THE EFFECTS OF THE CONSTANT CURRENT ON THE HEART.

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THE Frog and Toad were chiefly employed in the following observations. Several experiments however were made with the hearts of Tortoises and Dog Fish. For a supply of the latter the authors are deeply indebted to the kindness of Mr Henry Lee, of the Brighton Aquarium, and to the liberality of the Directors of that Institution.

The current was always applied by means of non-polarisable electrodes. Tracings of the heart's beat were generally taken by means of a very light simple lever, or levers, placed directly on the ventricle, or on the auricle and ventricle. Occasionally the endocardial method was employed, but all the main results were obtained by means of the lever. Undoubtedly the contact of even the lightest lever must be regarded as a stimulus; but this stimulus is at its maximum at the moment of application, and very rapidly sinks to zero. Practically there is no difficulty whatever in eliminating the effects of the lever from those of the currents.

The results of the observations may be naturally arranged according to the part of the heart subjected to the current, and according to the condition of the heart previous to the application of the current.

1. *The lower two-thirds of the ventricle.*

This portion was chosen as an especial object of study, because at the time our observations were begun it was generally admitted that a ventricle deprived of its basal third, on the one hand contained no ganglionic apparatus, and on the other never exhibited any spontaneous rhythmic beat. Since our observations were made we have read the interesting observations of Merunowicz[1], who has succeeded in obtaining good spontaneous rhythmic pulsations from this moiety of the ventricle. We cannot but regard his results as corroborative of some at least of our own conclusions.

The results which we obtained on subjecting such a portion of the ventricle to a constant current directed longitudinally, that is from base to apex or from apex to base, differed according to the strength of the current employed.

With very weak currents, sometimes no effect at all is produced; sometimes there is seen a beat at the making of the current, or at the breaking, or at both making and breaking, the tissue during the passage of the current remaining perfectly quiescent. The beat thus brought about is in all its features a normal beat.

In very many cases the making beat was distinctly seen to proceed from the kathode and to travel towards the anode, and the breaking beat to proceed from the anode and to travel towards the kathode. This was most clearly seen when the ventricle was bisected longitudinally almost up to the apex, where a bridge of tissue was left, and the limbs of the V-shaped mass extended into almost a straight line and pinned out in that position. Under favourable circumstances the beat was seen to move as a wave from one pole to the other, from the kathode to the anode or from the anode to the kathode, as the case might be. But the experiment did not always succeed, and occasionally, when probably the bridge left was too small, the two portions acted as two independent masses. We may remark in passing that this experiment quite corroborates Engelmann's[2] views on the *physiological* continuity of the whole ventricular tissue, views which we have fully adopted in our paper on the Snail's Heart[3], where we perhaps ought to have called attention to Engelmann's previous remarks on physiological continuity[4] more specially than we did.

Thus far the cardiac tissue seems to differ in no way from ordinary muscular tissue, and the above results, which remain

[1] *Berichte k. Sächs. Gessellschft. d. Wissenschft.* 1875, p. 254.
[2] Pflüger's *Archiv*, XI. p. 465.
[3] *Proc. Roy. Soc.* XXIII. p. 318.
[4] Pflüger's *Archiv*, II. p. 243.

the same after the heart has been treated with urari or with atropin, are merely illustrations of Pflüger's law.

When however stronger currents are employed, distinct rhythmic pulsations are set up on the making of the current, continue during the passage of the current, and cease with its cessation. The beats thus produced are in all their characters like to normal spontaneous beats; indeed are indistinguishable from them. We were able to obtain these beats from any piece of the ventricle, however small.

The frequency and force of the beats depend on the strength of the current in relation to the irritability of the heart. Thus if a current which is just strong enough to produce simply a making and a breaking beat, be slightly increased, the result is that the making beat is followed at a considerable interval by a second beat while the current is going on, and this perhaps by a third or fourth; and the breaking beat fails to make its appearance. As the current is still further increased in strength, the beats become more frequent and at the same time more forcible, until a point is reached at which the maximum of pulsation is obtained, *i.e.* at which the beats are at the same time strongest and most rapid. Beyond this the increase of frequency still goes on, but at the expense of the force of the individual beats. The beats then tend to overlap and so to convert the rhythmic pulsation into an ordinary tetanus; but for this a very strong current is required; and indeed we were never able to bring about a complete tetanus, such as could be fairly compared with the tetanus of an ordinary striated muscle.

Of the rhythmic pulsation thus brought about many varieties presented themselves, varieties which we can only refer, without completely explaining them, to the varying irritability of the heart.

The most common type is that which, following the phraseology of the Leipzig school, we may speak of as consisting of an ascending and descending staircase. In this the making of the current is followed immediately or after a short interval by a feeble beat, this by a stronger one, and so on in an ascending series until a maximum is reached, which after being maintained for a variable time gives place to a descending series in which the beats diminish in force and lose in frequency. With currents of short duration the descending limb, as might be expected, is frequently absent.

Very frequently the ascending limb is absent, the pulsations starting at a maximum, and declining either immediately or after a variable period; but, sometimes, even with currents lasting the greater part of a minute, no decline at all is seen, the heart continuing to beat uniformly and regularly during the whole time of the passage of the current.

In nearly all cases, and certainly in all cases where the pulsations are maintained to the end of the passage of the current, the distinct breaking beat is conspicuous by its absence. We have however occasionally but very rarely seen the pulsations survive the application of the current, two or three beats making their appearance after the current had been broken.

This power of the constant current thus to provoke a regular rhythmic pulsation in the part of the ventricle normally devoid of any spontaneous beat was observed long ago by Eckhard[1]; and indeed was the subject of a controversy between that physiologist and Heidenhain[2]. The general impression produced by that controversy seems to have been that the rhythmic pulsations caused by the constant current simply formed a particular case of the tetanus observed by Pflüger[3] as the result of the application of the constant current to an ordinary muscle-nerve.

Without denying that the two sets of phenomena may have a common origin in so far as they may be both due (as Pflüger suggests with regard to one) to electrolytic action, we must confess that in their general features the two are most markedly different. The tetanus set up by the application of the constant current to a nerve is a rapid tetanus; by no adjustment of the strength of the current can the rhythm of the contractions be graduated. With certain strengths of current, the tetanus is absent; and as the strength is increased, a tetanus of rapid rhythm suddenly

[1] *Beiträge zur Anat. u. Phys.* Bd. I. 147, also Bd. II. 123.
[2] Müller's *Archiv*, 1858, p. 479.
[3] Virchow's *Archiv*, XIII.

makes its appearance when a certain point is reached. Very striking is the contrast offered by the cardiac muscle under the same constant current. Under favourable circumstances, and by applying the current with great care, a whole series may be obtained ranging, according to the strength of current employed, from the initial simple make- and break-beat, through a rhythm of two or three beats a minute, to one of a beat every two or three seconds, and finally to one every second, or even to a still more rapid rhythm. Nothing like this is ever witnessed in any ordinary muscle. The beats moreover have all the features of normal beats. An observer, however experienced in cardiac experiments, would, on seeing the pulsations, suppose the heart to be beating naturally and spontaneously, if he did not know that the current was being applied. Indeed, the simplest and perhaps the truest mode of stating the facts is to say that the constant current provokes the heart to spontaneous beats.

Nor are these rhythmic contractions witnessed with the constant current alone. As one of us pointed out some time ago[1], when a quiescent lower moiety of the frog's ventricle is submitted to the action of an ordinary interrupted current for some little time, the irregular tetanic contractions which generally speaking first make their appearance, give place to a rhythmic beat, the features of which are in every way normal. On the supposition that the lower two-thirds of the frog's ventricle do not contain any ganglionic structures, these facts seem to point most distinctly to the conclusion that the less differentiated cardiac muscular tissue still retains a power of rhythmic pulsation, which power has been almost entirely lost by those muscles which are more completely under the dominion of the will. We say almost entirely, because in the first place theoretical considerations would lead us to suppose that if the property of rhythmic movement were a fundamental attribute of primitive protoplasm, traces of this property would be visible even in the most differentiated forms, and in the second place, such traces may indubitably be found[2]. But to say that the cardiac

[1] Foster. This *Journal*, Vol. III. p. 400.

[2] See the interesting paper of Mr Romanes which precedes the present

muscular tissue still retains the power of rhythmic pulsation, is very nearly the same thing as saying that the rhythmic pulsation of the heart is a fundamental property of its general muscular tissue and not of any special localized mechanism. Thus although the lower moiety of the ventricle does not under ordinary circumstances exhibit a spontaneous pulsation, its behaviour under the constant current warrants the conclusion that the power of rhythmic pulsation though latent is not absent, and only needs favourable circumstances for its complete manifestation. Those favourable circumstances are provided for by Merunowicz's (*loc. cit.*) mode of experimentation, and he accordingly finds that the lower moiety of the frog's heart beats with a regularity and spontaneity as distinct if not as ready as that of the entire ventricle. In fact, the distinction between the entire ventricle and the moiety is one of degree, not of kind. The entire ventricle will beat under many circumstances; in fact nearly, though not quite, as readily as the ventricle with the auricles attached. The moiety will only beat under certain favourable circumstances, *e. g.* when its fibres are extended by the distension of its cavity, and at the same time supplied with nutrient or invigorating material, or when it is subjected to a constant current of a certain intensity.

Now it may without any risk be affirmed that distinct ganglionic cells, like those which are found in the atrioventricular boundary and elsewhere, are absent from the lower two-thirds of the ventricle. Structures of that size could not be missed by the many acute observers who have searched for them. We may therefore without any fear say that the spontaneous beat of the heart cannot be due to the action of *such ganglionic cells as these.*

Future observers may discover in the lower moiety of the ventricle nervous structures of another order; and in that case it may become necessary to transfer to those structures the attributes which are now monopolized by ordinary gan-

article, and which bears very closely both on this and on many other points. We may perhaps be permitted to point out that, while the rhythmic pulsations observed by Mr Romanes were done away with by urari poisoning, we have not seen any fundamental changes introduced into our results by the exhibition of even large doses of that drug.

glionic cells. For ourselves, we must confess that it seems more in accordance with the tendency of physiological inquiry to suppose that the cardiac muscle-cells (they might be called neuro-muscular cells if there be any advantage in the name) have not yet lost that property of rhythmic movement which is seen to be exercised with varying but progressive regularity in all protoplasm, from that of a bacterium or a vegetable cell upwards.

The fundamental functional homogeneity and at the same time accidental heterogeneity of the cardiac tissue is shewn in the following observations.

When a large piece of the ventricle was employed, for instance the whole of the lower two-thirds, the rhythmic pulsation was always markedly much more easily obtained when the kathode was placed at the base than when the kathode was placed at the tip.

When the piece was small, *e.g.* when the mere tip of the ventricle was employed, rhythmic pulsations were more readily obtained when the kathode was placed at the tip and the anode at the cut surface, than when the current was sent in the contrary direction.

In a piece cut out from any part of the lower two-thirds, rhythmic pulsations were always more readily produced when the current was thrown in one direction than in another; that is, when one part rather than another was made kathodic. By carrying incisions in various directions we could almost at will convert any spot into a point, the kathodization of which appeared more favourable to pulsation than that of other points.

It seems impossible to attribute these results to any arrangement of localized mechanisms, save such a distribution of them as would be coextensive with the muscular tissue itself. Without being able fully to explain the facts, we are inclined to interpret them as being connected with the shape of the ventricle and the consequent unequal distribution of the anodic and kathodic areas.

It is exceedingly probable that the beats are kathodic in character, *i.e.* that they proceed from the kathodic region, and are connected with the katelectrotonic phase. We have not however been able to prove this satisfactorily. In many cases, as for instance when the piece of ventricle was divided longitudinally and the parts pinned out, the beats could be distinctly seen to proceed from the kathode. In many other cases, on the contrary, the beats seemed to start in the kathodic and anodic region at the same time. In the snail's heart (*loc. cit.* p. 326) the beats which the constant current evoked in an otherwise quiescent ventricle could very clearly be seen to proceed from the kathode and to travel towards the anode; but when the complicated arrangement of the fibres in the twisted tube which forms the frog's ventricle is compared with that of the fibres in the straight tube of the snail's heart, it is easy to understand why the regular progression from the kathode to the anode, which is so obvious in the latter, should be obscured in the former. On the other hand, the beats which are seen during the passage of the current have all the appearances of being repetitions of the initial beat. But this is a kathodic beat, and we may therefore infer that the following beats are kathodic also. If this be so, then we may go a step further, and conclude that the facility with which beats can be evoked by the constant current, will depend on the ease with which the katelectrotonic phase can be made dominant in the tissue under the influence of the current.

Now, in dealing with the effects of the constant current on nerve-fibres and ordinary striated muscular fibres, we have to do with cylinders of uniform diameter (neglecting, as we may do, the extreme ends of the muscular fibres) throughout, and the relative expanse of the katelectrotonic and anelectrotonic areas will depend entirely on the position of the neutral line, and that again on the strength of the current in relation to the irritability of the tissue. As far as we know, the case has never been considered where the tissue forms a physiologically continuous cone, one electrode being applied to the base and the other to the apex. There is no proof that the anelectrotonic and katelectrotonic phases (*and by these terms we mean the physiological and not the merely electrical conditions of the tissue*) are so related to each other that the movement, whatever it may be, in one direction is accompanied by an equivalent movement in the other direction, the sum of the two remaining null; we are not debarred, by anything that we know, from the supposition that when the kathode is applied broadly to the base of such a cone, the larger portion of the tissue is thrown into the katelectrotonic state, and when the anode is placed at the base, the smaller portion. In the behaviour of the snail's heart, which forms such a cone of physiologically continuous tissue, we thought we found positive indications of an influence of the form of the tissue in this direction; and since Engelmann has shewn that the ventricle of the frog's heart is similarly physiologically continuous, we have some ground for applying a similar hypothesis to that organ also. If we are allowed to do so, then we should say that the lower two-thirds of the ventricle, in spite of the injury caused by the section, still form a cone, so that when the current is applied with the anode at the tip, the larger portion of the tissue is thrown into katelectrotonus, and beats in consequence are more easily evoked than when the kathode is placed at the tip. When, on the contrary, a small piece only of the ventricle is being operated on, the injury at the lines of section, and the directions of the incisions, determine the position in which the electrodes should be placed in order that the katelectrotonic phase should be dominant, and in consequence beats more easily evoked. We throw out this view with great diffidence as a mere suggestion, put forward in the hope that it may provoke inquiry into what, on any hypothesis, seems a singular fact, that the beats should be produced more easily by applying the current in one direction than in another, and that the direction depends on the form of the piece of ventricle or at least on the directions of the incisions made.

We naturally turned our attention to the point whether the neutral boundary could be shifted, and the relative areas of katelectrotonus and anelectrotonus in consequence varied by varying the strength of the current.

According to the views just expressed it might be supposed that, since the neutral boundary in ordinary nerve electrotonus moves from the anode towards the kathode as the strength of the current is increased, the ease with which beats could be produced would diminish with the increase in the strength of the current. As a matter of fact the beats are more easily produced with the stronger currents; and this fact seems at first sight distinctly to disprove the hypothesis we have put forward. But, in the first place, it must be remembered that the rhythmically pulsating cardiac tissue differs from a nerve-fibre in this, that with the initial beat, and with each subsequent beat, the condition of the tissue is profoundly altered as the very result of the beat. In the second place, we have in the heart's beat to do with two distinct things; the force and extent of the individual beats, and the rapidity with which the beats are repeated. Between these two things there is a relation, and that relation is in large measure an inverse one. (In the ordinary explanations given of rhythmic action, the two are treated of as being absolutely in an inverse relation. When a gas is bubbling through a fluid the large bubbles come slowly: when they follow rapidly they become small. The problems of the heart would be very simple if this inverse relation were an absolute one for it also; it is not so, for we may have within limits rapid strong beats, and infrequent feeble ones; but nevertheless the inverse relationship does exist though obscured by other influences.)

Now, in operating on the ventricle with a constant current, it is seen that an increase in the strength of the current bears much more upon the rapidity of the rhythm than on the force of the individual beats. We have frequently observed that the beats, few in number, called forth by a weak current are individually as strong as those, many in number, which are produced by a stronger current applied for the same time. Nay more, when a certain limit has been passed the beats lose in force while they gain in rapidity, by increase of the current. In the last matter we have to do probably with the effect of one beat upon another in the shape of exhaustion; and indeed the whole of this part of the subject must remain obscure until we know the limits and conditions of the beneficial and of the injurious effects of any given beat on its successor; for these beneficial effects do exist, as shewn by the labours of Bowditch, and the injurious effects are readily shewn in any overtaxed heart.

If we might make a suggestion it would be in the direction that while the force of the beat is most (but not exclusively) dependent on the area of the katelectrotonus, the rapidity of the rhythm is more immediately connected with the intensity of the electrotonic phases. This would at least enable us to understand why, in spite of the diminished katelectrotonic area, the beats increased in rapidity with an increase in the current[1].

The absence of the break-beat when the current has during its passage evoked a series of pulsations, seems to us a point of interest as contrasted with its very regular presence when the current has simply caused a make-beat, and not given rise to any series. When the beats are maintained during the whole time of the passage of the current, the break-beat is almost invariably absent. It is only when the beats have ceased before the shutting off the current, so that a pause of some length is seen between the last beat and the actual breaking of the current, that the break-beat follows upon a series.

Now the break-beat in many cases was most distinctly seen to be, and in all cases probably is, an anodic beat; it proceeds from the anode, and is due to the disappearance of anelectrotonus. May we infer from this that the effect of a beat is to neutralize the (physiological) electrotonic condition, so that after each explosion neither the kathodic region is so katelectrotonic, nor the anodic so anelectrotonic, as immediately before the beat? that during the interval between that and the succeeding beat the heart is occupied in getting up, so to speak, the katelectrotonic and anelectrotonic phases? This would at least enable us to understand why the larger kathodic area is more favourable for the development of beats.

[1] It is impossible to avoid the conviction that the processes concerned in the production of a pulsation spontaneous or otherwise, are capable of being analysed, like the phenomena which belong to an ordinary muscular contraction, into those pertaining to the stimulus wave and those pertaining to the contraction wave. If this be granted, it is more than probable that the two sets of processes would be differently affected by the constant current; and that this difference might explain the results recorded in the text. Our efforts however to lay hold of this difference have been hitherto wholly in vain.

2. *The whole ventricle, when quiescent.*

As is well known, the entire ventricle, from which the auricles have been carefully removed, though still retaining the ganglia situated at the base of the ventricle, frequently remains perfectly quiescent, without offering any spontaneous beats at all.

Such a ventricle when submitted to the action of the constant current behaves exactly as does a ventricle from which the base has been removed. According to the strength of the current in relation to the irritability of the tissue, the effect of the current may be a simple make- and break-beat, a series of infrequent pulsations, or a series of rapid pulsations. The beats are more easily evoked when the kathode is placed at the base than when it is placed at the tip. In fact, we met with no one feature (except a greater irritability, that is, a greater readiness to respond to comparatively weak currents, and a greater endurance, that is, a capability of being submitted to the action of currents for a longer time without losing its activity) which we could point to as distinguishing the ventricle possessing the atrioventricular ganglia from one devoid of those structures. This fact shews very clearly, on the one hand, how entirely subordinate is the influence of the ganglia in question, as far as the intrinsic activities of the ventricle itself are concerned; and, in the second place, how little permanent damage is done to the ventricle, as a whole, by the rough section needed to remove the ganglia.

3. *The whole ventricle beating spontaneously.*

As is well known also, the frog's ventricle will, in the complete absence of auricles and sinus venosus, frequently go on beating spontaneously for a very considerable time.

When such a spontaneously beating ventricle is submitted to the action of the constant current, the effects are by no means so constant as in the two cases we have already discussed.

With weak currents, that is, with one or two Daniell's cells applied through small non-polarisable electrodes of considerable resistance, no effect whatever was visible. Both in respect to the rapidity of the rhythm and the force and duration of the individual beats, the heart behaved at the making, at the breaking, and during the passage of the current, in a perfectly normal manner.

By stronger currents, such as those supplied by three to six Grove's, the heart was visibly affected, both at the make and break, and during the passage of the current.

The make and break effects were fairly constant, with the exception that they varied according to the phase of the cardiac cycle which was being passed through at the moment when the current was made or broken. Thus, if the current were made during a certain part of the systole of any beat, that beat was followed by one which was at once premature and slight. This in turn was succeeded by an abnormally prolonged diastole ushering in a beat larger than the normal; after which, at least in the cases where the current was of such a strength as only to produce make and break effects, and not to affect the heart to any marked extent during the passage of the current, the pulsations were normal until the break occurred, which if it took place at the same phase of the systole, produced a similar effect to the make. Hence, both at make and break, a normal beat was followed, first by a short diastole and a feeble beat, and then by a long diastole and a strong beat; and in many cases, the long and short diastoles made up together the length of two normal diastoles, and the movements of the lever during the feeble and strong beats were together about equal to the movements of the lever during two normal beats. We do not, however, pretend to say that this compensation was always exact and complete; and it was certainly less exact as regards the force of the beats than as regards the length of the intervals.

When the current was made or broken at certain other phases of the cardiac cycle, the effects we have just described were replaced by others. Thus, sometimes the initial beat was enlarged; sometimes no obvious effect at all was produced. We did not make a sufficient number of observations to work the point out thoroughly, but hope to be able to do so at some future time, since the facts seem not without interest as promising to throw light on the varying conditions of the heart as it passes through its several phases, and to afford a means of more accurately measuring than has hitherto been done the duration of the latent period of a natural systole[1].

Far less constant than the above effects were those which made their appearance during the passage of the current.

The most frequently recurring effect was, that during the passage of the current the beats were most distinctly lessened, and with the stronger currents almost completely annihilated, without *any marked change of the rhythm.* This we have seen again and again, both when the kathode was placed at the base and when it was placed at the apex.

We sought, by placing two light levers, one near the base and the other near the apex, to gain some insight into the relative movements of different parts of the ventricle; but we found that the varying pressures of the two levers, and a variety of other circumstances, introduced so many sources of error, that we were unable to arrive at any satisfactory conclusion.

We thought that in many cases, especially where moderate currents were used, we had fairly distinct evidence that when the kathode was at the base there was an increase of movement at the base and a diminution of movement at the apex during the beats, and that, on the contrary, when the kathode was at the apex there was an increase of movement at the apex and a diminution at the base; there being in both cases a diminution in the movements of a lever placed midway between base and apex. But our results were not sufficiently constant to enable us to lay stress on this, which would point to a tolerably satisfactory explanation of the total lessening effect of the current in whatever way applied. We may add, that the same lessening was seen when the current was applied transversely or obliquely instead of longitudinally.

We also thought we noticed that there was a tendency to a quickening of the rhythm, though never very pronounced, when the base was kathodic, and inversely a tendency to retardation when the apex was kathodic; but on this point again we

[1] Since the above observations were made M. Marey (*Comptes Rendus*, 1876) has published a note in which he describes briefly very similar phenomena, and promises to deal with them in fuller detail than we have been able to do.

cannot, in face of the inconstancy of our results, assert anything distinct or certain.

Nevertheless there remains the striking fact that, taking the ventricle as a whole, its spontaneous pulsations are diminished by the passage of a constant current of sufficient intensity. So that between a quiescent ventricle and one which is beating spontaneously, there is this marked contrast in their behaviour under the constant current, that whereas the current evokes pulsations in the quiescent ventricle, it stops, or goes far to stop, the pulsations of the pulsating one. Thus the same current acting on the same ventricle, with the electrodes exactly in the same position, may at one moment all but stop pulsations, and a short time afterwards, when the ventricle has ceased to beat spontaneously, call forth pulsations which are in every way like to the pulsations it just before had stopped.

Both these effects were seen not only in a natural ventricle, but in one which previous to excision had been treated with urari or with atropin to a sufficient extent to do away with the inhibitory action of the vagus. And since the exciting effect on the quiescent ventricle has been shewn to be independent of the action of ordinary ganglia, we may fairly infer that the restraining influence on the pulsating ventricle has likewise but little to do with ganglia, the effects of both kinds being due to the direct action of the current on the cardiac tissue.

4. *The ventricle and auricles, removed from the body and beating spontaneously, with the cavities empty.*

The heart after excision was placed on a block of paraffin scooped out slightly so that the heart remained in one position. The electrodes were placed one at the apex of the ventricle and the other at the sinus venosus or at the upper border of the auricles by the side of the bulbus. Sometimes the heart was placed with the anterior surface uppermost, sometimes undermost. No essential difference was observed in its behaviour in the two different positions.

As far as the ventricle was concerned (and we paid no particular attention to the auricle, the movements of which it is extremely difficult to record satisfactorily) the effect of the current was exactly the same as when the spontaneously pulsating ventricle was alone operated on. There were the same break and make effects, and the same diminution of the beats during the passage of tolerably strong currents. The effects were essentially the same when urari or when atropin was given, as without those drugs; in fact we failed to distinguish any effects which could be attributed to the inhibitory mechanisms. It seemed as if the influence which the current exercised over the general cardiac tissue overcame altogether any effect which might be produced on the purely nervous structures, and hence ventricle and auricle acted as two organs physiologically isolated, the auricle serving only as a simple conductor of the current to the ventricle, modifying it only by offering resistance to its passage, but otherwise having no effect; and *vice versa*. In this point the frog's heart corresponded entirely with the snail's heart, in which we had[1] previously noticed the same physiological independence.

5. *The ventricle and auricles removed from the body and beating spontaneously, but with the cavities distended with serum.*

We commenced some observations with the current applied to the heart, fitted up for registering the endocardial pressure according to the method of Coates or of Bowditch. The heart was supplied with rabbit's serum or with rabbit's blood diluted with a ·75 per cent. solution of sodium chloride, and the electrodes were applied as usual. We found, however, that the application of the current produced at once such a profound and lasting change in the rhythm, the beats falling into Luciani groups immediately after the passage of even a comparatively weak current, and the groups developing themselves with such vigour, that all further observations were rendered impossible. We have rarely seen an intermittent rhythm so markedly shewn as it was under these circumstances.

[1] *l. c.* p. 325.

6. *The whole heart remaining in the body and the circulation maintained intact.*

The animal was sometimes pithed, but more frequently placed under urari. The heart was sometimes left in its natural position, but sometimes a ligature was thrown round the connective-tissue band which passes from the posterior surface of the ventricle to the adjacent pericardial wall, and the heart turned over, so that the apex pointed to the head, and fixed in that position by the ligature. Notwithstanding this unusual position the circulation went on very well; the advantage of the manœuvre lay in the fact that the levers could be more satisfactorily placed on the ventricle, and the electrodes applied to any part of the sinus venosus. One electrode was placed against the apex, and the other either at the upper border of the auricles or at the sinus venosus, or, in order to eliminate the auricle, at the auriculo-ventricular groove.

The main result which we obtained by applying the current under these circumstances was one which seemed to us very striking. Though we employed tolerably strong currents, *ex. gr.* six Grove cells, and as many as twenty-five Leclanché cells, we could produce no other distinct effects than a making and breaking one.

At the make and break we witnessed very frequently, as in 3 and 4, a premature feeble beat followed by a long pause and a strong beat, when the current was thrown or shut off at the appropriate time; but during the passage of the current itself the pulsations of the heart were in no obvious manner different from the normal.

There was perhaps a general tendency for the beats to be increased in force when the kathode was placed at the auricles or at the base of the ventricle, and a similar tendency for the beats to be diminished when the kathode was at the apex of the ventricle; but this was by no means present with sufficient distinctness and certainty to enable us to say that it was a definite effect of the current.

We applied the current again and again, and for several seconds at a time, without producing any other effects. It was only after the lapse of several hours, during which the current had been repeatedly applied, that an intermittence in the beat giving rise to irregular groups made its appearance during and for some time after the application of the current.

When one considers how profound are the effects which a constant current of much less strength than that supplied by six Grove cells produces when applied directly to a nerve, it certainly does seem surprising that the heart should be so little influenced by the constant current. The behaviour towards the constant current of the heart supplied under normal conditions with its proper nutritive fluid, when compared with the behaviour of the same heart, either deprived altogether of blood, or fed with serum only, indicates that the apparent indifference of the former is the result of recuperative influences exercised by the blood-supply, and absent in the case of the latter. Some share in the difference between the two might be referred to the isolation of the excised heart placed on the paraffin block, nearly the whole of the current under these circumstances passing into the heart, whereas when the current is applied to the heart in the body, some of it may escape into the surrounding tissues; but this share can only be a very slight one. The real cause of the difference lies in the fact, that the heart which enjoys a rich and continuous blood-supply can accommodate itself rapidly to the new circumstances in which it is placed by the passage of the current, while the nutrition of the heart without a blood-supply is too slow and too feeble to enable it to do so. That the current did produce an effect during the whole time of its passage, (though its action was at a maximum soon after the make), was shewn by the effect at breaking. During the whole of this time katelectrotonic and anelectrotonic phases were established in the ventricle, otherwise the occurrence of the breaking phenomena would be unintelligible. Yet in spite of this the heart continued to beat during the passage of the current at a rate and with a vigour which careful measurements shewed to differ but very slightly indeed, if at all, from the rate and the vigour which obtained previous to the application of the current. Even in the cases where a distinct break effect was absent (and the absence or character, when present, of the break effect seemed to depend chiefly on the exact phase of the cardiac cycle in which the heart was engaged at the moment when the current was broken), it would be unreasonable to suppose that the current was without effect or had ceased to have any effect; for it can hardly be imagined that the well-nourished and therefore more susceptible heart would be less affected by the current than the ill-nourished and therefore less susceptible heart. It is surely far more in consonance with all the facts to believe that, as we suggested above, the conditions which we know as katelectrotonus and anelectrotonus are developed in connection with spontaneous pulsations, so that, whenever a constant current is applied a struggle takes place between so to speak the natural and the artificial electrotonic conditions, resulting in a defeat of the heart when the heart is weak and the current strong, and in an apparent neglect of the current when the heart is sufficiently active. In this sense we could not speak of any permanent electrotonic condition lasting during the whole time of the passage of the current; since the intensity of the katelectrotonic and anelectrotonic changes would vary during the phases of each cardiac cycle, and thus develope or not a breaking effect, according to the moment at which the current was broken.

An idea presented itself, but only to be rejected, that the pulsations which occurred during the passage of the current were not real spontaneous beats, but artificial beats simulating true ones produced by a current which was strong enough at the same time to place *hors de combat* the ordinary automatic nervous mechanisms. This idea was negatived not only by the fact that the rhythm did not vary with the strength of the current, but also, and more distinctly so, by the fact that, as we subsequently found, the nervous (inhibitory) mechanisms were able to produce, when stimulated, their usual effects in spite of the presence of a strong current.

7. *The ventricles and the auricles brought to a standstill by Stannius' experiment (section of the boundary between auricles and sinus venosus).*

When the heart of the frog is brought to a standstill by this operation, any stimulus applied to the ventricle gives rise to a beat in which the ventricular systole occurs before the auricular. A series of beats in which this reverse rhythm is manifested, the auricle in each case contracting regularly after instead of before the ventricle, may follow upon the application of a single stimulus. This remarkable feature of the Stannius' standstill was observed by that acute observer Von Bezold[1] (whose early death physiology has so often to deplore), but apparently has not distinctly attracted the notice of subsequent investigators.

Bernstein[2] states that when a constant current is applied lengthways to the heart in this condition rhythmic pulsations (beginning with the making and ending with the breaking of the current) are produced in the direction of the current; *ex. gr.* that the ventricle beats before the auricle when the anode is placed at the apex of the ventricle and the kathode at the auricles, while the auricles beat first when the kathode is placed at the apex and the anode at the auricles.

Bernstein worked with somewhat strong currents, and did not sufficiently vary the strength in different experiments. We find that the result is in close dependence on the strength of the current; and in a series of experiments in which the strength of the current was progressively increased we obtained the following effects.

The animal was generally poisoned with urari in order to eliminate the effects of stimulation of the vagus due to the section from the direct effects of the Stannius' operation; the section was made through the junction of the sinus venosus and auricles; the heart was laid on a paraffin block, and when by its perfect quiescence the operation was seen to have been successful, the current was applied by means of non-polarisable electrodes.

With the weakest currents no effect at all was produced. With somewhat stronger currents rhythmic pulsations were set up on making the current, continued for a shorter or longer time during the passage of the current, and as a rule ceased on the breaking of the current. Both when the base was kathodic and when the apex was kathodic, the beat of

[1] *Physiol. d. Herzbewegung.* Virchow's *Archiv*, XIV.
[2] *Nerv und Muskel*, Abschnitt. v. s. 205.

the auricle succeeded instead of preceding the beat of the ventricle.

When still stronger currents were applied the difference between the case where the apex was kathodic and the case where it was anodic became evident. When the apex was anodic, rhythmic pulsations proceeding continuously from the ventricle to the auricle were set up, the rhythm being more rapid than with the weaker currents. The beats continued during the whole time of the passage of the current. When the apex was kathodic the beats were at first in the order ventricle-auricle; then came a pause of variable duration, after which rhythmic pulsations reappeared, but with *the auricles beating before the ventricle.*

With still stronger currents the events when the apex was anodic remained as before. When however the apex was kathodic the reversal of the order of rhythm took place very early, so that after one or two beats the order ventricle-auricle was replaced by the order auricle-ventricle.

The following details of a series of experiments will perhaps put the facts in a clearer light.

Rana esculenta; urari given. Stannius' experiment successful; heart perfectly quiescent.

Exp. 1. Current supplied by 1, 3 and 5 Leclanché cells respectively. No effect at all produced by the current applied in either direction for 30 seconds. Heart remains perfectly quiescent during and after the application of the current.

Exp. 2. Current supplied by 7 Leclanché cells. Current applied for 30 secs. V means beat of ventricle only. A, beat of auricles only. VA, beat in which the ventricle precedes the auricle. AV, beat in which the auricle precedes the ventricle. The first column gives in each case the time of each beat measured from the making of the current.

Apex kathodic.

After ·5 sec. V.
,, 1 ,, A.
,, 4 ,, VA.
,, 7 ,, VA.
,, 30 ,, current broken.
(No breaking beat.)

Apex anodic.

After 12 secs. VA. Beat of ventricle: very large.
,, 27 ,, VA. ,,
,, 30 ,, current broken.
(No breaking beat.)

Exp. 3. Current supplied by 7 Leclanché cells; No. 2 repeated.

Apex kathodic.

After ·5 sec. V.
„ 1 „ A.
„ 13 „ VA.
„ 25 „ VA.
„ 30 „ break.
(No breaking beat.)

Apex anodic.

After 1·5 sec. VA.
„ 10 „ VA.
„ 24 „ VA.
„ 30 „ break.
(No breaking beat.)

After the experiment with apex kathodic had been made, the heart was lightly touched, once only, with a camel's-hair brush soaked in a ·75 solution of sodium chloride. This was done for the purpose of moistening the surface of the heart. A beat in which the ventricle preceded the auricle immediately took place. This was followed by beats, in which the ventricle similarly preceded the auricle, at intervals of 10, 20, 40, 80, 120 seconds respectively after the application of the brush. The heart then became perfectly quiescent, and the other half of the experiment, *i.e.* with the apex anodic, was proceeded with.

Exp. 4. Current supplied by 10 Leclanché cells.

Apex kathodic.

After ·5 sec. VA.
„ 4 „ VA.
„ 7 „ VA.
„ 30 „ VA.

Apex anodic.

After 5 secs. V.
„ 5·5 „ A.
„ 16 „ VA.
„ 25 „ VA.
„ 30 „ VA.

In this case it was difficult to say if the last beat in each was a simple breaking beat or not. In the case where the apex was kathodic, the long interval preceding (from 7 to 30 secs.) would seem to shew that the beat was a breaking beat; but where the apex was anodic this is not so clear.

Exp. 5. Current supplied by 15 Leclanché cells.

Apex kathodic.

After ·5 sec. VA.
„ 3·5 „ VA.
„ 13 „ VA.
„ 21 „ VA.
„ 29·5 „ VA.
„ 30 „ break.
(No breaking beat.)

Apex anodic.

After 1 sec. VA.
„ 4 „ VA.
„ 9 „ VA.
„ 13 „ VA.
„ 18 „ VA.
„ 22·5 „ VA.
„ 26 „ VA.
„ 30 „ break.
(No breaking beat.)

Exp. 6. Current supplied by 20 Leclanché cells.

Apex kathodic.				Apex anodic.			
After	·3	sec.	VA.	After	1	sec.	VA.
„	3	„	VA.	„	4·5	„	VA.
„	5	„	VA.	„	8	„	VA.
„	7·5	„	VA.	„	11	„	VA.
„	10	„	VA.	„	15	„	VA.
„	13	„	VA.	„	19	„	VA.
				„	21	„	VA.
„	26	„	*AV.*	„	24·5	„	VA.
„	32	„	*AV.*	„	28	„	VA.
				„	30	„	VA.

The last beat registered with the apex anodic was not a strictly breaking beat; the contraction began before the current was actually shut off.

In the case where the apex was kathodic the current was kept on two seconds beyond the half minute, being broken immediately after the commencement of the last beat registered.

Exp. 7. Current supplied by 20 Leclanché cells.

Apex kathodic.				Apex anodic.			
After	·2	sec.	VA.	After	2	secs.	VA.
„	6	„	VA.	„	3	„	VA.
				„	6·5	„	VA.
„	10	„	AV.	„	10	„	VA.
„	14	„	AV.	„	13	„	VA.
„	16	„	AV.	„	17	„	VA.
„	19	„	AV.	„	19	„	VA.
„	22	„	AV.	„	22	„	VA.
„	25	„	AV.	„	24·5	„	VA.
„	28	„	AV.	„	28·5	„	VA.
„	30	„	AV.	„	30	„	VA.

In the case where the apex was anodic, at the beginning and at the end of the series a distinct interval was visible at each beat between the contraction of the ventricle and that of the auricles; in the middle of the series, on the other hand, the beat of the auricles came so rapidly after that of the ventricle that they appeared almost synchronous, and it became very difficult to say that the ventricle did really precede the auricles.

In this and several preceding experiments, the beat of the ventricle when it preceded that of the auricles was seen to be preceded in turn by a beat of the bulbus arteriosus.

It will be seen from the above, which is one of many experiments having exactly the same general features, that our results in large measure agree with those of Bernstein[1], though they differ to such an extent as to prevent our accepting the interpretation given by that inquirer.

That interpretation, if we understand it aright, is as follows. When the apex is made anodic,—when therefore the current may in relation to the heart be said to be ascending,—the nerves which descend from the atrio-ventricular ganglion to the ventricle, are at their origin from the ganglion thrown into katelectrotonus. This weakens the development of the molecular inhibitory processes in these nerves at their origin from the ganglion, and thus favours the development of a beat. The ventricle, thus assisted, in consequence beats before the auricle. When, on the other hand, the apex is made kathodic, and thus the current descending, the same ventricular nerves are thrown into anelectrotonus, which favours the molecular inhibitory processes. The ventricle thus hampered beats after the auricle. Further, while the nerves descending to the ventricle are thus being affected by the respective currents, the nerves ascending from the ganglion to the auricles are being affected in exactly the converse manner; so that while inhibition is being augmented in the ventricle, it is being decreased in the auricle, and *vice versâ*. Hence the dependence of the sequence of the rhythm on the direction of the current.

Now, in the first place, this view entirely overlooks the important fact that in the remarkable condition brought about by Stannius' operation the sequence of auricle upon the ventricle is the normal order of the rhythm of the beat. One instance of this has been mentioned in the foregoing experiment (3); and it will be observed that the stimulus, itself of the slightest character, was followed not by one but by a series of beats, in each of which the contraction of the auricle followed that of the ventricle. Many more instances of the same kind might be given. No great stress could be laid on a single beat with this abnormal sequence making its appearance; but the fact that a whole series having the same character should be regularly carried on, after being started only by the very slightest stimu-

[1] We failed altogether to observe the making and breaking "simultaneous contractions of all parts of the heart" of which Bernstein speaks. This is probably to be explained by the fact that our currents were in general weaker than those used by him.

lus, shews that the heart must, under the circumstances, be in a peculiar condition. No such change of the order of rhythm is witnessed in ordinary pneumogastric inhibition; and there are many reasons, to which we shall presently add a new one, for concluding that the standstill produced by Stannius' operation is fundamentally different in nature from that produced by stimulation of the pneumogastric.

Hence what needs to be explained is not so much why with the apex anodic (or current ascending) the ventricle-auricle order of rhythm is maintained, as why with the apex kathodic (or current descending) this natural order of rhythm is exchanged for that of auricle-ventricle, which in a heart during a Stannius' standstill is an abnormal rhythm.

In the second place, the reversal of the order is only obtained with comparatively strong currents, and in none of the cases we have had under our notice did it occur on the making of the current, being always preceded by one or more beats in which the order was ventricle-auricle, though we are not prepared to say that with still stronger currents than those we used the reversal might not coincide with the beginning of the application of the current. Bernstein[1] seems to have observed this reversal, but in the opposite sense, and he does not appear to have paid much attention to it. His explanation moreover fails to explain why a current of moderate intensity should produce a reversal in the course of or towards the end of its action; see *antea*, Exp. 6.

No solution of the phenomena can be considered satisfactory which is not at the same time a solution, or an approximation towards a solution, of the difficult problem, why in a normal heart-beat the sequence of the constituent contractions is always such as it is, even in a heart whose cavities are empty, and in which therefore the filling or distension of one cavity by the contraction of another can have no share in the matter. That the sequence is not the result of any fixed molecular constitution of the ganglia is shewn by the very fact of the possibility of its reversal. That the sequence may be changed by circumstances indicates that its normal character is due to a concurrence of circumstances, which concurrence is more readily

[1] *l. c.* p. 223.

brought about than any other arrangement. If we suppose the several parts of the heart, ventricle, auricle, sinus venosus, &c., to be mere passive instruments receiving stimuli or impulses to contraction from some common automatic ganglion (situate in the sinus venosus or elsewhere),—the sequence of the impulses being determined by molecular changes in that ganglion and in that alone,—then changes taking place in the ventricle can only affect the extent and character of its own contraction, and not in any way the sequence of the rhythm; and so with other parts. In the experiments above recorded a definite sequence of one kind or of the other was observed in the entire absence of the sinus venosus. On the above view they must be produced by a ganglion or ganglia situate in the auricles. We must further admit that this ganglion is the seat of the normal sequence in rhythm of the entire heart, or suppose that in the absence of the sinus venosus a ganglion, hitherto having no share in the direction of *the sequence*, comes into play. All of which is very complicated and unsatisfactory.

On the other hand, we have the undoubted fact that the ventricle alone (or even part of the ventricle), the auricles alone, the sinus venosus alone, and the bulbus arteriosus alone, can carry on each by itself a rhythmic pulsation of long duration and wholly like that of the entire heart. This means that each of these several parts of the heart has a rhythm of its own dependent on its own circumstances, including under circumstance everything which affects the nutrition both of its muscular and nervous elements. Now when ventricle and auricle are separated from each other, they beat each with an independent rhythm; but when physiologically connected, they beat in harmony and in sequence. It is impossible to conceive of this harmony being accomplished otherwise than by some mutual action of the two upon each other. We cannot suppose that any event connected with the contraction of the one (such as the negative variation of the natural current) by acting as a stimulus determines the contraction of the other. For, in that case, the systole of the ventricle would provoke a systole of the auricles, as well as the systole of the auricles a systole of the ventricle, and a rhythmic pulsation with long pauses between the whole beat (of both auricles and ventricle) would be impossible. Moreover, a weakly ventricle yoked to strong auricles would soon be driven to exhaustion, and *vice versâ*. We are thus driven to the conclusion that the beat of either organ is dependent not only on its own circumstances, but also on the circumstances of its fellow; that the rhythm of the auricles, for instance, is dependent not only on their own condition, but also on that of the ventricle. That just as the beat of the ventricle or of a part of the ventricle is determined by the condition of the whole of the ventricle or the whole of the part (the physiological continuity of the tissue permitting each fibre or bundle of fibres to influence all the other fibres by a sort of muscular sense, so that each fibre or bundle of fibres, instead of pulsating in a rhythm of its own, joins all the other fibres, or bundles, in a rhythm which is that of the whole tissue), in the same way the condition of the whole ventricle (the summation of the condition of the several fibres) is able, by the nervous continuity of auricle and ventricle, to affect, and in turn be affected by, the condition of the auricles, which again is the summation of the condition of the several auricular fibres. Were it permitted to speak of feeling in the absence of consciousness, we might say that just as each fibre of the ventricle (or auricle) feels the condition of and exerts in consequence an action on all the other fibres, whereby a harmony of the whole ventricle (or auricle) is established, so the auricles feel the condition of and exert an action on the ventricle, and *vice versâ*, whereby the harmony of the two is maintained; the nervous structures connecting them being the agents of the intercourse, the nerve-fibres probably serving simply as conductors, while in the nerve-cells processes may go on which stand in about the same relation to processes taking place in the more purely muscular elements that arithmetical operations on logarithms do to operations on the corresponding numbers.

If it be permitted to hold some such provisional view as that which we have just attempted to sketch, we should be obliged to add, that in the normal heart the nutrition of all parts of the heart is, so to speak, tuned for the production of a beat with the normal sequence of sinus venosus, auricle, ventricle, and bulbus. And further, that though the rhythm is at bottom dependent on the condition of the whole heart, yet each cardiac cycle is *set going* by the contraction of the sinus, the pulsation of that part having just the effect necessary to start the already prepared auricle, and this in turn the ventricle. Hence one might readily imagine that after removal of the sinus venosus (putting aside the effects of the section), the heart, having lost so to speak its leader, would be at a loss how to beat. When it did begin to beat we should expect it to beat in the order auricle-ventricle. The facts, however, that in Stannius' experiment the order ventricle-auricle makes its appearance, and that the ventricle separated from the auricles resumes its pulsations, while the auricles remain quiescent, shew that loss of leadership is not the sole cause of the standstill, but that some inhibitory work (not however of the pneumogastric kind) is going on, which inhibition bears more particularly upon the auricles. Both auricle and ventricle are prepared to beat upon a sufficient stimulus, but they are restrained from spontaneous pulsation by the (at present inexplicable[1]) inhibitory influences started by the section (or ligature) of the sinus venosus, the auricle being more restrained than the ventricle. Hence when a slight stimulus is applied to the heart, a beat, in the order ventricle-auricle, is produced; and that beat, as we know from the researches of Bowditch, being beneficial to the heart, and the inhibitory influences still continuing to work more upon the auricle than the ventricle, the initial beat may be followed by many others having the same sequence of ventricle-auricle.

So, with weak constant currents, which may be regarded as slight stimuli, the same kind of pulsation, the same sequence of ventricle-auricle, is produced, whether the current be ascending or descending.

It is well known that the make and break of a constant current is a more powerful stimulus on muscle than an induction-shock, there being in this point a remarkable differ-

[1] We say "at present inexplicable" because the Stannius' standstill has not yet, in spite of all that has been written on it, been fully cleared up. The fact that the standstill takes place when the endings of the vagus fibres have been paralyzed by atropin, proves that the inhibition is not due simply to vagus stimulation. On the other hand the curious results of Pagliani (*Moleschott's Untersuch.* XI. p. 358), shewing that *gradual* separation of the sinus will not produce standstill, disprove the view that the removal of an automatic ganglion in the sinus is the whole cause of the quiescence.

ence between ordinary muscle and ordinary nerve. In the course of our experiments we have been gradually impressed with the view that in applying the constant current to the heart, the effects which are produced (and we cannot help thinking that electrolysis has much more to do with these than is generally admitted) by the action of the current on the more distinctly muscular elements override those which are due to the action of the current on the more distinctly nervous elements. We may indeed go almost so far as to say that the former put the latter altogether on one side. So that in studying the action of the current on the auricles and ventricle, we have been led to consider merely its action on the muscular elements of the ventricle and of the auricles respectively, without paying any attention to either the inhibitory or any other nervous mechanisms present or supposed to be present. We have at least never met with any satisfactory evidence of the excitation of these nervous structures playing any part in the phenomena with which we have had to deal.

Hence in applying the constant current to the auricles and ventricle we have considered only the effects on the muscular tissue of the one and of the other. Now the ventricle, just as it is more muscular, is more susceptible to the action of the current than the auricle. It is more especially in the ventricle, we might say exclusively in the ventricle, that any difference is observable between the effects of the ascending and those of the descending current. In studying the snail's heart we were very much struck with the greater susceptibility of the ventricle as compared with the auricle. The latter is far less readily inhibited by the interrupted current than the former, less easily roused from quiescence into pulsations by the constant current, less easily checked by the constant current when beating spontaneously. Whether these facts are to be explained as mass effects or in some other way, the frog's heart, in spite of the presence of all its nerves and ganglia, acts in these respects very similarly to a snail's heart; and we venture to suggest that this greater susceptibility to extrinsic influences of the ventricle as compared with the auricle has to do both with the inverted order of sequence so characteristic of the heart during the

Stannius' standstill, and with the fact that the same order is also visible in pulsations called forth by weak constant currents.

The reversal which takes place during the action of the descending current is not so easy to explain; and it is with the greatest hesitation that we submit the following suggestions.

In the first place, in the course of many repeated observations, we were struck with the fact that the descending current had distinctly a more *exhausting* effect on the heart than the ascending current. During the minutes which followed upon the application of the descending current for 30 seconds, the heart was less irritable than it was after the application of the ascending current for the same time. So that, unless care were taken to allow sufficient intervals of restorative rest, the primary effects of the action of the current were obscured by the secondary effects of exhaustion. This exhaustion was of course more evident with strong than with weak currents. The fact that the reversal takes place with weaker currents towards the end and with stronger currents towards the beginning of the action of the current, points very distinctly to exhaustion as a prominent factor in its causation.

In the second place, if we may assume, in accordance with Pflüger's results on nerves, that with weak currents the neutral point lies near the anode, then so long as the current is not too strong a large part of the ventricle will always be in the condition of katelectrotonus, so that whether the base or the apex be kathodic, the area of katelectrotonic tissue in the ventricle is sufficient to maintain the greater susceptibility of the ventricle as compared with the auricle. As the current becomes stronger, the neutral line is driven nearer and nearer to the kathode. Under these circumstances, when the current is descending the base becomes largely anodic. This condition of the ventricle, with the base anodic and the apex kathodic, as shewn very distinctly by the phenomena of the snail's heart, and more or less forcibly illustrated by the foregoing observations on the frog's heart, is equivalent to a preponderating anodisation of the entire ventricle, more being lost by the anodic condition of the broad base than is gained by the kathodic condition of the narrow apex. And this anodic condition added to the exhaustion (of which it is probably the cause) so depresses the ventricle that the auricle gains the upper hand and precedes it in each beat; the depression of the ventricle however not being so intense as to prevent it from following the auricle at each beat.

When, on the other hand, a strong current is ascending, and the base therefore is kathodic, however much the neutral line is driven near to the base, there is always left an area of kathodic tissue at the broader pollent base sufficient just to maintain that preponderance of the ventricle over the auricle which is the characteristic of Stannius' standstill; and exhaustion not being produced so readily in this case as in the other, the rhythm ventricle-auricle is carried on in spite of the peculiar condition of the former.

We repeat that we put forward this explanation with much hesitation, but we submit that it is founded on at least no greater assumptions than that of Bernstein. At any rate our view has a certain value in reducing the phenomena to known actions of the constant current on irritable tissues.

8. *The heart brought to a standstill by stimulation of the vagus.*

So struck were we, in the course of our experiments, with the entire absence of any phenomena, which we could satisfactorily attribute to the action of the constant current on the termination of the vagus fibres, or on the various inhibitory and other mechanisms existing or supposed to exist in the vertebrate heart, the stimulation of which we, on starting our investigations, supposed would render the behaviour of the frog's heart under the current entirely different from that of the nerveless snail's heart, that we were led to suspect that the currents employed being so much stronger than those generally made use of in experimenting on nerves, exhausted on their first application all the nervous elements, and left us dealing with (so to speak) the naked contractile elements.

To have proved that this was the case would have been to bring an additional and strong argument in favour of the thesis of which all our experiments may be regarded as illustrations, that the causes of the rhythmic pulsations of the heart are to be sought for in the properties of contractile tissue. But we found, to our great astonishment, evidence that the most important and active nervous mechanisms of the heart were able fully to exert their influence in spite of a powerful constant current being passed through the heart. Seeing that a portion of the ventricle, or the whole ventricle when quiescent from whatever reason, or the whole heart when quiescent from the experiment of Stannius, is roused into rhythmic pulsations by the constant current, we very naturally expected that the same current would produce rhythmic pulsations when applied to a heart in standstill from stimulation of the vagus.

We found, however, that this was not the case.

Having brought the heart to a standstill by stimulating the pneumogastric with the interrupted current, we threw into the heart constant currents of various strengths, both ascending and descending. But not even with six Grove cells did we succeed in calling forth any rhythmic pulsations. The only effect which we could trace was a very marked reaction, when both the constant current and the vagus stimulation were removed, the heart soon beginning to beat with remarkable vigour and rapidity.

Having applied the constant current, both in the descending and ascending direction, we stimulated the vagus while the current was still passing through the heart. Inhibition was nevertheless produced, and, as far as we could see, took place very much as if no current were passing through the heart. We are not prepared to say that the current made absolutely no difference or that it would not be possible to call forth rhythmic pulsations in pneumogastric inhibition by applying still stronger currents; but we do say that currents distinctly stronger than those which readily rouse into rhythmic pulsations the naturally quiescent ventricle or part of the ventricle, or the whole heart brought to a standstill by Stannius' experiment, failed with us to bring forth pulsations in a heart brought to a standstill by stimulation of the vagus.

From this we draw the following conclusion. We have argued that the pulsations which the constant current calls forth in a piece of the ventricle must, until some hitherto unnoticed nervous elements have been discovered, be considered as pulsations caused by the direct action of the current on the cardiac muscular tissue. Since these pulsations are also seen in the whole ventricle (otherwise quiescent), and indeed in the whole heart (under Stannius' experiment), when the constant current is applied, it is clear that previous division of the ventricle is not necessary to their production, that the continuity of the ganglionless apex of the heart with those portions of the heart which do contain ganglia, is no bar to pulsations arising in the former as the result of the application of the constant current. Now, in the generally accepted theory of inhibition, the action of the pneumogastric is supposed to stop at certain ganglionic centres. In these centres the impulses descending the vagus so exalt, either directly or by the mediation of various mechanisms, the molecular inhibitory forces that the accustomed rhythmic stimuli are no longer set free, and the muscular fibres lie idle till the struggle in the ganglia is over. According to this view then, whether the muscular fibres are removed from the influence of the ganglia by section or by profound urari or other poisoning, or by the ganglia being preoccupied in an inhibitory struggle, the constant current acting directly on the fibre ought in all three cases to produce the same effect, viz. a rhythmic pulsation. As a matter of fact, it does so in the two former cases but not in the third. From this it follows that stimulation of the vagus, in addition to whatever effect it may have on the ganglia, has also an effect of such a kind that the irritability of the cardiac muscular tissue itself is impaired, and the production of rhythmic pulsations hampered in their muscular origin. The depression of irritability thus caused is not so great but that a mechanical stimulus will produce a contraction, and hence the heart, in standstill from stimulation of the vagus, will beat when pricked. Such a method of estimating irritability is however a very rough one. That a mechanical stimulus calls forth a beat, proves that the irritability is not extinguished, but is no evidence that it is not impaired: the more delicate test of the constant current manifests the muscular weakness which stimulation of the vagus has caused.

We are thus led to the conclusion that the pneumogastric, like any other motor nerve, acts when stimulated directly on the muscular tissue with which it is connected; from which conclusion there follows, as a corollary, the view that the peculiar inhibitory effects of stimulation of the pneumogastric are due, not to a specific energy of the nerve itself or of any mechanism in which it terminates, but to the fact that while ordinary nerves are connected with muscles ordinarily at rest, the pneumogastric is connected with a muscle in a state of continued rhythmic pulsation. To which we may add, that the other marked inhibitory nerves, the vaso-dilator nerves, are also in connection with muscles normally in a state of activity (tonic action) which is more closely allied to rhythmic pulsation than to any other form of muscular activity; indeed, in many cases, as in the rabbit's ear, the two merge into each other, and it seems difficult to regard the tonic contraction of blood-vessels in any other light than that of an obscure rhythmic pulsation.

If this view be accepted, the phenomenon of inhibition of the snail's heart by direct application of an interrupted current ceases to be extraordinary; for both that form of inhibition, and the ordinary pneumogastric inhibition, fall into the same category, being both at bottom due to the fact that in them stimulation is brought to bear on a spontaneously active tissue. Against the identity of the two, there may be urged two strong objections, one that the interrupted current applied directly to the vertebrate heart never produces a distinct inhibition similar to that seen in the snail's heart, but a tumultuous irregular sort of tetanus (never however reaching the distinct form of tetanus, and eventually giving rise to a standstill), and the other that stimulation of the pneumogastric never causes (however strong the current) a tetanic contraction of the heart, such as is seen when a too strong interrupted current is applied directly to the snail's heart. Without prolonging the discussion any further, we may be permitted to say that these objections do not seem to us insuperable, and that the study of the vaso-dilator and vaso-constrictor nerves appears likely to afford a solution of the difficulties.

The conclusions then to which our observations point, we do not pretend to say satisfactorily establish, are as follows.

The vertebrate heart, such as that of the frog, behaves towards the constant current in a manner very closely resembling that in which the snail's heart behaves.

The well known, easily recognised, ganglia of the heart play a subordinate part in the production of the heart's spontaneous rhythmic pulsations. The real origin of these is to be sought for in the phenomena of muscular tissue, unless some new form of nervous tissue which has hitherto escaped detection be discovered.

The constant current may according to circumstances call forth or put an end to rhythmic pulsations: calling them forth when they are absent and diminishing or destroying them when they are spontaneously present. Hence, here, as in the case of the snail's heart, stimulation and inhibition are shewn to differ from each other in degree, or according to circumstance, rather than in kind.

Stimulation of the vagus produces an effect on the muscular tissue of the heart; its inhibitory action is not confined to the ganglia; and hence vagus inhibition does not differ so essentially from the inhibition of the snail's heart by direct stimulation as might at first appear.

POSTSCRIPT.

WHILE the above paper was in the printer's hands we received the *Centralblatt f. med. Wissenschaft*, of May 27th (No. 22, 1876), containing a brief communication from Prof. Bernstein *Ueber den Sitz der automatischen Erregung im Froschherzen.*

In it the author relates an experiment in which the ventricle of a frog's heart is violently compressed for a few seconds across its middle with a fine pair of forceps. The line of tissue thus injured breaks the physiological continuity between the upper and lower half of the ventricle; though, there being no actual physical solution of continuity, the apex is still as before supplied with abundance of fresh blood. Since under these circumstances the apex, though irritable towards stimuli, remains perfectly quiescent, never exhibiting any spontaneous pulsations, Bernstein argues that the pulsations witnessed in Merunovicz's experiment are not really automatic, but the result of the rabbit's blood or serum acting as a stimulus "upon certain motor mechanisms in the cardiac muscles, and thus causing in them an intermittent discharge of energy."

Without waiting for the results of the counter experiments which naturally suggest themselves, we should like at once to remark that, if a stimulus so constant in its nature and action as serum or blood must be is capable of producing rhythmic movements so varied in their rate of development and character as those which made their appearance in Merunovicz's experiments, the hypothesis of an automatic centre confined to the sinus venosus needs a fresh definition.

The old view, and the one against which we have in foregoing pages argued, taught that the impulses which caused the heart's beat proceeded *in a rhythmic manner* from the ganglia in the sinus, that the rate and character of the rhythm was determined there, and that the muscular apparatus of the heart had no other task than to respond to those rhythmic impulses according to the measure of its irritability. If however, in accordance with Bernstein's new view, the muscular tissue of the heart with its "motor mechanisms" is capable, when affected by a constant stimulus (whether chemical, as blood and sodium chloride, or electrical, as the constant current), of developing rhythmic pulsations *which in no way, except as far as relates to their causation, differ from normal spontaneous beats,* the need of any intermittence in the action of the automatic ganglia in the sinus is done away with; its presence would shew a wasteful want of economy.

Looking at the matter from an evolution point of view, and seeing that muscular or neuro-muscular tissue is anterior in evolution to strictly differentiated nervous tissue, it is in the highest degree improbable that, supposing the power of generating automatic rhythmic impulses were at some time transferred from undifferentiated protoplasmic or neuro-muscular tissue to purely nervous mechanisms, the muscular remnant, from which spontaneity had been removed, would retain a power of intermittent action which it could never, in actual life, have an opportunity of manifesting, since its intermittence would ever afterwards be determined by its nervous master.

It becomes necessary, therefore, to modify the hypothesis of an automatic centre in the sinus in the sense that the action of that centre is not an intermittent but a continuous one. From this modified view to the one which we ourselves have urged in the foregoing pages, the step is very slight.

We may add that the 20th number of the same *Centralblatt* contains an original communication from Herr Fischer which, while confirming the presence of a considerable number of fine nervous plexuses between the fibres in the ventricle of the dog's heart, throws much doubt on the nervous character of the elements described by Gerlach, as abounding in the striated muscle and in the tissue of the frog's ventricle, elements which might be regarded by some as the long sought for motor mechanisms.