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COMPRESSION OF THE CARDIAC NERVES OF LIMULUS, AND SOME ANALOGIES WHICH APPLY TO THE MECHANISMS OF HEART BLOCK.[1]

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INTRODUCTION.

THE experimental work which will be described in this paper was undertaken with the view of ascertaining the effects of compression upon conduction in nerves. The chief object in view was to determine whether the changes in conduction in the nerves of the heart of Limulus polyphemus were comparable to the changes in the atrio-ventricular bundle of the mammalian heart when clamped by the method of Erlanger.[3] It was believed, and this belief has been justified, that such an investigation would throw further light on the mechanisms of heart block.

The effects of compression upon conduction in motor nerves have been noted in numerous investigations. In recent years Ducceschi[4] has made the most extensive observations, while the work of Meek and Leaper[5] merits especial attention owing to the refinement and accu-

[1] These investigations were reported to the American Physiological Society, December 29, 1911, at which time numerous tracings illustrating the details were reproduced. A report was also made to the St. Louis Medical Science Club, January 9, 1912. The paper is abstracted in this Journal, 1912, xxix, Proceedings of the American Physiological Society, p. xxi.

[2] I am indebted to the Commissioner, Hon. Geo. M. Bowers, for the opportunity of conducting these investigations, and to Mr. H. D. Aller, Director of the Beaufort Laboratory, for his co-operation in placing at my disposal the conveniences and facilities for prosecuting the work.

[3] ERLANGER, J.: Zentralblatt für Physiologie, 1905, xix, p. 9, and Journal of experimental medicine, 1906, viii, pp. 8–58.

[4] DUCCESCHI: Archiv für die gesammte Physiologie, 1901, lxxxiii, p. 38.

[5] MEEK and LEAPER: this Journal, 1911, xxvii, p. 308.

rate quantitative character of the method employed by them, and owing to the further fact that they also hoped to throw light upon the nature of the conducting tissue in the atrio-ventricular bundle. While Meek and Leaper found only a slight difference between the amount of pressure required to block impulses in motor nerves and in skeletal muscle, it is none the less highly probable that quantitative differences in the reaction to compression between the types of conducting tissue extant in the vertebrate heart do exist. This view is based upon a previous communication by the author,[6] in which it was shown that it requires a greater degree of compression to block inhibitory nerve impulses than normal autogenous impulses in the turtle's heart. One is led, from this and other facts, to expect that, qualitatively at least, all types of conducting tissue comport themselves in a similar manner when compressed. It is not the least surprising, therefore, that the results of our experiments upon nerves are, in the main, in harmony with the previous findings in experiments upon the auriculo-ventricular bundle of His, showing only such deviations as are to be expected from tissues with the physiological properties found in the Limulus heart.

The Method.

a. Material. — The heart of Limulus polyphemus ("King crab," "Horseshoe crab") was chosen as most suitable for this investigation. As has been pointed out by Carlson,[7] the impulses in this heart are neurogenic. They originate in a ganglionic nerve cord which is situated on the dorsum of the tubular, segmented heart. The chief mass of the ganglion lies upon the posterior segments. The impulses are transmitted to the anterior segments by nerves exclusively. There are three of these nerve paths: the anterior prolongation of the ganglionic cord and the two lateral or marginal nerves. This anatomical arrangement makes it possible to cut or clamp each or all of the conducting nerve paths. The myocardium is syncytial, and arranged circularly in nine segments. The only physiologic connection between these segments is to be found in the nerve paths just mentioned. The myocardium contracts, like skeletal muscle, with a force graded to the

[6] Garrey, W. E.: this Journal, 1911, xxviii, p. 249. Also Fredericq, L.: Archives internationales de physiologie, 1912, xi, p. 405.

[7] For literature concerning the heart of Limulus, *cf.* Carlson, A. J.: Ergebnisse der Physiologie, 1909, viii, p. 373.

strength of the impulses which reach it. It is therefore possible to get graphic records which show the results of compression.

b. Procedure. — The conditions under which this investigation was prosecuted did not admit of the use of the liquid transmission method employed by Meek and Leaper. In its stead a modified Gaskell clamp, open at one side, the jaws of which were covered with thick smooth pure gum tubing, was employed. In the earlier experiments these elastic pads were not used, but were resorted to as soon as it became evident that it would otherwise be impossible to graduate the amount of pressure with sufficient accuracy, or to avoid permanent injury to the nerves. For adjustment and graduation of pressures the clamp was provided with a very fine micrometer screw. The clamp was placed in most instances at about the junction of the second and third segments. This location was chosen because the bulk of the rhythm-initiating nerve cord is posterior to this point, and because after section, or clamping to complete block, at this point, the anterior segments only rarely initiate an automatic rhythm. Various procedures were resorted to in the application of the clamp. In some instances the whole cross section, including the muscle tissue and the three nerve paths, was compressed. In other instances the lateral nerves were cut and the central nerve cord only was clamped; or again, the nerve cord was cut or dissected back from the anterior segments, and the clamp applied to both lateral nerves or to one of them after section of the other. The results are identical in all these procedures as far as the effects of compression are concerned, being modified only by the fact that the height of contractions of the anterior segments is much decreased by any procedure which materially decreases the number of nerve fibres conducting impulses to their musculature. Although many experiments were performed upon the heart *in situ*, it was found to be more convenient and satisfactory to work upon the excised organ immersed in its own plasma or in sea water. The latter method was therefore most generally used.

A light heart lever was attached to a muscle segment posterior to the clamp (usually the sixth); its movements served as an index of the strength of the impulses sent out by the nerve cord. The movements of a second lever attached to a segment anterior to the clamp afforded an accurate measure of the effects of compression. In such a preparation the posterior segments may be likened to the auricles and the an-

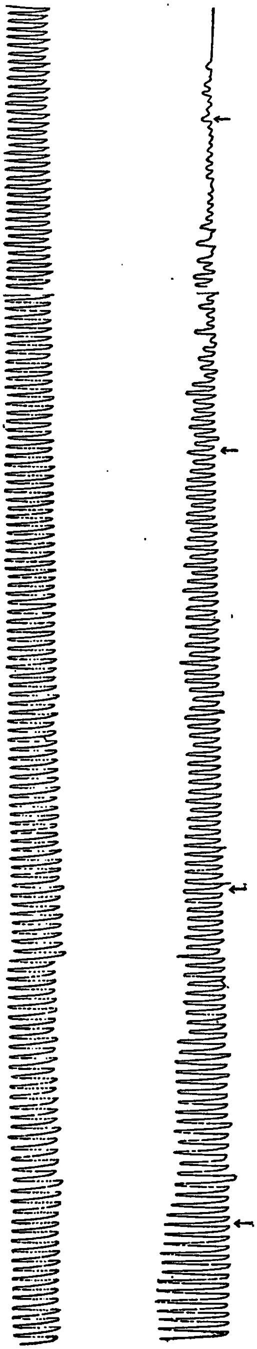

FIGURE 1. — Shows the weakening of impulses and their irregular strength resulting from compression of the nerve cord between the second and third segments. Upper tracing from the sixth segment. Lower tracing from the second segment anterior to the clamp, which was tightened at the points marked with arrows. Rate = 20 beats per minute. About two thirds the original size.

terior segments to the ventricles; the conducting nerve to the atrioventricular bundle.

GENERAL RESULTS OF COMPRESSION.

The most striking effect of the gradual application of compression to one or all of the conducting nerves was a reduction in the height of contraction of the muscle of the anterior segments, distal to the clamp. When the compression was very gradual, the reduction in the contractions was also very gradual and perfectly uniform (Fig. 1). When the compression was induced by more rapid approximation of the jaws of the clamp allowing an interval of time between successive manipulations, the tracings presented a series of step-like reductions in the height of contraction, each step corresponding to an increase in pressure (*cf.* Fig. 6). With the application of a given degree of compression, the major effect is immediate, but the appearance of the full effect requires the lapse of a certain time, during which, if the pressure is maintained constant, the height of the contraction gradually decreases. The importance of a similar time factor has been noted by Ducceschi and by Meek and Leaper (*loc. cit.*) in their observations upon compression of motor nerves.

When a given amount of pressure had been so graded that complete block was just obtained, and the pressure was then removed, the nerves gradually, and in many instances completely, recovered their conductivity and the subsequent contractions reached their original height. While recovering, however, as well as during the application of the severer grades of pressure, the individual contractions may show considerable variations in height, a fact to which detailed reference will be made later. Occasional instances were noted in which after the contraction had reached a minimum a partial recovery ensued, although the compression was maintained constant. This recovery during compression never resulted if the degree of compression was severe. When the severer degrees of compression were sustained for some time, only partial or no recovery ensued, a permanent injury to the nerves having resulted.

Analysis of results. — The weakened contractions are the result of alterations in the conductivity of the nerves at the point of compression, which demand further analysis. Carlson [8] has shown that stimuli applied to the lateral nerves or to the anterior portion of the nerve cord may cause an inhibition of the ganglionic impulses in the Limulus heart, and this finding has been confirmed by the author. Ducceschi [9] and others have also shown that compression may stimulate motor nerves mechanically. Such mechanical stimulation with resultant inhibition could explain a weakening of ganglionic impulses, but does not account for our findings as recorded above, for examination of our tracings shows that the contractions of the anterior segments distal to the clamp are the only ones affected by the compression. There was no inhibition of the ganglionic impulses, since the contractions of the segments posterior to the clamp showed no alteration in rate, rhythm, or strength. Our results can be attributed solely to alterations in conductivity of the conducting nerve fibres at the site of clamping.

Comparison of Compression with Section of the Conducting Nerves.

From the very nature of the method employed some nerve fibres must inevitably have been more affected by the compression than

[8] Carlson, A. J.: Ergebnisse der Physiologie, viii, p. 434, and this Journal, 1905, xiii, p. 229.

[9] Zederbaum: Archiv für Anatomie und Physiologie, 1883, p. 161; Efron: Archiv für die gesammte Physiologie, 1885, xxxvi, p. 467; Ducceschi: *Loc. cit.*; Meek and Leaper: *Loc. cit.*, Fig. 2, p. 317.

others. It seemed possible, then, that our results might be explained by assuming that the conductivity of some of the nerve fibres was completely suppressed while other nerve fibres were still able to conduct normally. To test this possibility Carlson's [10] experiments on the section of the nerves were repeated with certain variations. It was found, in confirmation of Carlson's work, that a decrease in the number of conducting nerve fibres by section decreased the height of contraction

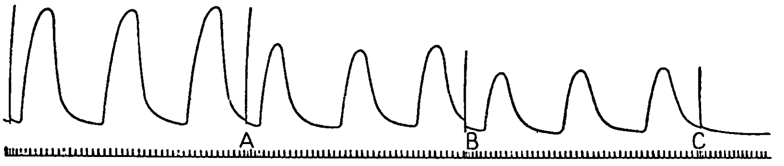

FIGURE 2. — About four fifths the original size. Effects upon the strength of contractions of the anterior segments, produced by section of the conducting nerves. The nerve cord was cut at *A*, the right lateral nerve at *B*, and the left lateral nerve at *C*, thus stopping further contraction of these distal segments. Time = one fifth of a second.

of the myocardium innervated (Fig. 2). Further experiments revealed the cause of this diminution in the height of contraction, and showed that the muscle elements involved were those which were most directly innervated by the sectioned nerves. Thus upon section of a lateral nerve the chief effect is upon the homolateral half of the myocardium. This is shown in Fig. 3, which was taken from an experiment conducted in the following manner. The heart was fastened by pins to a paraffin block, weighted and submerged in sea water. The pins were inserted about the margin of the posterior seven segments. In the anterior two segments they were placed in the median line, just avoiding the central nerve cord. Tracings were then taken from the lateral halves of these anterior segments. When the left lateral nerve was cut (at *X*, Fig. 3), the contractions of the left side were at once diminished to about one sixth of the original height. After about eight minutes (at the point *Z*, Fig. 3) recovery had taken place and was almost complete.

Discussion. — In interpreting these findings we believe we are justified in postulating a predominant homolateral innervation of the myocardium of Limulus. Impulses passing along a given path affect more especially those cells which they innervate most directly, and in case the more direct path is interrupted then recovery and co-ordina-

[10] CARLSON, A. J.: Ergebnisse der Physiologie, 1909, viii, p. 408, Fig. 15.

tion are effected by transmission of the impulses by a more indirect or circuitous route. Functional integrity of the myocardium is thus re-established either by conduction from muscle cell to muscle cell (which does not seem probable in the light of Carlson's [11] work) or by the establishment of new paths in the peripheral nerve plexus.[12] In this way function, lost by the section of the more direct paths, is re-established. The whole arrangement is strongly suggestive of the disposition of inhibitory nerve fibres found by Garrey [13] in the heart of the turtle. In the turtle the action of the inhibitory nerves is more pronounced on the homolateral side of the heart — a bilateral effect is obtained with stronger stimuli. The view that a similar condition may exist in Limulus is strengthened by the results of stimulation of the nerves. After ablation of the nerve cord from the posterior segments, a procedure which produced quiescence of the heart and prevented inhibitory phenomena, stimulation of a lateral nerve with very weak induced currents (either faradic or single) produced a much stronger contraction on the homolateral half of the anterior segments. Strong shocks produced a bilateral effect. These results are in perfect accord with those obtained upon the turtle's heart when a vagus nerve was stimulated. The effects of section of the nerves of Limulus heart as here outlined furthermore remind one forcefully of the experiments of

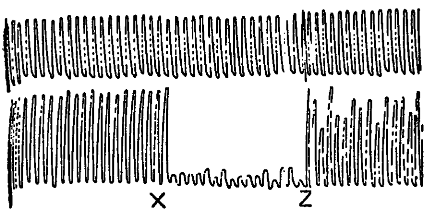

FIGURE 3. — Upper tracing from the right half and lower tracing from the left half of the second segment. The left lateral nerve was cut at *X* and produced only a homolateral effect. Note the recovery at *Z*. Heart's rate = 20 per minute.

[11] CARLSON, A. J.: this Journal, 1907, xvii, pp. 478 *et seq.*

[12] Section of some of the fibres of a motor nerve paralyzes the fibres of skeletal muscles which they innervate. The contraction of the muscle as a whole is correspondingly weakened. It is somewhat surprising that a similar condition is to be found in the Limulus' myocardium, which is a syncytium. CARLSON has shown, however, that in spite of this anatomical condition conduction does not take place by transmission of the impulse directly from muscle element to muscle element, but, normally, is always by way of the nerve plexus. After treatment of the myocardium with sodium chloride (or other chemicals) a direct muscular conduction may be established.

[13] GARREY, W. E.: this Journal, 1911, xxviii, p. 330.

Gaskell on the turtle's heart. He produced blocks of varying degrees by successive sections which narrowed the conducting bridge; similarly in our experiments the response of the muscle is also affected by decreasing the number of conducting nerve fibres, *i. e.*, the functionating area of cross section.

The results of section and stimulation of nerves, as we have outlined them above, justify the conclusion that the effects of clamping of the nerves may be due in part to destruction of function (temporary or permanent) of some of the compressed fibres, *i. e.*, by actually cutting off certain paths of conduction while others still function. By this procedure a corresponding portion of the myocardium contracts less efficiently. Many of the phenomena, however, cannot be ascribed to this mechanism, and are compatible only with the alternative view that they are produced by an alteration in the property of conduction in all the fibres.

After a clamp has been tightened on the nerve cord, say at the level of the junction of second and third segments, till the myocardium of the anterior segments fails to respond to the impulses from the posterior part of the nerve cord, recovery more or less complete, depending upon the severity of the compression, will take place (see Fig. 8). This fact alone speaks strongly for an involvement of all of the fibres in the altered conduction. Other facts which speak for this view will be considered in the subsequent sections.

The Relation of Strength of the Impulses to Block.

a. Experimental variations in the strength of impulses. — A degree of compression which will block a weak stimulus will not block a stronger stimulus; strong induction shocks, for example, applied to the lateral nerves posterior to the clamp after the normal impulses had been completely blocked, frequently caused contractions of the anterior segments. Strong autogenous neurogenic impulses may also break through a block which is complete for weaker impulses. One of the most striking methods of demonstrating this relation of strength of stimulus is to produce complete block by clamping the nerves, and to then subject the ganglionic nerve cord in its posterior portion to the action of stimulating chemicals, such as isotonic solution of chloride, citrate, or tartrate of sodium, which is added to the sea water or Limulus' blood plasma in which the nerve cord is immersed. These chemicals increase the rate of discharge and the force of all impulses sent out by the ganglion. In all hearts thus treated, as soon as the impulses had reached a sufficient strength the previously existing block disappeared and the segments anterior to the clamp began to contract. This is illustrated in a somewhat typical way in Fig. 4, in which the nerve cord was transferred from sea water to isotonic sodium chloride at the point *A*. The

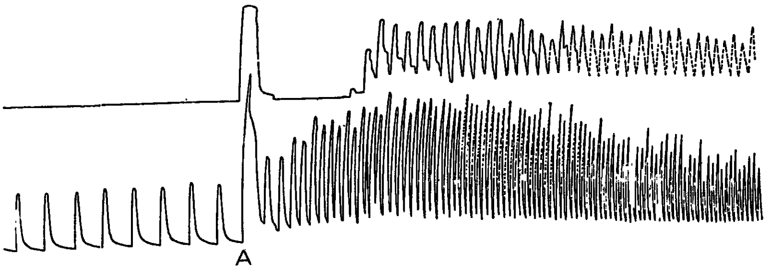

FIGURE 4. — Illustrates the disappearance of block upon stimulating the nerve cord (but not the site of compression) with 3 per cent sodium chloride at *A*. Also shows the refractory condition of the nerve due to clamping and activity, only alternate impulses producing full effects. Frequently the alternate impulses produce no effect, thus establishing the 2/1 rhythms of partial block. The smoked paper moved 24 millimetres per minute.

increased strength of impulses is recorded in the contractions of the posterior segments (lower tracing). Four seconds later the strengthened impulses forced the block, and the anterior segments contracted. In cases in which the increased strength of the impulses was sustained by the proper admixture of sea water and sodium chloride solution, it was found that the impulses continued to force their way through the compressed area. As soon, however, as the nerve cord was replaced in sea water and the impulses were thereby weakened, the condition of block was re-established. When the stronger impulses had forced a block, it was found that the block was easily re-established by increasing the amount of compression by tightening the clamp, and that the block again disappeared when the clamp was released. In perfect accord with these experiments are the results of Meek and Leaper,[14] who found that strong artificial stimulation of a motor nerve would cause an impulse to pass a region of compression when weaker stimuli produced no

[14] MEEK and LEAPER: *Loc. cit.*, p. 315.

effect. An examination of the published tracings of Ducceschi[15] shows also that, as a result of compression of motor nerves, the effects of the weaker make induction shocks disappeared before those due to the stronger break shocks, although the author makes no reference to the finding.

b. Partial block due to impulses of various strength. — It was very commonly found that the impulses originating in the ganglion varied

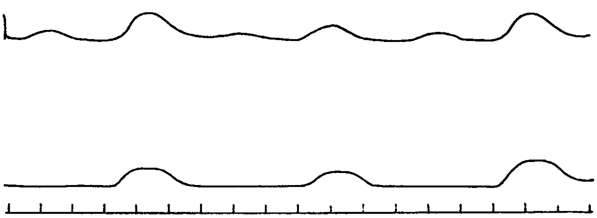

FIGURE 5. — A 2/1 rhythm established by blocking out the weaker of two unequal impulses, as seen in the upper tracing taken from the posterior segments. Lower tracing from anterior segments. The clamp was placed between the two. Time record indicates seconds.

in strength in a perfectly regular manner, for example, a strong impulse frequently alternated with a weak one. In other instances the impulses appeared in groups of three or four; the first of the group producing the strongest contraction, the last impulse producing the weakest contraction, while the intermediate contraction had a strength graded between the other two. In several such instances the clamp was applied and the conducting nerve paths compressed. There always resulted a gradual weakening of the contractions anterior to the point of compression after the manner already described. In every instance a stage ultimately was reached at which the weak impulses were blocked while the stronger impulses were still transmitted. Fig. 5 shows the results of one of these experiments. In this instance the nerve cord generated impulses alternately weak and strong, as is shown in the upper tracing. Clamping produced a 2/1 rhythm, since the weaker impulses were blocked and only the stronger caused contractions of the anterior segments (lower tracing).

The same condition is shown in a very striking way in Fig. 6. At *A*, *B*, and *C* the clamp was tightened but complete block was not produced. Near the middle of the record an alternating rhythm sud-

[15] DUCCESCHI: *Loc. cit.*, Fig. 4, p. 44.

denly made its appearance.[16] The weaker impulses failed to get through the compressed region, and a 2/1 rhythm was instituted. That the result was due purely to a diminution in the strength of the impulses is clearly demonstrated by the fact that whenever a strong impulse replaced a weak one, as at 1–1, 2–2, and 3–3, it was conducted through in the normal way and produced contraction. These examples indicate clearly that in any condition in which the impulses vary in strength, compressing the conducting paths may lead to the establishment of a partial block. It can be readily seen that the type of block will depend upon the grouping of the unequal impulses and the degree of compression. A strong impulse alternating with a weak one can give only a 2/1 rhythm. Other types of partial block are developed, however, in such groupings as are indicated in Fig. 7, which diagrammatically represents two types of grouping, tracings of which have been obtained in the course of this work. Slight compression represented by the line *a* eliminates the weakest contraction

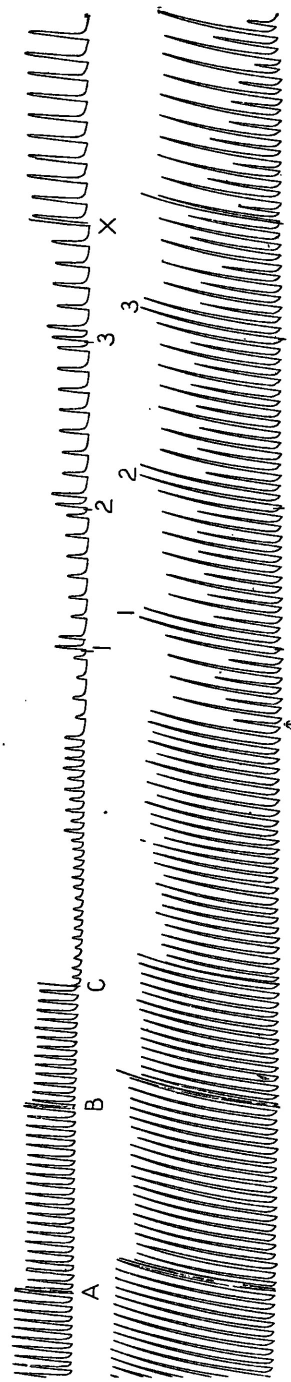

Figure 6. — Seven ninths the original size. Effects of clamping shown at *A*, *B*, and *C*. With the development of impulses of alternating strength (↑) the weaker fails to reach the anterior segments (upper tracing), thus establishing a 2/1 rhythm. When strong impulses replace the weaker, as at 1–1, 2–2, and 3–3, they overcome the block at the compressed area. At *X* a solution of disodium phosphate was added to the plasma about the anterior segments, and increased their irritability so that the weaker impulses produce a just perceptible contraction. The smoked paper moved 22 millimetres per minute.

[16] The preparation had previously been subjected to the action of potassium permanganate and of calcium chloride solutions.

(4) in both group *A* and group *B*. There thus is developed a partial block with a 4/3 rhythm. Greater compression (represented by the line *b*) causes a 4/2 block in group *A* and a 2/1 block in group *B*. The amount of compression indicated by the line *c* develops a 4/1 rhythm of partial block in both groups.

It is thus seen that a variety of different types of partial block may be developed as a result of inequalities in the strength of the impulses generated in the rhythm-producing tissue. The number of types of block which may be produced in this way is, however, limited for each grouping of the impulses. This fact places a distinct restriction upon the application of this mechanism to the partial blocks produced in the vertebrate heart by similar compression. Although it is conceivable that there may be distinct variations in the strength of the rhythmic impulses which develop in the vertebrate heart, and that such variations may cause certain types of block upon compression, yet such a factor ordinarily can serve only as a modifying influence upon the other mechanisms involved. This is clearly understood when we remember that both Gaskell and Erlanger have shown that it is possible to pass step by step through all the intermediate stages from the slightest degrees of partial block to the most complete block. This result cannot possibly be obtained in the case of partial blocks due to differences in the strength of the impulses such as have just been considered.

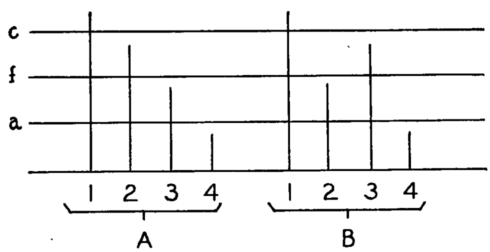

FIGURE 7. — Diagram representing two groups of four impulses (1, 2, 3, 4) showing some variations in strength of impulses frequently encountered in automatic tissues. The lines *a*, *b*, and *c*, established on the ordinates at different distances, represent different degrees of compression of conducting tissue. The portions of the ordinates above these lines represent the impulses which pass through the clamp and their relative strength. Compression *a* established a 4/3 rhythm in both groups; compression *b* results in a 4/2 rhythm in group *A* and a 2/1 rhythm in group *B;* while compression *c* establishes a 4/1 rhythm in both groups.

PARTIAL BLOCKS INDUCED BY THE PASSAGE OF IMPULSES THROUGH THE COMPRESSED REGION.

In addition to the partial blocks produced by the coincidence of variations in the strength of impulses and the proper degree of compression, our experiments show that partial block may also be instituted by changes in the physiologic properties in the compressed portion of the nerves. The changes are due to the passage of the impulses themselves, and are of such a nature that the passage of one or more impulses through the compressed area renders the nerve incapable of conducting succeeding impulses effectively. These alterations in the properties of the nerve occur independently of any alteration in the strength of the ganglionic impulses or of any alteration in the excitability of the myocardium.

Indications of these changes are to be found in nearly every tracing. In their simplest form they appear as a distinct irregularity in the height of contraction of the anterior segments, distal to the point of compression. These irregularities are most noticeable in the severer grades of compression, when all impulses are much weakened, and in the interval following the release of the clamp subsequent to compression. The variations in the height of contraction may recur with distinct regularity. This is to be seen in Fig. 4. In this tracing it is to be noted that when the block was overcome the impulses affecting the anterior segments were alternately strong and weak. The weaker impulses are in evidence as a slight shoulder on the descending limb of the stronger contraction. When the ganglionic impulses became weaker, this shoulder disappeared because the weakened impulse could not pass the block. A 2/1 rhythm of partial block was thus instituted. The experiment represented in Fig. 8 brought out very clearly the irregularities and partial blocks established by severe compression at *A*. Following decompression at *R*, recovery gradually ensued, but during this stage there is furnished a very striking instance of the type of partial block under consideration. It may be noted that at first there was a short stage in which every second impulse was ineffective. Following this it is to be noted the contractions appear in groups which are separated by intervals in which the ganglionic impulses failed to pass through the block. Toward the end of the tracing the block disappeared and the normal sequence of beats was re-established and maintained. The condition is quite comparable to the stages of slight block which may be established in the vertebrate heart by clamping the auriculo-ventricular junction. That the groups in the blocks of the vertebrate heart appear more regularly is only a relative matter. They may appear irregularly in vertebrates and occasionally with perfect regularity in the heart of Limulus. There is then justification for believing that this mechanism is applicable to the explanation of

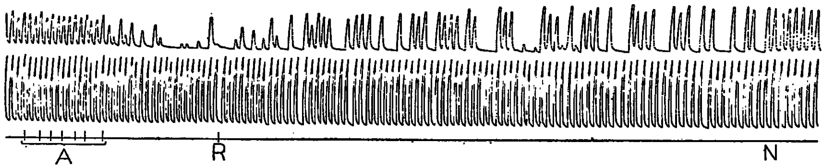

FIGURE 8. — Shows partial block with groups of contractions separated (irregularly) by dropped beats. Effects of clamping at *A*, clamp released at *R*, and normal sequence re-established at *N*. Upper tracing is from the second segment, the lower from the sixth segment — clamped between the second and third segments. The smoked paper moved 22 millimetres per minute. About one half the original size.

partial block as it appears in the vertebrate. The tracings of Ducceschi [17] show that compression of a motor nerve transforms a complete tetanus of the muscle into an incomplete tetanus, and also show that the impulses which pass through the area of compression vary greatly in strength and number. These results harmonize with our findings as outlined above. Our experiments, however, show how important this factor of lengthened refractory period or fatigue, if we may so designate it, really is in the explanation of the mechanisms of partial block.

a. **Condition of the nerve which results in this type of block.** — The condition which results from compression of a nerve is one of general sluggishness. The ability of the nerve to conduct impulses is distinctly diminished, and while conclusive proof has not been adduced to show that conduction time is lengthened, yet there are grounds for believing this to be the case. Any procedure which tends to increase the excitability and conductivity of the compressed nerve may cause the irregularities which have just been considered to disappear. This happened, for example, in the experiment from which Fig. 4 was taken. When sodium chloride was applied at the site of clamping, the partial block disappeared at once and every impulse passed readily through the clamp.

[17] DUCCESCHI: *Loc. cit.*, p. 49, Figs. 6 and 7.

Attention is again directed to the obvious fact that although one or more impulses may pass the clamp they leave the nerve in such a condition that one or more succeeding impulses are conducted with difficulty. They are weakened or rendered ineffective by the physiological activity of the nerve. This condition of the nerve remains until a certain, although somewhat variable, time interval has elapsed. We may look upon this interval as a prolonged refractory period, not unlike that produced in nerves by Fröhlich [18] through the agency of asphyxia and anæsthetics. To test this idea, a condition of partial block was produced by clamping. The ganglion was then cooled, while the temperature of the clamped portion of the nerves remained constant. Cooling from 28° C. to 20° C. produced a slowing of the heart rate from 16 per minute to 9 per minute. The effect of this procedure upon the strength of the impulses, as recorded by the posterior segments, was almost imperceptible, but the condition of partial block immediately disappeared. The impulses all passed to the anterior segments and produced contractions when the rate was slow. When the ganglion was again warmed to 28° C., the condition of block again supervened.

b. **Discussion.** — It is our belief that the result of cooling the ganglion was due wholly to the slower rate which gave ample time between impulses for the nerve to recover from the abnormal state occasioned by their transmission. It is a tempting field of speculation to attribute the phenomenon of block, which is produced by the conduction of impulses, to a condition similar to Wedensky's [19] "parabiosis"; a condition which Semenoff [20] has shown may be produced by compression of nerves. The applicability of this explanation is, however, rendered highly improbable by the work of Hoffmann,[21] who has demonstrated with the string galvanometer that each contraction of the myocardium of Limulus is not a single twitch, but a tetanus. We cannot be more specific than to state that we believe the blocks are due to a refractory condition of the nerve which is the result of fatigue. Fatigue has been demonstrated by Meek and Leaper [22] in nerves which have been sub-

[18] Fröhlich, F. W.: Zeitschrift für allgemeine Physiologie, 1904, iii, pp. 474 *et seq.*

[19] Wedensky: Archiv für die gesammte Physiologie, 1903, c, p. 182.

[20] Semenoff: *Ibid.*, 1903, c, pp. 1–144.

[21] Hoffmann (Paul): Archiv für Physiologie, 1911, pp. 142 *et seq.*

[22] Meek and Leaper: *Loc. cit.*, p. 318.

jected to pressure; fatigue of nerves is in fact a general accompaniment of general sluggishness such as may be produced by cold (Tait [23]), by anæsthetics (Fröhlich [24]) and by yohimbin lactate (Tait and Gunn [25]).

The Relation of Depressed Excitability of the Myocardium to Heart Block.

It has developed regularly in the course of our experiments that clamping of the nerves weakened the impulses to a point where the myocardium failed to give a mechanical response. In many such instances it was found that if the excitability of the muscle was increased, contractions were again obtained. This result was produced in individual cases by warming the myocardium or by adding small quantities of isotonic solutions of sodium chloride, citrate, tartrate, or dibasic phosphate to the sea water in which it was immersed. An indication of this result is to be seen in Fig. 6. At *X* 5 c.c. of n/2 disodium phosphate were added to the 50 c.c. of sea water in which the anterior segments were immersed. The increased excitability is shown in the increased height of contractions, and careful inspection of the tracing shows that there are, interpolated between the higher contractions, very small contractions which were caused by the weaker impulses from the nerve cord, contractions which were recorded in spite of the fact that the impulses giving rise to them were actually weaker than in the preceding portions of the tracing, where they produced no effect. That a partial block existed in this experiment was due then not only to alternating strength of impulses, but also to the fact that the myocardium was not excitable enough to respond to the weakened impulses. There can be no question, then, that impulses may actually pass the clamp without being effective, nor that the effects which are produced by impulses which reach the muscle through the clamped region are determined in a certain measure by the physiologic condition of the musculature.

An illustration of a peculiar but not infrequent response of the

[23] Tait: Quarterly journal of experimental physiology, 1908, i, pp. 92 *et seq.*

[24] Fröhlich: *Loc. cit.*, p. 478.

[25] Tait and Gunn: Quarterly journal of experimental physiology, 1908, i, pp. 191 *et seq.*

muscles of Limulus heart is shown in Fig. 9. The contraction of certain segments appear in groups in which the individual contractions get progressively weaker (lower tracing), although the impulses which caused these contractions remain fairly constant (upper tracing), or at least do not vary uniformly with the grouping.[26] It is apparent that a uniform decrease in the strength of all the impulses, such as would result from clamping the nerves, would lead to a dropping out of the

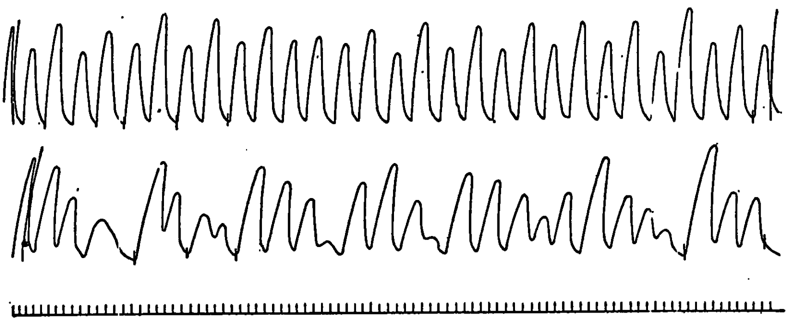

FIGURE 9. — Owing to treatment with chemicals, the contractions of the myocardium of the posterior segments (lower tracing) are not commensurate with the strength of impulses as indexed by the contractions of the anterior segments (upper tracing). Clamping conducting tissue in such a condition of the myocardium would establish partial blocks even if the impulses were of equal strength.

weakest contractions of each group and that a condition of partial block would thereby be produced. This was tested by an actual clamping experiment and the expected result obtained; a condition of partial block appeared.

GENERAL APPLICATION TO HEART BLOCK OF THE VERTEBRATE HEART.

Our work on the nerves of Limulus heart has given detailed information concerning the actual factors which must be considered in any explanation of heart block due to compression of the conducting system. It remains for us to see how well they fit into the explanation of heart block in the vertebrate heart. The striking similarity of our results to those obtained on vertebrate hearts leads us to believe that

[26] This condition of the muscle was induced by treating successively with a number of solutions; the actual cause of the peculiarity of this muscle is, however, not known to us.

the same factors are involved when all types of conducting tissue are compressed, and that the differences which do appear can readily be accounted for when we consider that the myocardium of Limulus acts like skeletal muscle, while the vertebrate contracts according to the "all or none" rule, and possesses a refractory period of a distinctive character. That the conducting paths are nerves in the cases we have considered above, and that they probably are not in the vertebrate heart, we feel certain makes little, if any, difference in the general application of our findings.

In applying our results we turned at once to the admirable schematic representation of the mechanism of heart block due to clamping the His' bundle which Erlanger [27] has given us. This investigator lays special emphasis upon two factors as the probable causes of the partial blocks which he observed. One of them is the gradual and progressive weakening of the impulses which pass the clamp when it is gradually tightened; the other is the variation in the excitability of the ventricular musculature subsequent to contraction. Our experimental results harmonize perfectly with this conception of the mechanisms involved; compression weakens the impulses transmitted, and the effects produced by these impulses depend upon the excitability of the musculature.

Our experiments show that at least two additional factors must be considered in individual cases of heart block. The first of these is the not infrequent variations in the strength of the impulses which originate in the rhythmic tissues. While this is undoubtedly much more a factor in the neurogenic heart of Limulus than in the vertebrate heart, still it occasionally becomes a factor in the latter. It is a not infrequent occurrence to find cases in which the vertebrate auricles beat, first weakly then strongly, with rhythmic variability. Clamping in such instances could result in a block of a fixed type. The limitations of this factor as a mechanism of importance are, however, apparent, and have already been referred to in the discussion of our experiments.

The other factor to which we wish to direct attention, one which has not been found by previous investigation, is the change in the conductivity of the compressed tissue which is brought about by the

[27] Erlanger, J.: this Journal, 1906, xvi, p. 183, and American journal of medical sciences, 1908, cxxxv, p. 797.

passage of impulses; as shown above, the tissue is thus fatigued or rendered refractory, so that succeeding impulses are blocked until recovery has occurred. This factor should not be overlooked in the application of Erlanger's mechanism, for it will serve in the explanation of certain irregularities which are frequently encountered in the grouping of contractions in partial block.

Erlanger's diagram makes it clear that in partial block, experimentally produced, many impulses actually pass the clamp, but fail to produce any effect because of their reduced strength and the reduced excitability of the ventricular musculature subsequent to its contraction. This fact is not commonly recognized and has never been put to the experimental test. Our experiments, however, show that the condition actually existed in some of our cases, that impulses which were completely blocked, so far as any contraction of the myocardium was concerned, actually passed the compressed area but were below the threshold for the muscle. When the excitability of the latter was raised by appropriate treatment with chemicals, these stimuli became effective.

Summary.

1. Progressively increasing the compression upon the nerves of Limulus heart causes a progressive reduction in the height of contraction of the myocardium supplied by the corresponding nerves; the full effects do not come on immediately, but gradually increase with a constant pressure.

2. Recovery may take place after releasing from compression.

3. Cutting, clamping, or stimulating the cardiac nerves causes changes in height of myocardial contraction which are mainly homolateral in the case of lateral nerves, but bilateral in the case of the nerve cord. After cutting the lateral nerves the decreased height of contraction may be recovered from, probably as a result of impulses which pass by new or more circuitous paths.

4. Clamping nerves may block out weak impulses, while stronger impulses are only weakened; thus variations in the strength of nerve impulses may give rise to various types of partial block depending upon the degree of compression of the conducting paths.

5. Compression establishes in nerves a condition as a result of

which the passage of one or more impulses renders it refractory to a succeeding impulse, thus accounting for certain conditions of partial block.

6. Impulses may pass a clamped region and yet be below the threshold of the myocardium, or they may find it in a refractory state; thus in certain cases the condition of the myocardium may be the factor determining the type of partial block established by clamping the nerves.