because the atropinized muscle contracts with the very first stimulus at its full strength that neither the cardiac nerves nor the interrupted current is any longer able to diminish those contractions; it is because atropin repairs the conduction power that stimulation of the vagus is no longer able to prevent the contraction wave passing from the sinus into the auricles.

Atropin, however, has a further action which is not possessed by muscarin. It not only prevents the action of the vagus nerves by its direct influence on the cardiac muscle, but also by its action on the intra-cardiac nerves themselves, and perhaps especially on their ganglionic nerve cells. Muscarin, on the other hand, influences the muscular tissues, leaving the nervous action intact, at all events, until a very large dose has been given. Thus in my former paper I noticed in the case of the frog that atropin, applied to the sinus and auricle alone, prevented the whole action of the vagus not only on those parts of the heart, but on the ventricle as well; while, on the other hand, muscarin when applied to the sinus and auricle only may affect those parts even to complete standstill, without in the least abolishing the power of the vagus to increase the contractions of the ventricle.

In the tortoise the influence of atropin upon the action of the vagus can be demonstrated by the effect upon both the force of the auricular contractions and the conduction power of the auricular muscle, when the atropin is applied locally to the point of entrance of the coronary nerve into the auriculo-ventricular groove. Thus in one case, where the auricle was slit up until only every second contraction passed the block, it was found that stimulation of the right vagus and of the coronary nerve was in each instance able to remove that block, and also, as is always the case, stimulation of each nerve diminished the contractions of the part of the auricle on its own side. Atropin (1 p. c. solution) was then applied to the ventricle and its junction with the ventricle-auricle, with the result of preventing the action of the coronary nerve upon the force of the contractions of the ventricle-auricle and upon the conduction of the contraction wave over the block (as is seen in Fig. 19, Pl. V.). On the other hand, the right vagus was still able to slow the rhythm, reduce the force of the contractions of the sinus-auricle and remove the block of the contraction wave, just as efficiently as before atropin had been given (Fig. 19). Similarly atropin applied to the sinus and sino-auricular junction will remove the whole action of both right and left vagus nerves, without affecting the action of the coronary nerve, provided that the auricle has been previously slit up, and so all chance of the drug reaching the auriculo-ventricular junction removed. Atropin then not only influences the muscular tissue, but also the nervous structures of the heart in such a way that neither the direct action of the interrupted current nor stimulation of the vagus nerves are any longer able to produce their usual effects upon the various functions of the cardiac muscles.

The views put forward in this paper necessitate a revision of the opinions at present held in respect to the action of a large number of cardiac poisons: a task, which it is impossible to undertake in this present paper without swelling it out to an inordinate length. I will therefore confine myself to one or two remarks on the action of curare as illustrative of the position I desire to maintain.

The difference between the action of curare and atropin is one of the main arguments in favour of the existence of an inhibitory centre capable of being paralysed by atropin but not by curare. Both poisons prevent the inhibitory action of the vagus nerve; but while after curare inhibition can still be caused by the direct stimulation of the venous sinus; after atropin this is no longer possible. The inhibition caused by muscarin can be removed by atropin, but not by curare. These facts do not in my opinion in the slightest degree prove the existence of an

inhibitory centre; they simply confirm the well-known fact that curare is essentially a poison which affects nervous and not muscular structures, and give another proof of the affinity of the cardiac muscle and nerve to the ordinary striated muscle and nerve. Thus curare prevents the inhibitory action of the vagus, because it paralyses some part or other of the nerve endings. It does not prevent the inhibition caused by the direct stimulation of the venous sinus, because unlike atropin it does not act upon the muscular tissue of the sinus, and therefore cannot prevent the inhibitory action of the current applied directly to that muscle. For the same reason it is unable to influence the inhibitory action of a muscular poison like muscarin.

PART V.

Conclusion.

The conception of the cardiac function advanced in the preceding pages represents the heart as a specially modified portion of the vascular system; the heart is to be considered as a piece of artery or vein, the muscular walls of which have developed in a special manner. The key-note therefore of the peculiarities of the cardiac muscle consists in its structural position, intermediate between unstriped and striated muscle fibre. Muscular tissues exhibit three different modes of responding to stimulation according to their structure. These modes may be expressed by saying that certain muscles possess essentially the power of "tonic contraction," others the power of "rhythmical contraction," and others that of "rapid contraction." A comparison of the tetanizing action of a strong interrupted current upon a strip of muscle from the bladder of the tortoise and from the heart of the tortoise with the ordinary tetanus curve of the frog's gastrocnemius shows clearly the difference of the three kinds of muscular tissue.

The unstriped muscle of the bladder contracts slowly after a long latent period, the contraction increasing steadily in force during and even after the cessation of the tetanizing current, and then the strip returns with excessive slowness to its original length. In other words we see a prolonged tonic contraction as the result of the stimulation.

With the striated muscle we have the well-known curve of tetanus composed of the superposition of a series of rapid contractions.

The cardiac strip gives a curve which is intermediate between the two and may be described as consisting of a long-continued tonic con-

traction upon which a number of rapid contractions are super-imposed. These separate rapid contractions never succeed one another so quickly as to fuse together. The cardiac muscle then, when tetanized, gives in virtue of its relationship to unstriped muscle, a tetanus of tonicity (to use Ranvier's expression), and at the same time a series of rapid contractions in consequence of its affinity to ordinary striated muscle. When the vitality of the tissue is impaired by exhaustion, by injury, by malnutrition, the cardiac muscle loses its power of rapid contraction, and the less-specialized tonic power alone remains, the muscle strip tetanized when in that condition contracts with a prolonged tonic contraction in the same way as unstriped muscle.

In another respect too the intermediate position of the cardiac muscle between the slowly contracting, slowly exhausted unstriped muscle and the rapidly contracting easily exhausted striated muscle is clearly shown; the vitality of unstriped muscle after the death of an animal is wonderfully long; the irritability of the cardiac muscle after death is less than this, but decidedly greater than that of the ordinary striated muscles.

Again, the evidence that the power of rhythmical contraction is a property of muscular tissue, common to many of the different kinds of muscle found in the animal kingdom increases in importance day by day. Not only do we know that the unstriped muscle of the ureter and the veins of the bat's wing are as capable of contracting rhythmically as the apex of the frog's heart under the influence of the mechanical stimulus of distention, but we also have evidence that the more highly developed striated muscle fibres are capable of rhythmical contractions under the influence of a constant stimulation, whether electrical or chemical. This is especially the case, as the experiments of Schœnlein[1] prove, in the striated muscles of the invertebrata, which contract rhythmically upon stimulation by a weak interrupted current in a manner very similar to the muscular tissue of the apex of the frog's heart. We see then that the power of rhythmical contraction is not confined to cardiac muscle, but exists also to a certain extent in unstriped and striated muscles, and just as this power has been developed to a greater extent in some unstriated muscles than in others, so too it has reached a still higher stage—the stage of rhythmical automatism—in some kinds of cardiac muscle than in others. We may then make a comparison between the development of function in the three kinds of muscular tissue as follows:—

[1] *Archiv f. Physiologie* von du Bois-Reymond, 1882, p. 369.

Striated muscle of vertebrates—
Rapidity of contraction most highly developed.
Tonicity rudimentary.
Rhythmic action still more rudimentary.
Cardiac muscle—
Rhythmic action most highly developed.
Rapidity of contraction well marked.
Tonicity well marked.
Unstriped muscle—
Tonicity most highly developed.
Rhythmic action well marked.
Rapidity of contraction most rudimentary.

Further, the development of the full rhythmical power in a piece of cardiac muscle is strikingly similar to that of the full contraction power. Thus the rate of the automatic rhythm increases by successive increments in the same way as the contraction force, and just as the isolated muscle in Bowditch's experiment responds weakly to the first stimulation, so the isolated auricle or ventricle of the tortoise remains still for some time before the first automatic contraction takes place.

The meaning of this preliminary standstill—the standstill of the first Stannius ligature—has always been a difficult problem to solve, and many attempts at an explanation have been given. It is therefore of special interest to examine the conditions necessary for its appearance and for its non-appearance. It is clear from what has already been said that this standstill is of the same nature, whether it occurs as a preliminary to the automatic rhythm of the auricle, of the ventricle, or of the apex of auricle or ventricle. It is associated with the development of the automatic rhythm in each case, and is not due to the action of any special inhibitory mechanism. The laws of the development of rhythm are throughout very similar to the laws of the development of the contraction force, and the reason why the tissue when first isolated commences its automatic contractions at so slow a rate as to give occasion to the use of the term "standstill" is the same as the reason why the first artificial contraction of the muscular tissue of the apex in Bowditch's experiment is so much weaker than the subsequent contractions. If it were possible to ensure that the conditions of the experiment should be the same in every case, it would in all probability be found that the length of the standstill after isolation of the tissue was strictly in proportion to the rhythmical power of the tissue. We ought therefore to find that the auricle commences its automatic beats sooner

after isolation than the ventricle, and the ventricle sooner than the strip from the apex. Undoubtedly the standstill is longer in the case of the apex than of the whole ventricle, and sometimes it is very clear that the isolation of the ventricle is followed by a longer standstill than that of the auricle, as the following case shows.

Feb. 14, 1883. Heart suspended, aorta held. Auricle fixed to upper lever, ventricle to lower. Contractions perfectly regular at about 12 per minute. The sinus was then cut away; 5 excitation contractions occurred at the moment of section and then the auricle and ventricle remained still for 11 minutes, after which the first automatic contraction of the auricle took place, followed by a contraction of the ventricle. The auriculo-ventricular rhythm then developed in its usual manner, the lengths of time in seconds between consecutive beats being as follows—

260, 170, ?, 90, 80.

A fresh drum was here necessary, and as soon as the beats were again recorded the durations in seconds of consecutive pauses were

33, 33, 27, 27, 28, 24, 23·5, 23, 22·5, 22, 21·5, 22, 21, 20, 19·75, 19·5, 19, 19, 19, 18·5, 18, 18.

and again on the next curve

16·5, 16.

The auricle was now cut away and a rhythm of excitation was immediately set up in the ventricle with pauses between the beats as follows—

7, 8, 9, 10, 10, 22, 22, 20, 23, 25, 26, 28, 35, 40, 106, 100, ?, 193, 170, 154, ?,

and then complete standstill for 12 minutes.

After this the ventricle began to beat automatically with the following lengths of time between the contractions—

150, 145, 138, 134, 130.

The first standstill lasted therefore 11 minutes and the second standstill including the time of the rhythm of excitation at least 34 minutes.

Throughout, the length of the standstill is relative and not absolute, so that it is not possible to compare different experiments on different animals without making an extensive series of experiments with all possible precautions in order to solve this one particular point. This I have not yet done and cannot therefore assert positively that the length of the standstill varies inversely as the rhythmical power of the heart segment which is isolated, although such a proposition is highly probable.

The nature of this standstill is further shown by the conditions necessary for its non-appearance. These conditions may be summed up in the assertion: Any influence which increases the develop-

ment of the rhythmical power removes at the same time the preliminary standstill; just as in Bowditch's experiment, atropin brings the force of the contractions to an immediate maximum. Such influences are in the case of the ventricular standstill the supply of a blood solution through the coronary vessels and the application of atropin to the auriculo-ventricular groove. In both cases the ventricle beats immediately upon isolation, the standstill is gone.

Again, when the contractions of the frog's ventricle have reached their maximum by means of a series of single induction shocks at equal intervals, and then the stimulations are discontinued for some time, a new set of contractions caused by a second series of induction shocks does not begin with contractions of the maximum strength of the previous series, but the first of the new set is smaller than the last of the old and a staircase is again formed. So too an automatic rhythm which has developed up to a certain rate may recommence at a slower rate after it has been interrupted. This is exemplified in the following way. The auricle is slit until a block occurs; in many cases this block lasts so long as to allow time for the commencement of the development of a rhythm of the ventricle and that part of the auricle in connection with it, which is entirely independent of the rhythm of the sinus. At this time then the two parts of the heart which are separated by the blocking point are beating quite independently of each other and the rhythm of the ventricular side is gradually gaining in rapidity in the usual manner. The block is now removed by the application of salt solution and stimulation of the vagus, until at last in favourable cases every contraction again passes and the sequence is fully restored. With the restoration of the sequence the independent rhythm disappears, the ventricle and ventricle-auricle are again completely under the domination of the sinus. The sinus is now removed by the section of the sinus-auricle, without therefore injuring in any way the ventricle and ventricle-auricle; and it is found that a standstill again occurs and again the independent auriculo-ventricular rhythm is slowly developed up to and beyond its former rate. Although the second rhythm does not commence at the rate that had previously been reached, yet some beneficial effect of the previous development is usually noticed; the second standstill is not as long as the first, and a third standstill produced in a similar manner may be less still, until at last the production of a block is not followed by any standstill at all.

The similarity between the laws governing the rhythmical power and the contraction force of the cardiac muscle is not the only similarity

found between two different muscular attributes. The excitability of the muscle as measured by its capability of response to a stimulus, and its power of conducting a contraction from muscle cell to muscle cell present many resemblances to each other. It has been shown that a block can be produced, either by artificial section of the auricle or by an increase in the natural block at the auriculo-ventricular junction, such that only every second contraction which starts from the sinus passes over the block. Such a partial block has been shown to be dependent upon the rate of the contractions and not upon the strength of the stimulus which initiates the contraction wave. Thus the conduction power of the muscle at the blocking point may be such that every contraction at ten seconds intervals will pass, while only every second contraction at intervals of five seconds is able to pass. In precisely the same way we know that the cardiac muscle will respond to every stimulus when a sufficient length of time elapses between the stimuli, but only to every second stimulus when that time is too short, provided that the strength of the stimulus remains unaltered. Again, in consequence of stimulation of the vagus, every contraction may pass a block over which only every second contraction had previously been able to pass, even though at the same time the force of the contractions has been greatly diminished. The conduction power is not dependent upon contraction force. So too the excitability of the muscle may be increased by the same action which depresses the force of the contractions. Thus as already mentioned the strip of muscle from the apex of the frog's ventricle or tortoise auricle may respond to every second induction shock, when the induction shocks are sufficiently weak and are sent through every five seconds; yet upon sending through a weak interrupted current, the muscle may respond to every stimulation, though at the same time the force of the contractions is markedly diminished. I have not yet attempted to work out the relations which exist between the strength of the interrupted current, the alteration of the contraction force and the alteration of excitability, and can say therefore at present nothing more definite than that the excitability of the muscle may be influenced by the interrupted current in a direction opposite to the contraction force. In other words, the interrupted current affects the muscular excitability in a manner similar to the effect of the vagus upon the conduction power; another proof of the resemblance between the action of the vagus and a weak interrupted current and also of the close relationship between muscular excitability and conduction power.

Again, I have shown clearly that the vagus depresses and exalts

all the different functions of all the different muscular tissues of the heart, whether the function in question is rhythm, contraction, conduction, tone, or excitability. Also I have shown that depression of one function is not necessarily accompanied by a simultaneous depression of another function, and so also with the exaltation of function. Further, the exaltation of each function is not necessarily dependent upon a previous depression; in each case the primary effect may under certain circumstances be exaltation and not depression. Combining these two facts together we are driven to accept one of two alternatives, either the vagus contains a multiplicity of fibres, which can be divided into two groups after the fashion of Heidenhain[1].—1. Depressors (Hemmungs-fasern); 2. Augmentors (Verstärkungs-fasern); and further each member of each of these groups has again its own special function, so that for instance the rhythm-inhibiting nerve fibre is different in kind from the contraction-depressing fibre and so on; or else, the same trophic nerve fibre produces all the different effects observed, according to the nature of the muscle which it supplies, and the condition of that muscle at the time.

In this paper as well as in my previous paper all the facts have tended strongly to prove that the vagus acts in the same manner upon the rhythm of the heart and upon the force of its contractions, so that if separate inhibitory and accelerator nerve fibres exist for the one, separate depressor and augmentor fibres must exist for the other. If therefore it can be shown that such diminution and augmentation of the strength of the contractions are due not to different influences reaching the muscle, but to the same influence affecting the muscle when its conditions are different, then it is, to say the least, highly probable that slowing and acceleration are also due not to different nerve fibres but to the action of the same nerve fibre under different circumstances. In the frog, as I have previously pointed out, such a complete gradation exists between a primary excessive diminution of the contractions and a primary augmentation in consequence of nerve stimulation, as to render the hypothesis that such curves depend upon the simultaneous stimulation of two antagonistic nerve fibres very improbable. I have now proved in addition that a weak interrupted current applied to the smallest strip of cardiac muscle produces the same two opposite effects, and that here the depressing effect may be removed and the augmenting alone remain, when the condition of the muscle is altered by the application of atropin. In

[1] *Op. cit.*

order therefore to still hold to the view of specific nerve fibres acting in opposite directions upon the force of the contractions, it is necessary to assume, not only that those nerve fibres possess opposite qualities up to their very termination in the muscle, but that even when the muscle itself is stimulated the relative action of these two sets of nerves still holds its ground. In addition, atropin would have to be considered as acting upon these two sets of nerve endings and not upon the muscle, paralysing the depressor nerve endings before those of the augmentor nerves. The experiments of Luchsinger and Szpilman[1] which lead them to the conclusion that atropin has a special action upon unstriped muscle fibre, those of Bowditch already referred to, and my own all point to the conclusion that atropin affects the cardiac muscle directly, in consequence of its affinity to unstriped muscle fibre. The whole evidence goes to show that the vagus is a constructive and not a destructive nerve, that the initial depression of function is not of the nature of exhaustion but is preliminary to a greater functional activity. The phenomenon presented by the muscular tissue of the frog and tortoise under the influence of an induced current is of exactly the same nature as that seen in the muscle of the snail's heart (as pointed out by Foster[2] and Dew-Smith), when a constant or weak interrupted current is sent through it. In both cases augmentation of function occurs as well as depression; in the one case the evidence is as strong in favour of special inhibitory and accelerator nerves as in the other. Clearly in the case of the snail it is simply impossible, as Foster[3] has said, to explain such results by the presence of accelerator and inhibitory fibres in every strip of muscular tissue, when as a matter of fact, cardiac nerves of any kind whatever have not been proved to exist. Clearly also whatever explanation will ultimately be found for the action of the current upon the muscular tissue of the snail's heart will also explain the same phenomena in the heart of the frog and tortoise. The problem which demands solution is essentially, Why is the condition of the muscle ultimately improved in every one of its functions by the direct application to it of a continuous stimulus which is not strong enough to produce motor effects? and why is that improvement of function preceded in many cases by a diminution of function? When these two questions have received a satisfactory answer, it will no longer be strange that the vagus produces throughout two opposing effects, and the action of atropin will become clear; then the relationship between trophic and motor action will be understood,

[1] Pflüger's *Archiv*, Vol. xxvi. p. 459. [2] *Op. cit.*

[3] *Journ. Anat. and Physiol.* Vol. x. "Some effects of Upas Antiar on the frog's heart."

and the true function of the ganglion cells found in connection with nerve fibres will be indicated. At present it can only be said that the vagus is the trophic nerve of the cardiac muscle, its action resembling that of a stimulus too weak to produce motor effects, and therefore it is possible that the function of the ganglion cells in the course of the nerve is to convert an otherwise motor into a trophic nerve.

Throughout this paper I have confined myself to observations upon the heart of cold-blooded animals. I am not yet in position to say how far, in the more highly-developed mammalia, the phenomena of the heart may have become changed under a greater differentiation of function, and an increased complexity of structure. Such questions therefore as the real interpretation of the action of the accelerans nerves, as distinguished from that of the main vagus fibres in these animals, must be left for subsequent investigation. I trust to be able at some future time to deal with the matter, which has naturally already been the object of investigation by others.

DESCRIPTION OF FIGURES. Pl. II.—V.

All curves read from left to right. The fractions in brackets after certain of the figures denote the extent to which the original curve has been reduced by photography. The letters *S*, *A*, *V* in all cases denote beats of the sinus, auricle and ventricle respectively.

Fig. 1. Feb. 23, 1882. Development of the rhythm of the auricle.

Curve *A*. Sinus cut away at arrow. The first curve after section is marked I.; II. is the continuation of this curve on the same drum.

Curve *B*. Continuation of curve *A*. Drum changed as rapidly as possible.

Curve *C*. Continuation of curve *B*. Fresh drum. Time marker every 2 seconds.

Fig. 2. Feb. 9, 1882. Development of the rhythm of the whole ventricle.

Clamp tightened in auriculo-ventricular groove. A rhythm of excitation was set up in the ventricle which gradually slowed down to the minimum rate shown at the commencement of curve I. From this point the ventricular rhythm slowly and regularly quickened as shown in curves I.—VII. Time marker every 2 seconds.

Curve I. was taken at 12.15 p.m.

Curves II. and III. follow immediately on curve I. and were therefore taken at about 12.30 and 12.45 p.m. respectively.

Curve IV. was taken at 2.45 p.m.
„ V. „ „ „ 4.0 p.m.
„ VI. „ „ „ 5.15 p.m.
„ VII. „ „ „ 6.40 p.m.

Fig. 3. Nov. 7, 1882. Development of the rhythm of the ventricular strip.

Strip from apex of ventricle suspended at 3.30 p.m.

Single induction shocks every 10 seconds sent in at one end; interrupted current sent through the whole strip at intervals as marked on the upper stimulation marking line.

Curves I., II., III. are samples taken during the first hour after suspension; each contraction corresponding to a single induction shock. Time marker every 10 seconds.

Curves IV., V. are samples of the automatic beats taken between 5.30 and 6 p.m. Time marker every 2 seconds.

Curve VI. was taken at 11 a.m. on Nov. 8; the strip remaining undisturbed during the night. Time marker every 2 seconds.

Fig. 4. Feb. 27, 1882. Comparison of artificial with natural block.

Aorta held; auricle slit up.

Curve *A*. Each auricular beat is composed of three parts.

First the contraction of the sinus-auricle (*As*); then the contraction of the ventricle-auricle (*Av*); and then the ventricular contraction (*V*) which follows *Av* and is transmitted to the upper lever.

Curve *B*. Between curves *A* and *B* the auricle was slit up further; the pause between the contractions of *As* and *Av* was increased, and every second contraction of *As* was unable to pass the block and therefore no contraction of *Av* or *V* followed. Time marker every 2 seconds.

Fig. 5. May 8, 1882. Stimulation of L. Vagus, R. Vagus and Coronary Nerve.

Aorta held. Time marker every 10 seconds. Sec. coil at 10 c.m.

Fig. 6. May 20, 1882. Stimulation of Coronary Nerve (central end).

Auricle cut away from ventricle, leaving coronary nerve in connection both with ventricle and sinus. Aorta held; electrodes on coronary nerve near ventricle. Contractions of auricle only given, ventricle quiescent. During both stimulations given in curve, sec. coil at 10 and 12 c.m. respectively, the ventricle remained absolutely quiescent. Time marker every 2 seconds.

Fig. 7. Feb. 27, 1882. Stimulation of R. Vagus when the coronary nerve is the only channel of communication.

Aorta held. Auricles cut away from sinus, leaving coronary nerve intact. Stimulation of R. Vagus in the neck after the establishment

of a regular independent auriculo-ventricular rhythm. Sec. coil at 5 c.m. Time marker every 2 seconds.

Fig. 8. Feb. 13, 1882. Development of an independent ventriculo-auricular rhythm made manifest by vagus stimulation.

Clamp in auriculo-ventricular groove. Curves I.—V. are samples taken at intervals of the effects of stimulation of the R. Vagus; sec. coil at 12 and 10 c.m. The arrows *V.A* and *A.V* denote the beginning and the end of the unmasked ventriculo-auricular rhythm during each stimulation. In this case the after-acceleration is well marked. Time marker every 2 seconds.

Fig. 9. March 23, 1882. Stimulation of R. Vagus.

Heart in the body and circulation intact. Beats of ventricle only registered. Sec. coil at 6 c.m. Time marker every 2 seconds.

Fig. 10. Nov. 6, 1882. Removal of a partial block by stimulation of R. Vagus.

Aorta held. Auricle slit up until only every second contraction passed the blocking point. Stimulation of R. Vagus caused all the contractions to pass for a time.

Fig. 11. March 1, 1882. Removal of a partial block by stimulation of R. Vagus.

Aorta held. Auricle slit up until only every second contraction of *As* passed. Stimulation of R. Vagus; sec. coil at 8 c.m. After the second stimulation given in the Fig. the contractions all passed permanently, so that a new block had to be made in order to repeat the experiment. Time marker every 2 seconds.

Fig. 12. May 8, 1882. Increase of partial block by stimulation of the Coronary nerve.

Aorta held. Auricle slit up. Stimulation of coronary nerve. Sec. coil at 8 c.m. Time marker every 10 seconds.

Fig. 13. April 27, 1882. Increase of a partial block by stimulation of the R. Vagus nerve.

Aorta held. Auricle slit up. Sec. coil at 6 c.m. Time marker every 2 seconds.

Fig. 14. Oct. 10, 1882. Sinus beats continue during R. Vagus stimulation.

Aorta held. R. Vagus stimulated; sec. coil at 10 and 11 c.m. respectively. Rhythm of sinus remains unaltered during the stimulations. With the stronger stimulation the beats of the sinus were diminished in strength to a greater extent than with the weaker stimulation. Time marker every 2 seconds.

Fig. 15. Oct. 28, 1882. Lengthening of the pause between the beats of the sinus and auricle during stimulation of the R. Vagus.

Sinus beats (*S*) are made evident by the stimulation of the nerve. Sec. coil at 10 c.m.

Fig. 16. Snake's auricle. Shortening of the pause between the beats of the sinus and auricle during stimulation of the R. Vagus.

In the two curves given the stimulation of the nerve commences at the arrow (α) and ends at the arrow (ω). Sec. coil at 6 c.m. Drum moving rapidly.

Fig. 17. Nov. 21, 1882. Action of a weak interrupted current upon the spontaneous contractions of a strip from the apex of the auricle.

By the application of single induction shocks every 5 seconds combined with the interrupted current at intervals the strip had been brought into the condition of spontaneous beating.

Curve I. gives two examples of the effect of an interrupted current sent through the strip upon the strength of these spontaneous contractions. Sec. coil at 9.5 and 8.5 c.m. respectively.

The strip was kept moist through the night and at 12.30 p.m. on Nov. 22 curve II. was taken and shortly afterwards curve III. Sec. coil pushed gradually from 8—5 c.m. and from 8—6 c.m. respectively. In both curves the contractions of the strip are spontaneous. Time marker every 5 seconds.

Fig. 18. Nov. 15, 1882. Action of single induction shocks applied to the R. Vagus.

Aorta held; auricular beats only registered.

Curve I. shows the effect of a single strong (sec. coil at 0 c.m.) induction shock applied to the R. Vagus in the neck.

Curve II. gives the effect of a series of single induction shocks to the R. Vagus every 3 seconds. Time marker every 3 seconds. Sec. coil at 0 c.m.

Fig. 19. May 8, 1882. Action of atropin applied to junction of auricle and ventricle.

Aorta held. Auricle slit up so as to cause partial block. Atropin sulphate (1 per cent.) applied to junction of auricle and ventricle. Stimulation of coronary nerve (sec. coil at 6 c.m.) is no longer able to influence either the force of the contractions of *Av* or the passage of the contraction from *As* to *Av*.

Stimulation of R. Vagus (sec. coil at 6 c.m.) acts as before the application of the atropin. Time marker every 10 seconds.

Fig. 1, A. ($\frac{1}{4}$)

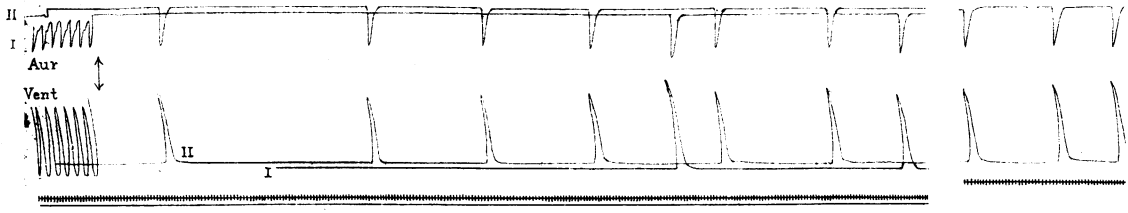


Fig. 1, C. ($\frac{1}{4}$)

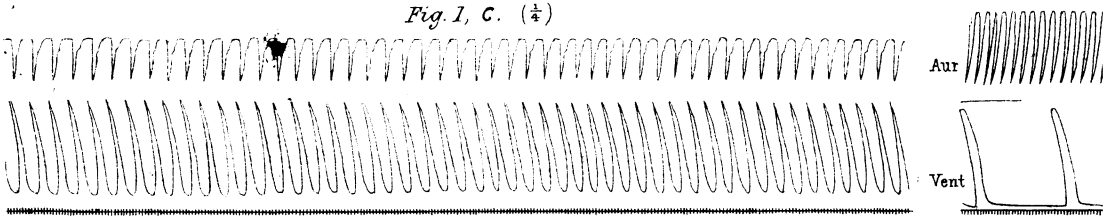


Fig. 2, II. ($\frac{1}{4}$)

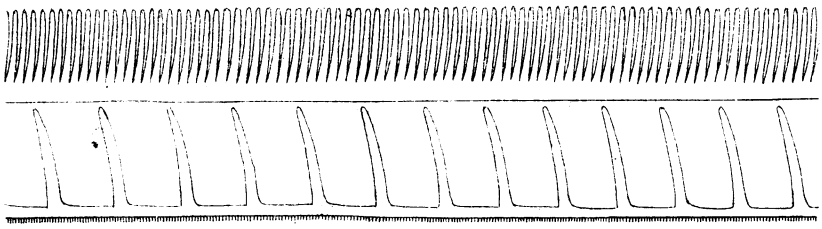


Fig. 2, III. (

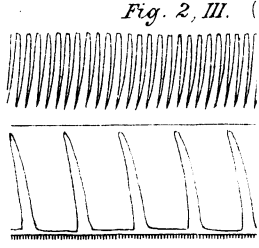


Fig. 3, I. ($\frac{1}{2}$)

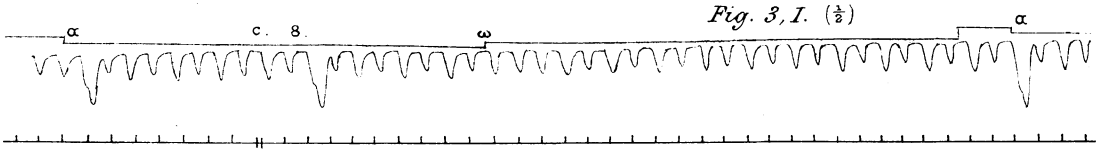


Fig. 3, II. ($\frac{1}{2}$)

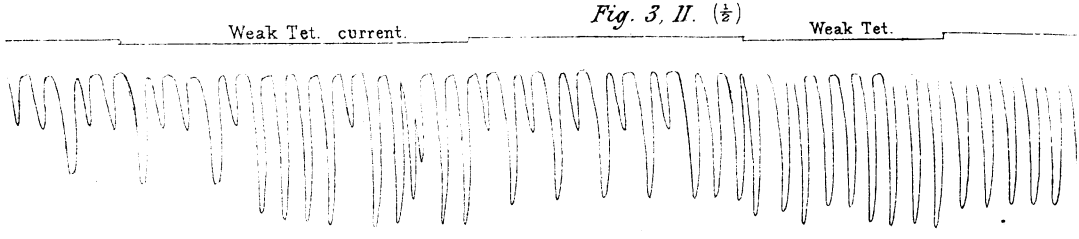


Fig. 3, III. ($\frac{1}{2}$)

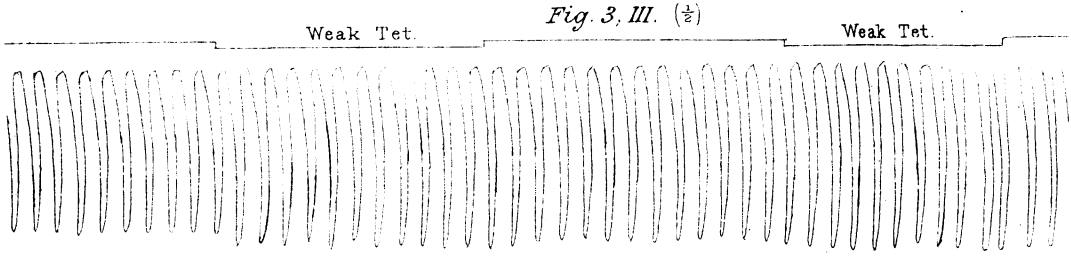


Fig. 1, B. ($\frac{3}{4}$)

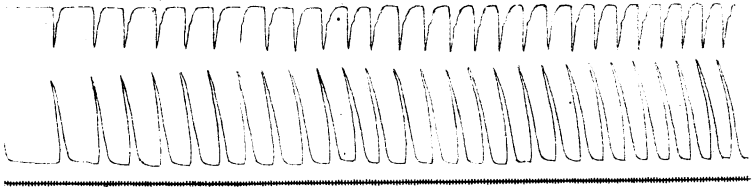


Fig. 3, IV. ($\frac{1}{2}$)

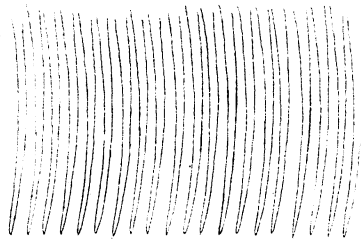
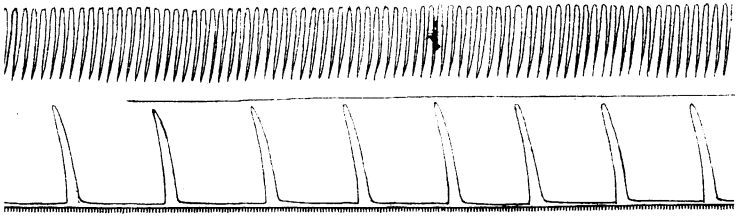


Fig. 2, I. ($\frac{1}{4}$)



Spontaneous beats.

($\frac{3}{4}$)

Fig. 2, IV. ($\frac{1}{4}$)

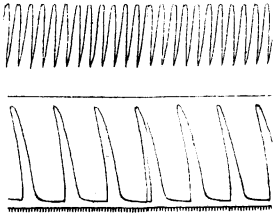


Fig. 2, V. ($\frac{1}{4}$)

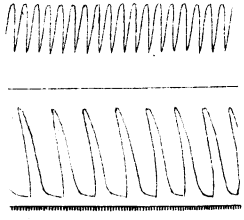


Fig. 2, VI. ($\frac{1}{4}$)

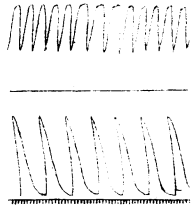
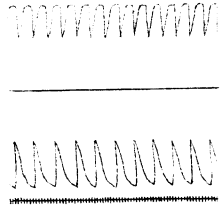


Fig. 2, VII. ($\frac{1}{4}$)



C. S. ω

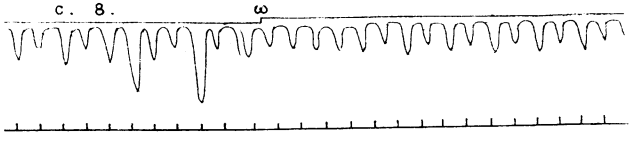
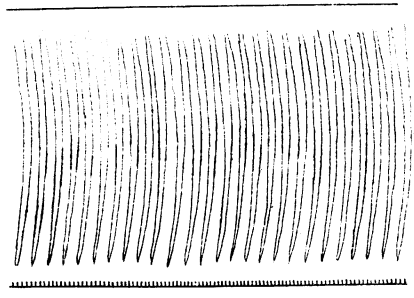


Fig. 3, V. ($\frac{1}{2}$)



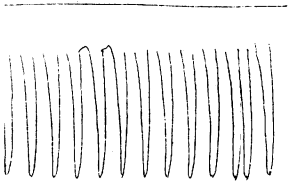
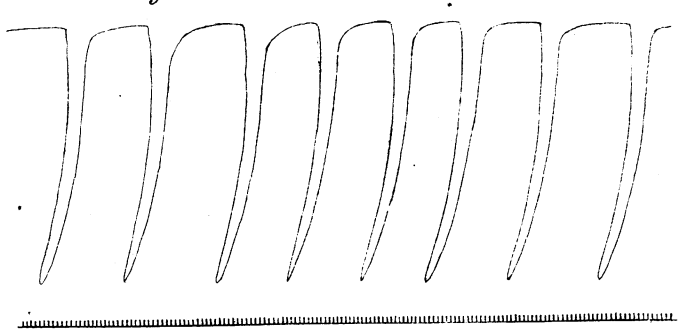


Fig. 3, VI. ($\frac{1}{2}$)



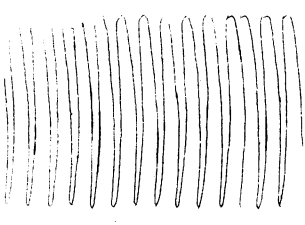
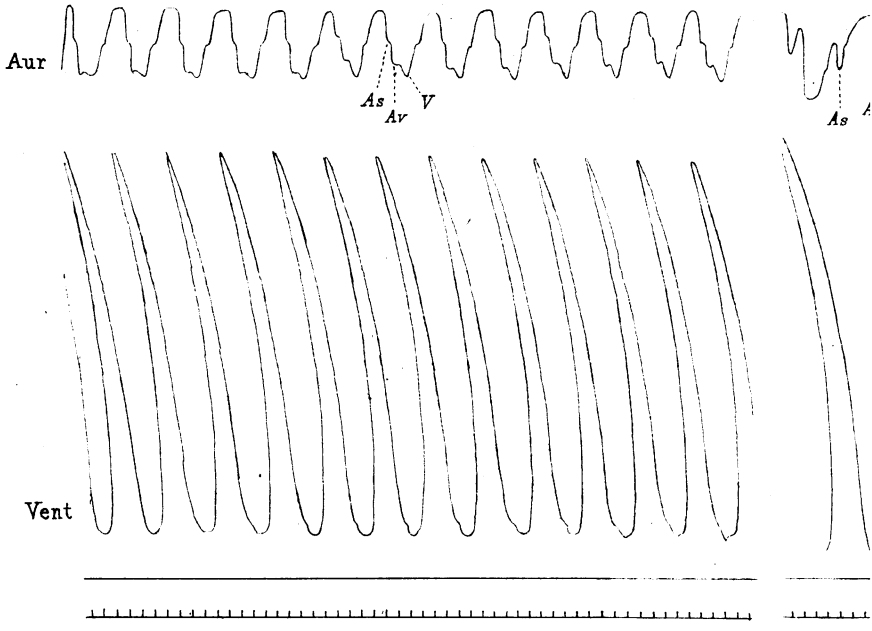


Fig. 4, A.



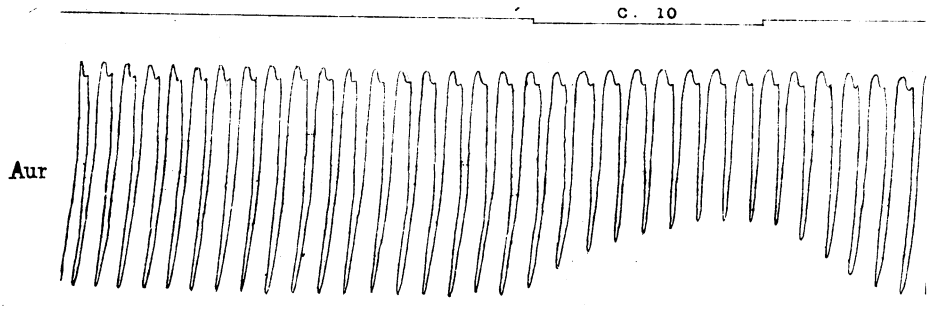
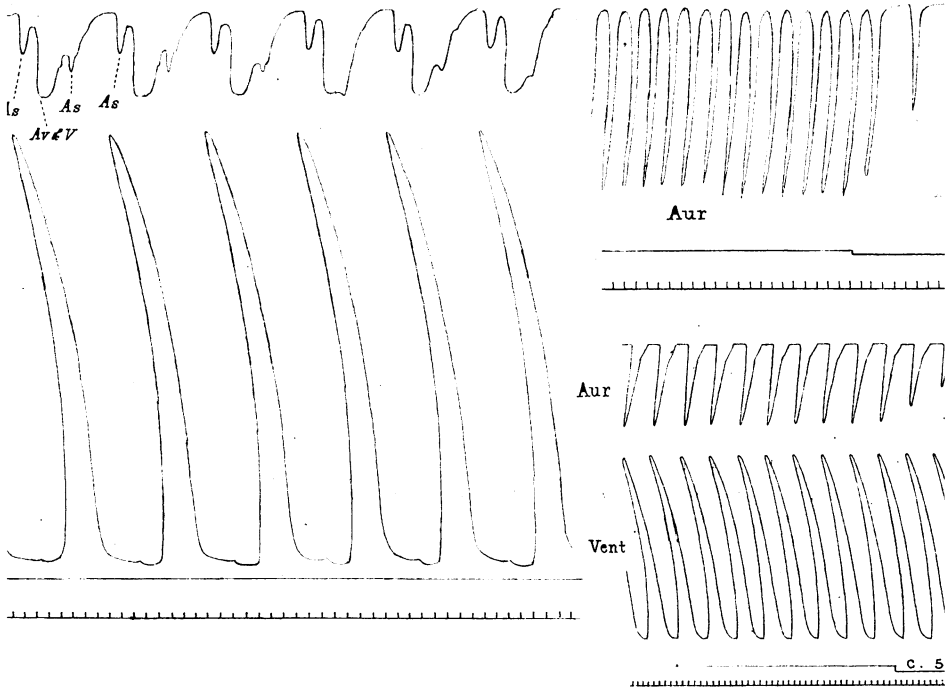
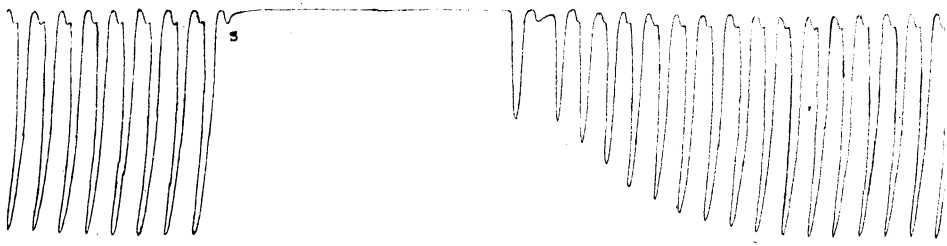


Fig. 4, B.



C. 10.

Fig.



R. Vagus.

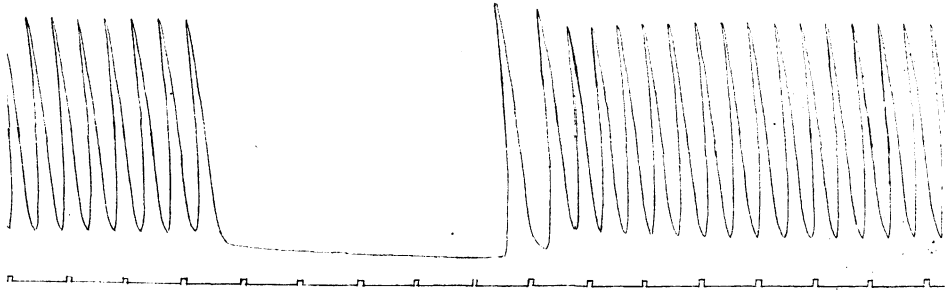


Fig. 6.

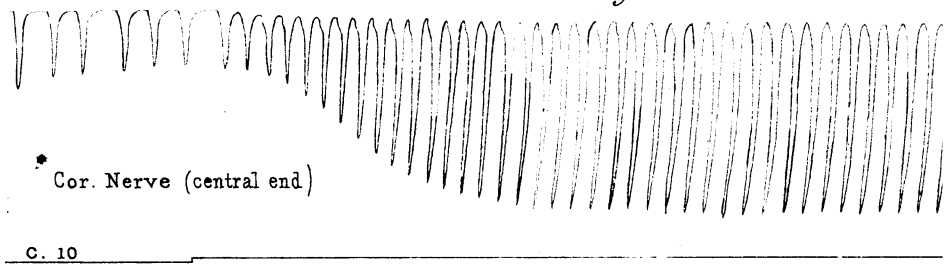
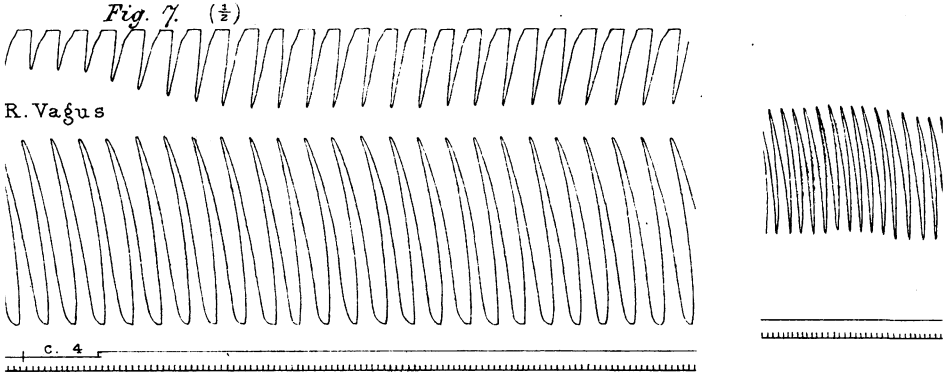
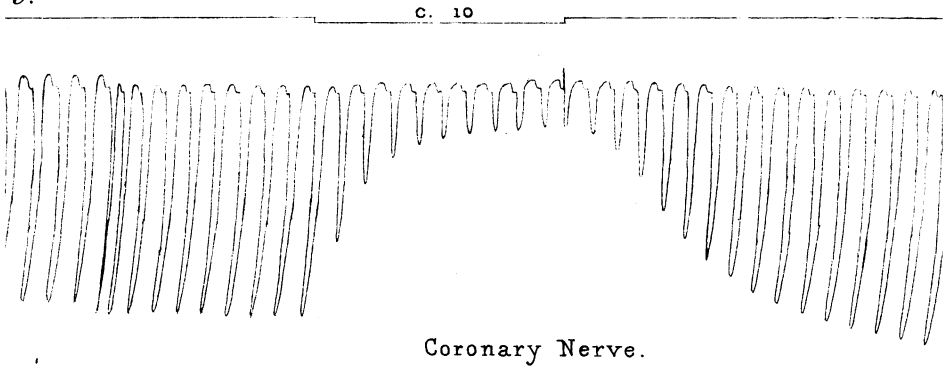
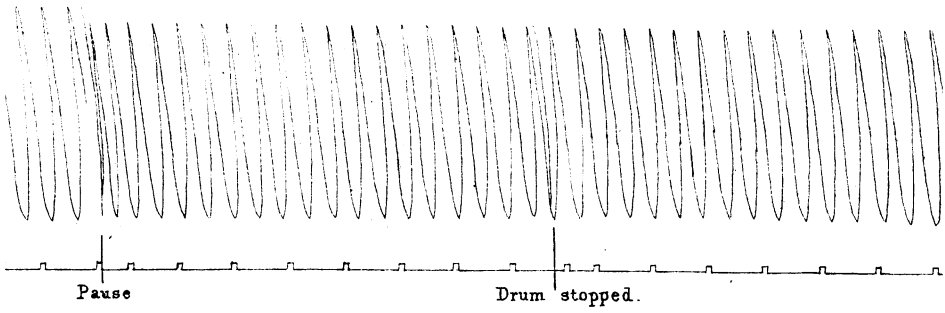

Cor. Nerve (central end)
C. 10

Fig. 7. (½)


R. Vagus
C. 4

5.


C. 10
Coronary Nerve.


Pause
Drum stopped.

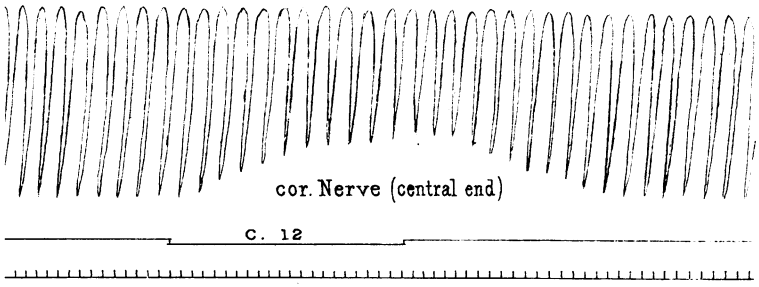
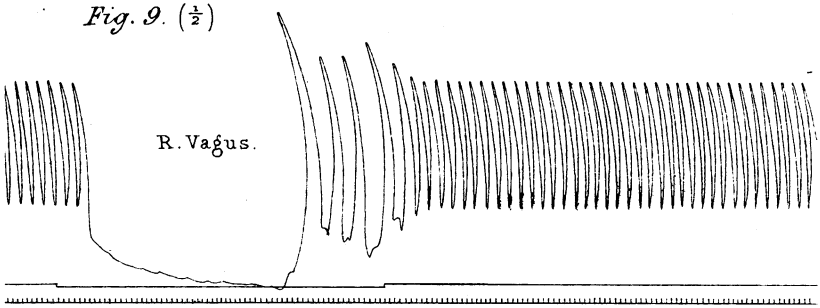
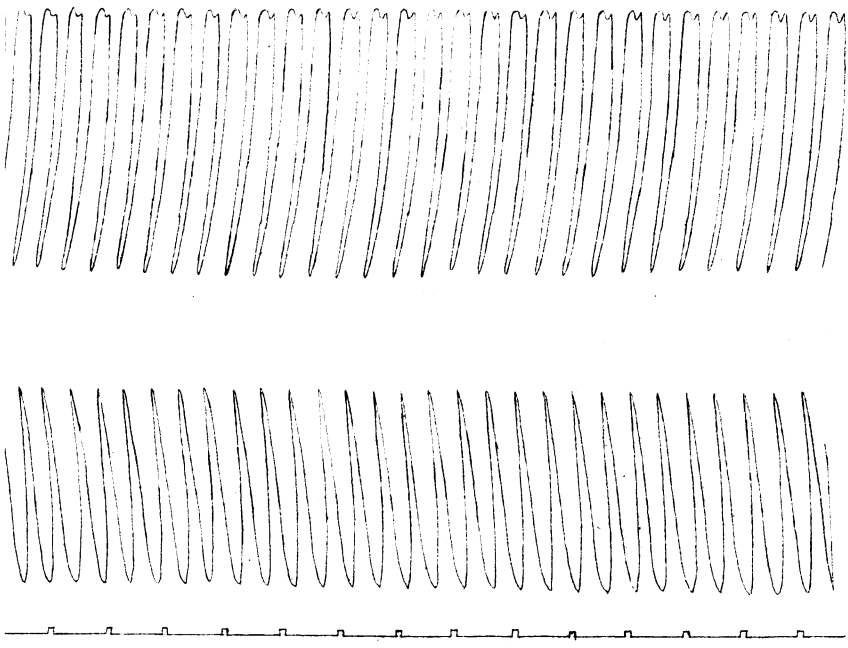


Fig. 9. $(\frac{1}{2})$





F Huth, Lith^r Edin^r

Fig. 8, I. ($\frac{1}{4}$)

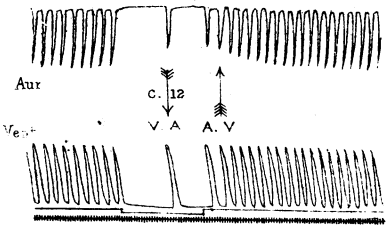


Fig. 8, II. ($\frac{1}{4}$)

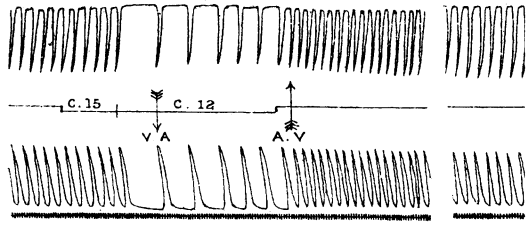


Fig. 10. ($\frac{1}{2}$)

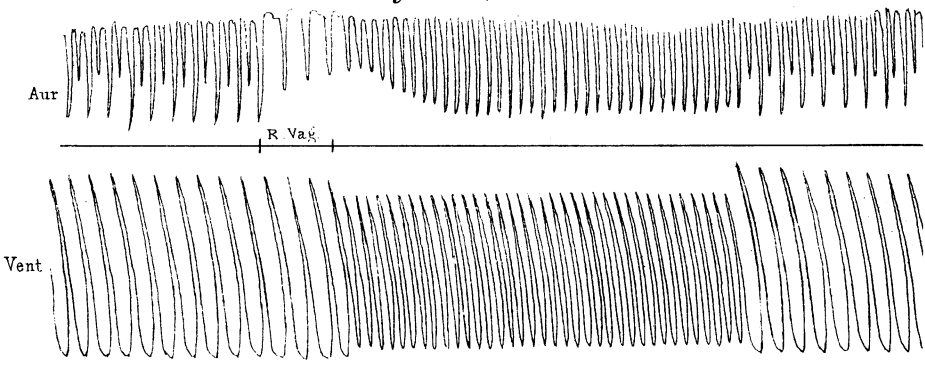


Fig. 14.

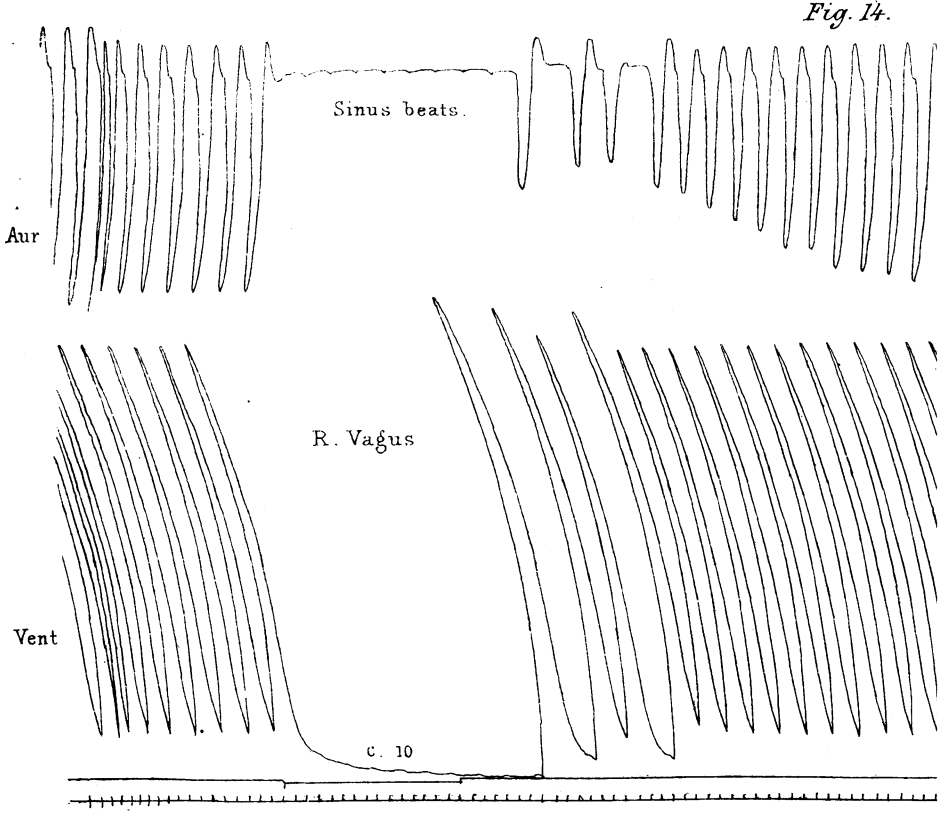


Fig. 8, III. ($\frac{1}{4}$)

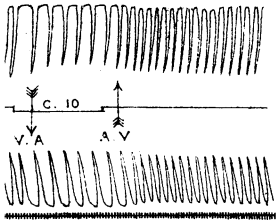


Fig. 8, IV. ($\frac{1}{4}$)

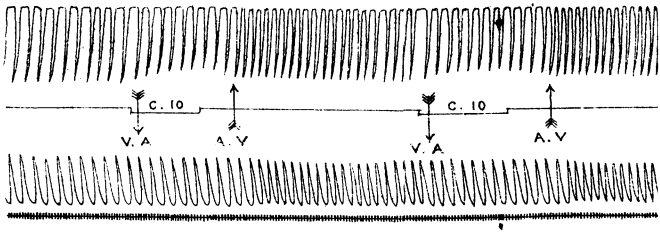


Fig. 12. ($\frac{1}{2}$)

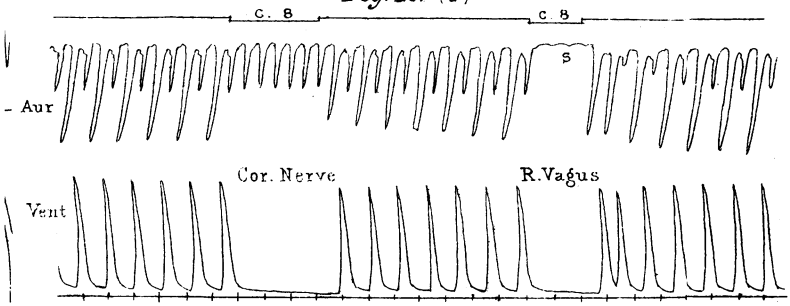
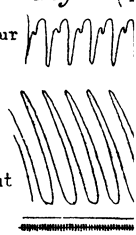
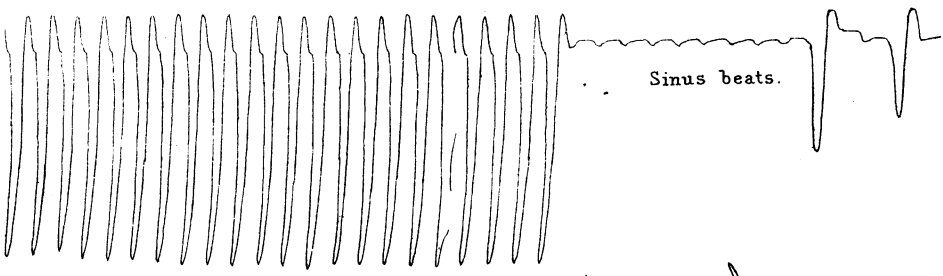


Fig. II. ($\frac{1}{4}$





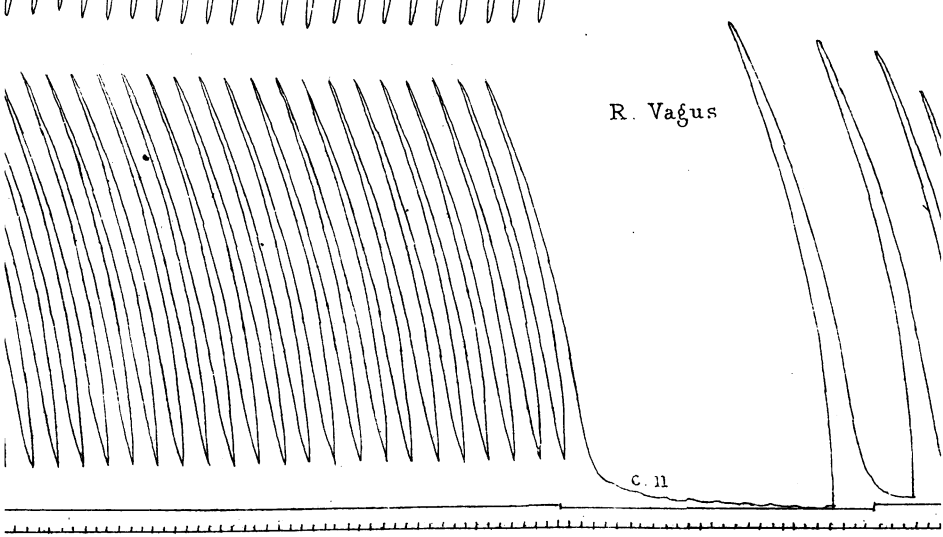


Fig. 8, V. (3/4)

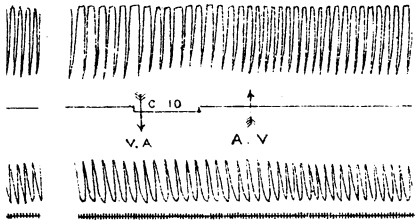
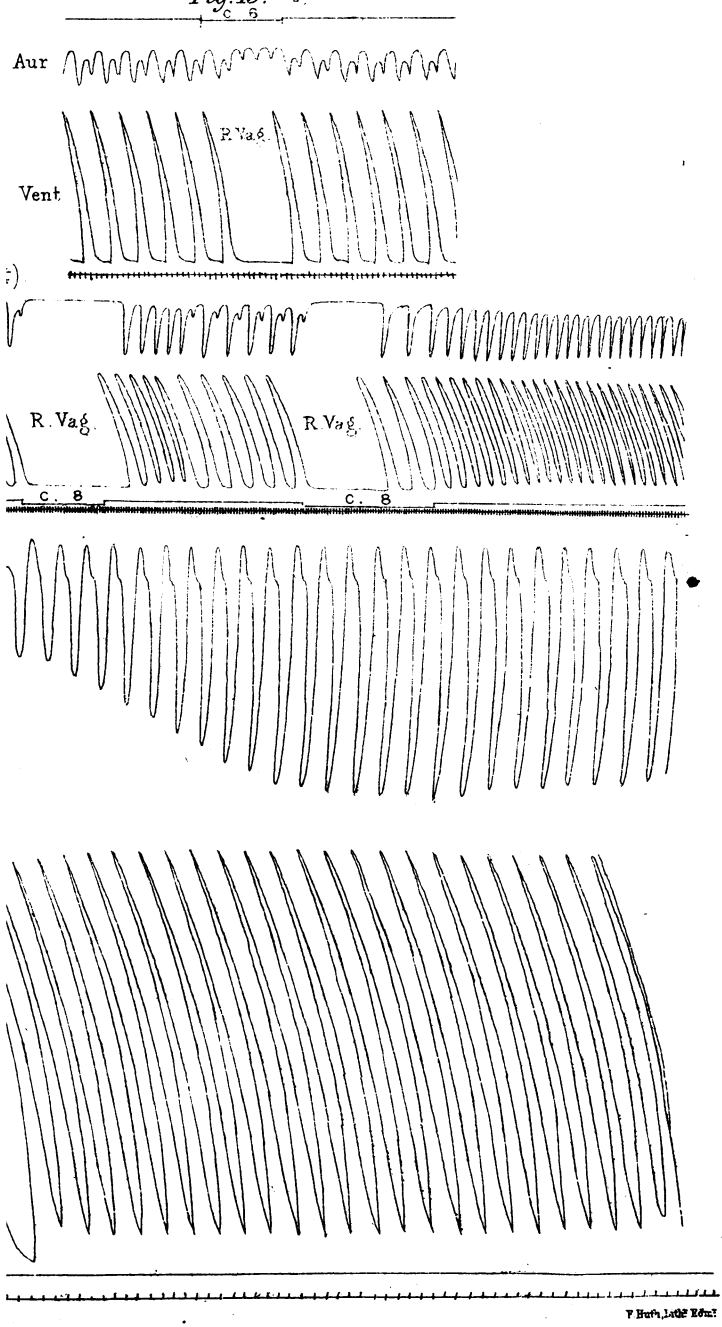


Fig. 13. (3/8)



F. Huth, Lith. Edin.

Fig. 19. ($\frac{1}{2}$)

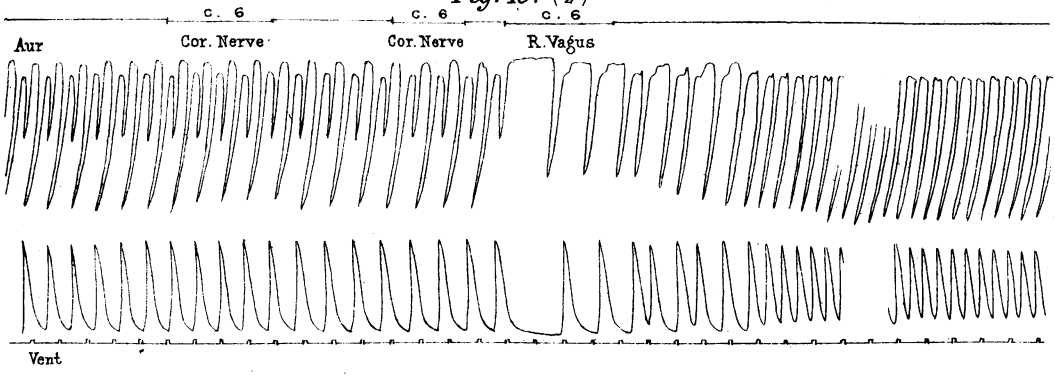


Fig. 17, I. ($\frac{1}{2}$)

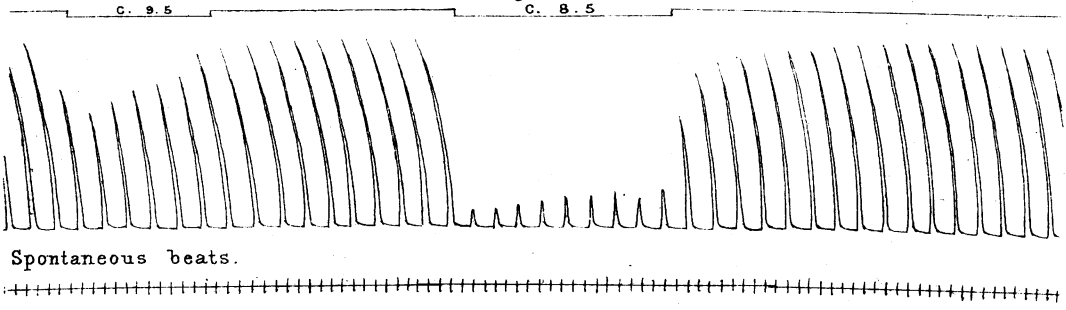


Fig. 17, II. ($\frac{1}{2}$)

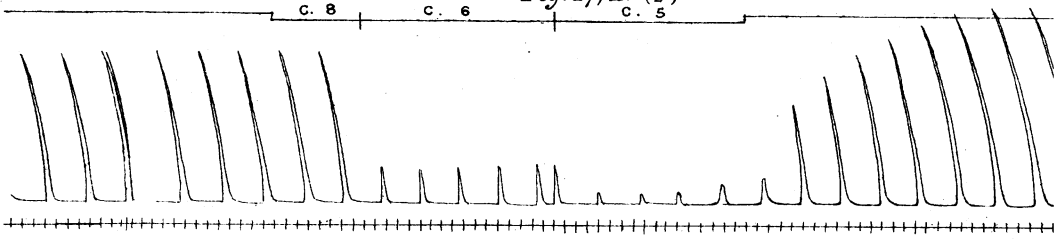


Fig. 17, III. ($\frac{1}{2}$)

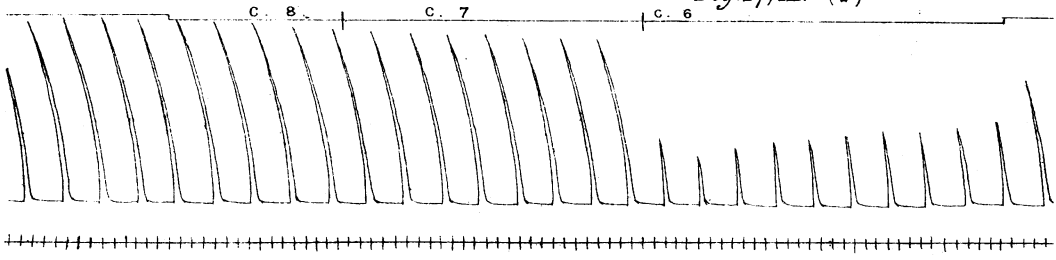


Fig. 16.

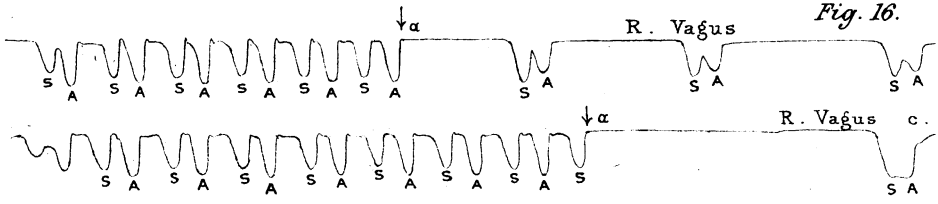


Fig. 15.

C. 10

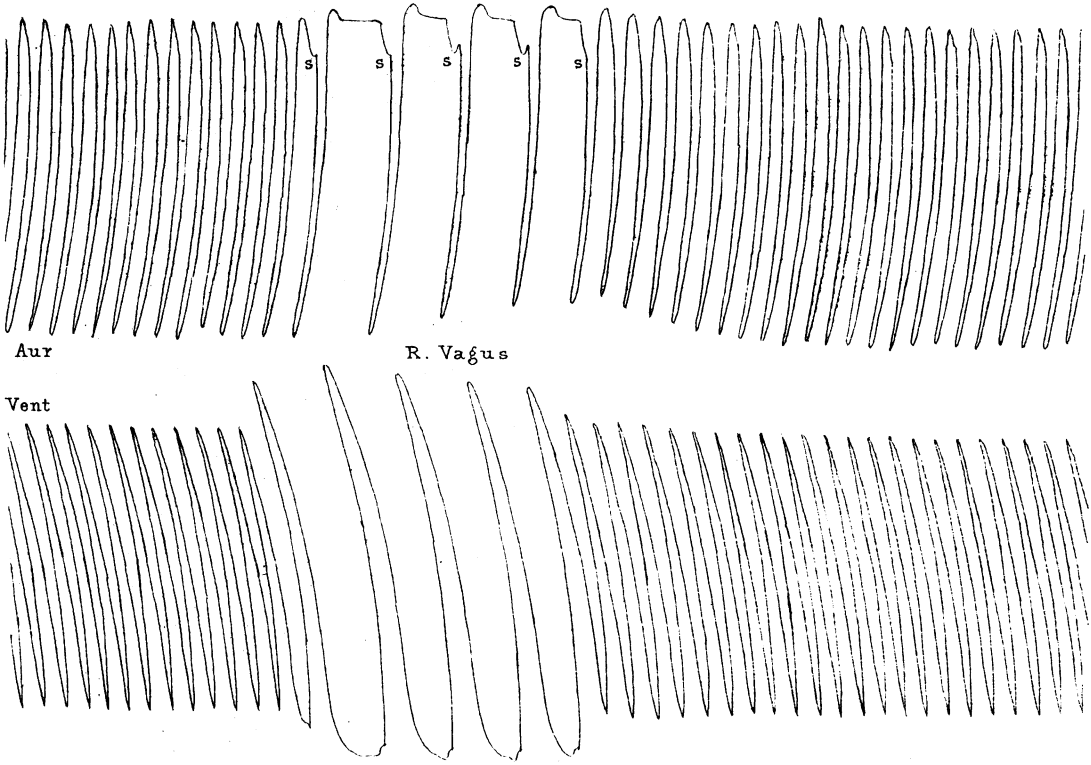


Fig. 18, II. $(\frac{1}{2})$

C. 6

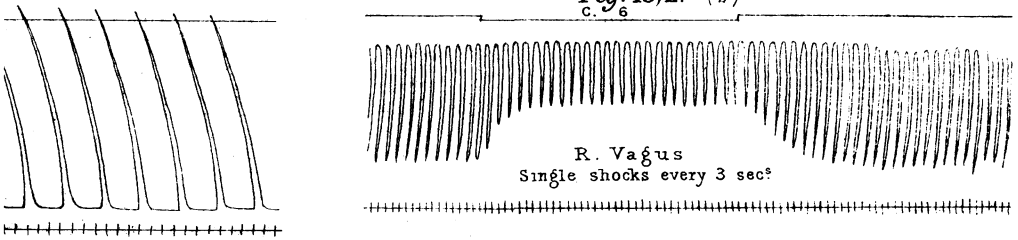
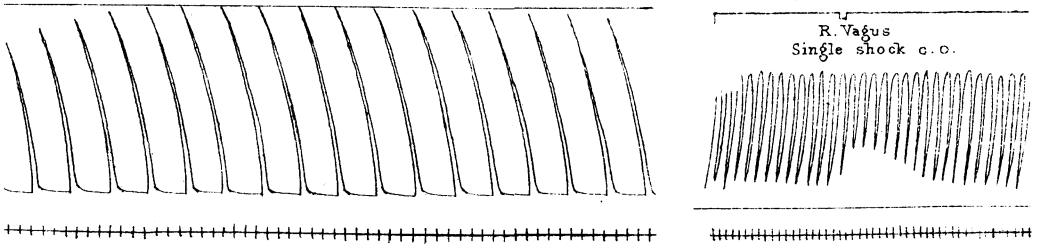
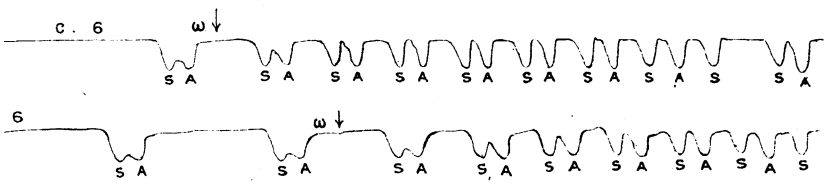


Fig. 18, I. $(\frac{1}{2})$





T. Huth Lith. Edin.