Critical Digest.

RECENT VIEWS ON THE INNERVATION OF THE HEART.¹

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AMONGST the vital problems connected with the heart, some of the most prominent and important are: (a) The construction and mode of action of the mechanism by which its contractions are produced and regulated (its automatic muscular and *motor* nerve arrangements); (b) the sensorium is informed of its condition (its sensory nerve arrangements); (c) the nutritive condition of its muscular fibre is maintained and regulated (its trophic nerve supply); (d) the construction and nature of the nerve arrangements, by means of which it is brought into relationship with the other parts of the vascular system, and with the other organs of the body.

THE AUTOMATIC MECHANISM OF THE HEART.

The nervous mechanism of the heart is extremely complicated, and the manner in which it acts is far from being perfectly understood. It is a subject, however, of the greatest importance, and we must, therefore, consider it in some detail.

In the *first place*, it is necessary to remember that the contraction of the heart is automatic, *i.e.* it is due to impulses arising within the heart itself, and that, in conditions of health, the action of the two sides of the heart, *i.e.* of the two pumps, is synchronous. Under ordinary circumstances the heart beats in a perfectly rhythmical and regular manner, the number of contractions being, in the adult male, about 72 per minute.

Until quite recently it was supposed that the rhythmical action of the heart was entirely due to the periodical and orderly discharge of motor nerve force in the nerve ganglia, which are scattered through the organ; but recent physiological observations, more especially the brilliant researches of Gaskell, seem to show that the influence of the cardiac ganglia is not indispensable, and that the muscular fibre itself, in some of the lower animals at all events, possesses the power of rhythmical contraction.

¹ Part of the first of a course of lectures on the Diseases of the Heart, delivered in the Edinburgh Extra-Academical School of Medicine.

Gaskell's observations seem to prove conclusively, that, in the tortoise, the automatic action of the heart does not depend upon any special rhythmical nervous apparatus, but that it is due to a property of rhythmical contraction inherent in the muscular tissue itself.

It is perhaps premature to conclude that the automatic contractions of the human heart are produced in exactly the same manner as the automatic contractions of the heart of the tortoise. We may, however, safely say, that in man, the rhythmical action of the heart must be due, either to the periodical and orderly discharge of motor nerve force from the ganglia which it contains, or to a rhythmical property possessed by the muscular tissue independently of any special nervous mechanism; and if we may judge by analogy, the latter view is possibly the correct one. And this we may term the *first step* in the comprehension of the mechanism of these complicated arrangements.

In the *second place*, it would appear that the stimulus to muscular contraction is the presence of blood, or rather the presence of blood under a certain pressure, in the cardiac cavities.¹ If the pressure is too low the stimulus is insufficient, and the muscle does not contract. If, on the other hand, the pressure is too great over-distension and a paralytic condition may result. Indeed the recently published experiments of Sewall and Donaldson seem to prove "that, within its working limits of internal pressure, the heart muscle has a remarkable power of accommodating the intensity of its discharges of energy, to the resistance to be overcome."²

"A fact continually forced upon our attention," say these writers, "was the great dependence of the systole, as to its energy and completeness upon the amount of fluid within the heart. Particularly was this noticed in regard to the thin walled sinus and auricles, when isolated in the manner to be described. Within tolerably low fluid pressures, the sinus and auricles become so distended as to be powerless to contract; as the pressure within them is reduced they contract feebly, and when the quantity of blood flowing into them is only just sufficient to bring about full distension during diastole, they contract powerfully, and empty themselves completely at each vent. As the supply of blood is further lessened by lowering the pressure flask, the contractions apparently again become feebler, and in the sinus hardly visible."³

"The exact manner in which the cardiac muscle is stimulated

¹ In some of the lower animals, the frog for instance, the heart continues to beat even after the cavities have been cleared of blood, and indeed when they are almost empty of fluid. In the frog, therefore, the presence of blood is not absolutely necessary to produce cardiac contractions, but it is nevertheless probable that the pressure of the blood in the cardiac cavities, under ordinary circumstances, acts as a stimulus, and excites the contraction of the cardiac muscular fibres.

² 'The Journal of Physiology,' vol. iii., p. 361.

³ Loc. cit., p. 361.

by the presence of blood under a certain pressure is obscure. If the muscular contraction can occur independently of the ganglia, we must suppose either that the muscular fibre is *directly* stimulated by the mechanical stretching which it undergoes when the cardiac cavities become distended; or, that the contraction is indirect, and is due to stimulation of the fine nerve fibres¹ which, as Schweigger-Seidel² has shown, form a rich plexus in the endo-cardium. If we grant that the ganglia are concerned in the process, we may suppose, as some physiologists have for long held, that the mechanism is a reflex one. A cardiac ganglion-cell may be regarded as the centre of a reflex arc, to which a sensory nerve fibre passes from the endo-cardium, and from which a motor nerve fibre proceeds to the cardiac muscle (see fig. 1); the reflex mechanism being thrown into action by the presence of blood, under a certain pressure, in the cavities of the organ.

Fig. 1.

FIG. 1.—*Diagrammatic representation of the reflex mechanism by which (it has been theorised) the cardiac muscle (or muscular coat of the blood-vessels) is thrown into contraction, under the influence of the blood pressure.*

E' E, the endo-cardium; B, the blood in the cardiac cavity; M, the muscular fibre of the heart; G, ganglion cell, the reflex centre; n, sensory nerve fibre conducting the impression generated by the blood pressure on the sensory nerve terminations under the endo-cardium to the reflex centre; n', motor nerve fibril conducting the impulse from the reflex centre to the muscle.

In the case of blood-vessels, E E' is the endothelium; the other references will be readily understood.

In the *third place*, the experiments of Gaskell, and of Sewall and Donaldson, seem to show that in the frog and tortoise at least, and when the heart is acting normally, the motor impulse originates in the sinus, and passes from the sinus to the muscular fibres of the auricle, and thence to the ventricle, the rhythm of the sinus determining that of the whole heart.

¹ This view necessarily supposes that these fine nerve fibres are motor.

² Quoted by Power, Carpenter's 'Physiology,' p. 276.

Those authorities who believe that the automatic action of the heart is due to the periodical discharge of its motor ganglia, necessarily conclude, in order to explain these results, that the action of the ganglia, which are situated in the sinus venosus, is more powerful than that of the ganglia situated in other parts of the organ; and indeed some authorities have supposed that the ganglia of the sinus venosus are the true automatic centres, while the action of the other ganglia requires to be excited reflexly, or in some other manner. The supporters of the neurotic theory further believe that the sequence of the cardiac contractions (the fact that the contraction of the auricle follows at a regular interval upon the contraction of the sinus, and the contraction of the ventricle at a regular interval upon that of the auricle) is due to nervous influences.

Dr. Gaskell, whose experiments seem to show, as I have already mentioned, that the automatic rhythm originates in the muscular tissue itself, explains the fact that the contractions originate in the sinus, by the peculiar structure of the cardiac muscle in this part of the heart; while he states that the sequence of the contraction of the ventricle to the auricle is not due to separate stimuli passing along nerve fibres from the sinus to the ventricle—not, in short, to any nervous mechanism—but to the fact that a wave of contraction passes directly from the muscular fibres of the auricle to the muscular fibres of the ventricle, through the muscular fibres forming the auriculo-ventricular groove. The pause, or, more correctly, the alteration of rate in the progress of the contraction wave, which takes place between the contraction of the auricle and the contraction of the ventricle, is, he says, due to an alteration in the conducting power, which naturally exists at the auriculo-ventricular ring. "This diminished conducting power or natural block, exists not only because the auriculo-ventricular muscular ring is narrow, and that a somewhat abrupt change occurs in the direction of the muscular fibres along which the contraction wave passes when it reaches and leaves this ring, but essentially because the structure of the muscular fibres here is different from those of the auricle or ventricle.

"The muscle fibres throughout the heart¹ are," he states, "of the same type, any differences which are seen are differences in the prominence of the various structural peculiarities of the cardiac type of muscle, and are not so great as the differences between unstriated and striated muscle fibres. Thus all the muscle fibres are, to a greater or less extent, transversely striated; but the prominence of this striation varies considerably. Similarly the thickness of the fibre, the extent of parallelism of its edges, the size of the nucleus in relation to the size of the fibre, and therefore the extent of crowding of the nuclei in any strip, all present differences in different parts of the heart. The greatest contrast is seen when the muscular fibres of the ground layer in the sinus are teased out and compared with the muscle fibres of the spongy

¹ He is speaking, it must be remembered, of the adult heart of the tortoise.

tissue of the ventricle. The sinus muscle fibre is thin and delicate, tapering somewhat at both ends, with a large central oval nucleus which causes a distinct bulging of the fibre; the substance of the fibre shows a striation which is decidedly indistinct, presenting often a granular rather than a distinct banded appearance. On the other hand, the ventricular muscle fibre is boldly and strongly striated, it is much thicker than that of the sinus, its edges are parallel, and the thin elongated nucleus is small in comparison to the size of the fibre. The muscle fibres of the reticulated tissue of the auricle are not so large or so coarsely striated as those of the ventricle, though larger and much more distinctly striated than the sinus muscle fibres. Their edges also are more parallel than in the fibres of the sinus. The muscular ring forming the junction of the auricles and ventricle, and to a certain extent the whole junction wall joining the two auricles, are composed of muscle fibres, with a structure intermediate between the sinus and the auricle muscles. The nuclei are large, conspicuous on section both in size and number, the striation is not so well marked as in the bulged portion of the auricles, and the fibres are thin and delicate with somewhat parallel edges.

"Such a structure as above described is very suggestive, not only as an explanation of the causes which occur naturally in the course of the peristaltic wave of contraction, but also of the differences of rhythmical power exhibited by different parts of the heart."¹

Dr. Gaskell, therefore, conceives "that the variations in the rhythmical power and in conductivity, which are characteristic of the different parts of the adult heart of the tortoise, may all be accounted for on the supposition, that the development of the muscular tissue of the originally tubular heart has not proceeded at the same rate throughout the tube, so that in the adult heart greater variations in rhythmical power are apparent in the different sections of it, than in the original tubular heart; the peristaltic wave of contraction which originally passed smoothly from end to end, passes finally along a tube of irregular calibre, the muscular walls of which have become so modified in their rates of contraction and conduction, as well as in the arrangement of the fibres, as to form out of a simple peristaltically contracting tube such an efficient muscular pump as is represented by the adult heart."²

"The conception advanced above, that the rhythmical beating of the heart is due to a series of peristaltic contractions which start from that particular portion of the muscular tissue of the heart in which the property of automatic rhythm has been most largely developed, brings the heart's action into harmony with the rest of the vascular system and with the rhythmical properties which are so often manifested by the less specialized forms of muscular tissue."³

Space will not allow me to detail the facts and arguments on

¹ Loc. cit., pp. 72, 73.

² Loc. cit., p. 77.

³ Loc. cit., p. 80.

which Dr. Gaskell founds this theory, which obviously has most important practical bearings on the pathology of the human heart. I would, however, strongly advise my readers to peruse the original for themselves.

In the *fourth place*, Gaskell has distinctly proved that the ventricle is supplied with afferent nerve fibres, which are "able to regulate the force of the auricular contractions, as well as in all probability the rate of rhythm. It is then conceivable that the function of many of the nerve fibres which pass into the ventricle is by their action upon the force of the auricular contractions to regulate the amount of blood thrown into the ventricle, and therefore the amount of work done by the heart."¹

But although the movements of the heart are automatic, it is intimately connected both with the sympathetic and cerebro-spinal nervous centres; and its action can, as each one of us so well knows, be readily affected by general nervous influences. But in order that this most important and difficult part of our subject may, if possible, be clearly understood, I must now describe the nervous supply of the heart in some detail.

A description was here given of the nerves supplying the heart, and the subject was illustrated by means of a large coloured drawing, of which the wood-cut on p. 516 is a copy.

THE MANNER IN WHICH THE VAGUS AND SYMPATHETIC NERVES AFFECT THE HEART.

I have now described the construction of the mechanism concerned in the innervation of the heart, and I must next point out the manner in which that mechanism works.

We have already seen that while the movements of the heart are automatic (i.e., are due to impulses arising within the heart itself), they can be profoundly modified by the condition of distant parts; and that the impulses which produce these modifications are conveyed to the heart through certain branches of the pneumogastric and sympathetic nerves. Now, until recently, we might have summed up the effects of these impulses by saying, that *impressions passing to the heart through the pneumonogastric retard, while impressions passing to the heart through the sympathetic accelerate its movements* (hence the terms "*inhibitor*" and "*accelerator*" of the heart which are given to the two nerves respectively); but recent observations seem to show that the action of the vagus on the heart is much more complicated, and that it affects not only the rhythm, but also the force of the cardiac contractions, and that it exerts a trophic influence upon the cardiac muscle. It will be necessary, therefore, to consider each of these functions separately.

The Inhibitory Action of the Vagus.

As the result of the laborious investigations of many able observers, physiologists have concluded:—*Firstly*, that there exists

¹ Loc. cit., p. 92.

in the medulla oblongata a cardio-inhibitory centre, which is continually exerting a restraining influence upon the heart; and *Secondly*, that the action of this cardio-inhibitory centre may be intensified, i.e. the action of the heart may be still further retarded by:—

(a) Direct stimulation, i.e. by certain changes in the medulla itself.

(b) Impressions passing to it from the brain.

(c) Impressions passing to it from peripheral parts (reflex stimulation).¹

“Some authorities also believe that the cardio-inhibitory centre may itself be inhibited, i.e., its restraining power taken off the heart, by impressions passing to the medulla from other parts of the central nervous system, or from the periphery.”

The most important local changes which stimulate the cardio-inhibitory centre, appear to be increased blood-pressure within the cranium, and irritative lesions in the medulla or in the neighbourhood of the vagi roots, e.g., inflammatory affections at the base of the brain, etc.; while reflex inhibition of the heart seems to be chiefly brought about by impressions passing to the medulla from the abdominal viscera.²

It has also been supposed that the action of the heart may be inhibited by impressions passing from the heart itself. Rutherford's experiments certainly seem to show that reflex inhibition of the heart can be produced in the rabbit by stimulation of the central cut end of the superior cardiac nerve, the impression passing up to the cardio-inhibitory centre in the medulla oblongata, and back, through the vagus and its inferior cardiac branch, to the heart.

“The *superior cardiac branch* arises by two roots, one connected with its superior laryngeal branch crosses down the neck close to the cervical sympathetic, and joins one or two branches of the inferior cervical ganglion with which it proceeds to the heart. This branch is a purely sensitive nerve; and is in fact the sensitive nerve of the heart. On cutting it across, and stimulating its inferior (peripheral) end no effect is produced; while stimulation [p. 518]

¹ Whether the action of the cardio-inhibitory centre is automatic or not, is still undecided.

² Powerful stimulation of any afferent or sensory nerve can probably produce reflex inhibition of the heart. Rutherford found that the cardio-inhibitory fibres of the vagus may be thrown into action by stimulating: (1.) The central end of the vaso-inhibitory or superior cardiac branch of the vagus (depressor nerve); (2.) The central end of the vagus of the opposite side; (3.) Almost any sensory nerve, in the case of warm-blooded animals; (4.) The abdominal viscera of the frog; (5.) The splanchnic and sympathetic.—‘Lancet,’ Dec. 16, 1871, p. 483. Michael Foster states that “the regulative action of the inhibitory mechanism is brought into more or less close connection with all parts of the body.”—‘A Text Book of Physiology,’ p. 174.

FIG. 2.

Description of FIG. 2.—Semi-diagrammatic representation of the nervous supply of the heart.

RCP, right, and LOP, left coronary plexuses; SCP, superficial cardiac plexuses; DCP, right, and D'C'P', left half of the deep cardiac plexus; P, right, and P', left pneumogastric nerves; 1CG, right, and 1'C'G', left superior ganglia of the sympathetic; 2CG, right, and 2'C'G', left middle ganglia of the sympathetic; 3CG, right, and 3'C'G', left inferior ganglia of the sympathetic; RV, right, and LV, left ventricles; RA, right, and LA, left auricles; SVC, superior vena cava.

1cn, 2cn, 3cn, 4cn, 5cn, 6cn, 7cn, 8cn, branches of the right, first, second, third, fourth, fifth, sixth, seventh, and eighth cervical nerves, proceeding to the sympathetic ganglia.

1'cn', 2'cn', 3'cn', 4'cn', 5'cn', 6'cn', 7'cn', 8'cn', branches of the left, first, second, third, fourth, fifth, sixth, seventh, and eighth cervical nerves, proceeding to the sympathetic ganglia.

1DG, right, and 1'D'G', left first dorsal ganglia of the sympathetic; 1dn, branches of the right, and 1'd'n', left first dorsal nerves proceeding to the first dorsal ganglia of the sympathetic.

SL, right, and S'L', left superior laryngeal branches of the pneumogastric; EL, right, and E'L', left external laryngeal nerves; rel, right, and r'e'l', left recurrent laryngeal nerves at lower part of neck, and in the thorax respectively.

a, branch from right coronary plexus to right auricle; b, branch from right coronary plexus to right ventricle; c, branch from the superficial cardiac plexus to the right coronary plexus; d, branch from the right half of the deep cardiac plexus to the right coronary plexus; e, branch from the left half of the deep cardiac plexus to the left coronary plexus; f, branch from the right half of the deep cardiac plexus to the left coronary plexus; g, branch from the left coronary plexus to the left auricle; h, branch from the left coronary plexus to the left ventricle; i, branch from the left coronary plexus to the right ventricle.

1CN, right, and 1'C'N', left first or superficial cardiac nerves.

2CN, right, and 2'C'N', left middle cardiac nerves.

3CN, right, and 3'C'N', left inferior cardiac nerves.

1, branch from the right, and 1', branch from the left external laryngeal nerves to the superior cardiac nerves; 2, branch from the right, and 2', from the left pneumogastric nerves to the superior cardiac nerves; 3, communicating branch from the right, and 3', from the left recurrent laryngeal nerves to the first cardiac nerves on the right and left sides respectively; 4, communicating branch between the right, and 4', communicating branch between the left superior and middle cardiac nerves; 5, communicating branch between the right, and 5', between the left middle cardiac and recurrent laryngeal nerves respectively; 6, communicating branch between the right, and 6', communicating branch between the left, middle and inferior cardiac nerves; 7, communicating branch between the right, and 7', between the left inferior cardiac nerves and the recurrent laryngeal respectively; 8, communicating branch between the right inferior cardiac nerves and the trunk of the pneumogastric, 8', on the left side this branch of the pneumogastric proceeds directly to the superficial cardiac plexus; 9, 9, branches from the trunk of the right pneumogastric, and 9', from the left recurrent laryngeal nerve to the right and left halves respectively of the deep cardiac plexus.

of its upper (central) end causes pain, retardation of the heart, and, as I shall afterwards more particularly point out, such a striking diminution of blood-pressure, that the term *depressor* nerve has been given to it.

"In the rabbit the vagus gives two branches to the heart, a superior and an inferior cardiac branch (see Fig. 3).

FIG. 3.—The last cervical and first thoracic ganglia in the rabbit. (Left side.) (Somewhat diagrammatic, many of the various branches being omitted.) (After Foster.)

Trach., Trachea. *Ca.*, carotid artery. *sb.*, subclavian artery. *n. Vag.*, the vagus trunk. *n. rec.*, the recurrent laryngeal. *sym.*, the cervical sympathetic nerve, ending in the inferior cervical ganglion, *gl. cerv. inf.* Two roots of the ganglion are shown, *rad.*, the lower of the two accompanying the vertebral artery, *A. vert.*, being the one generally possessing accelerator properties. *gl. thor. pr.*, the first thoracic ganglion. Its two branches communicating with the cervical ganglion surround the subclavian artery, forming the annulus of Vieussens. *sym. thor.*, the thoracic sympathetic chain. *n. dep.*, depressor nerve, which, though running by the side of the sympathetic, is really a branch of the vagus, from which it separates higher up. This is joined in its course by a branch from the lower cervical ganglion, there being a small ganglion at their junction, from which proceed nerves to form a plexus over the arch of the aorta. It is this branch from the lower cervical ganglion which possesses accelerator properties—hence the course of the accelerator fibres is indicated in the figure by the arrows.

"The *inferior cardiac* branch leaves the vagus below the origin of the inferior laryngeal nerve, and proceeds directly to the heart.

It is a purely motor nerve, and stimulation of its inferior cut-end gives rise to the same effects as stimulation of the vagus itself (i.e., stimulation above the origin of this branch), viz. (with weak currents) retardation of the heart from prolongation of the diastole, and (with stronger currents) complete arrest during diastole."

In the human subject, two branches of the vagus seem to correspond to the superior cardiac branch of the vagus in the rabbit; while the inferior cardiac branch of the vagus of the rabbit seems to be (mainly at all events) represented in man by the large branch which leaves the vagus trunk at the lower end of the neck (inferior cervical branch).

Now it has been supposed that these two nerves, together with the cardio-inhibitory centre in the medulla, constitute a reflex arc; and that stimulation of the peripheral terminations of the superior cardiac nerve in the heart may generate an impulse which, being conveyed to the cardio-inhibitory centre, and being reflected back to the heart along the vagus, may retard the action of the heart. Whether the superior cardiac nerve has any special function of this description, other than is possessed by all sensitive nerves, is extremely doubtful; and it seems certain that increased blood-pressure within the heart, as a whole, does not, as was at one time supposed, produce reflex inhibition of the organ.

Physiologists are not yet agreed as to the exact manner in which the vagus causes inhibition of the heart.

Until quite recently it was believed that while weak stimulation of the nerve prolonged the diastole, the duration of the ventricular systole being very little affected, more powerful stimulation caused complete arrest during diastole (complete relaxation), the next systole being as it were indefinitely postponed; and it was generally supposed that the vagus inhibited the contractions of the heart by preventing motor impulses being sent from the automatic ganglia to the muscle, i.e., by holding in, as it were, the motor energy of the ganglia; and this would appear to be the view which Sewall and Donaldson take. They think that their experiments "point pretty clearly to the conclusion, that the inhibitory action of the vagus nerve exerts itself in the same indirect manner (as a motor stimulus does), influencing the ventricle by damping in sinus and auricles the excito-motor discharges arising in these parts of the heart."¹

Dr. Gaskell takes a different view. He has shown:—*Firstly*, that the vagus is able to modify all the great functional attributes of the cardiac muscle, viz.:—

(a.) The rate at which automatic contractions are produced. (The *automatic rhythm*.)

(b.) The force with which the contractions, more especially the contractions of the auricle, are carried out. (The *force of contraction*.)

¹ Loc. cit., p. 367. 'Journal of Physiology,' iii.

(c.) The facility with which the contractions are conducted by the muscular fibres. (*The power of conduction*).¹

Secondly, that it sometimes produces depression, at other times exaltation of function.

He believes that the vagus may produce standstill or inhibition of the heart (auricles and ventricles) in the three following ways:—

(1.) By producing cessation of its automatic contractions, i.e. by depressing the rhythmical power of the muscular fibres of the sinus in which the automatic rhythm originates. (This has been established in the frog, tortoise, and snake.)

(2.) By reducing the force of the auricular contractions, so that they become invisible, i.e. by depressing the contraction power of the rapidly contracting reticulated muscular fibres of the auricle. (Frog.) The contractions he states may be so small as only partly to be visible, so that to the naked eye the heart appears to stand still.

(3.) By blocking the contraction wave at the sino-auricular ring, i.e. by depressing the conducting power of the muscular fibres connecting the sinus and auricle. (Snake, tortoise, frog.)

The Trophic Function of the Vagus.

As I have previously remarked, Dr. Gaskell² has advanced the important theory that the vagus is the trophic nerve of the heart. "Although," he says, "the initial effect of the vagus is to depress some function, its final and most enduring power is to exalt, intensify, and repair that function. Thus, although it slows rhythm, yet its stimulation makes the rhythmical power last longer than it otherwise would, and makes the heart beat with regularity when it was previously irregular; although it reduces the force of the contractions, yet its ultimate effect is to improve and sustain the contraction force, although it may diminish the conduction power, yet in the end it completely repairs that power. *For these reasons*," he says, "*I look upon the vagus as essentially the trophic nerve of the heart.*"

Since this chapter was written I have learned from Dr. Gaskell that the term "trophic" as it is commonly used and understood does not exactly express the function which he supposes the vagus to have over the cardiac muscle. "I have felt," he says, "all along that the word trophic is somewhat misleading as applied to the results of my experiments on the action of the vagus. I wanted a word to express what appears to me to be the fact, in the cold-blooded animals at all events, that the inhibitory process is not destructive but constructive in its nature, but could not find any good term. I therefore used the term 'trophic,' not

¹ In the tortoise the force of the contractions of the ventricle was uninfluenced by vagus stimulation. In the frog, on the other hand, the vagus influences the force of the ventricular as well as of the auricular contractions.

² Loc. cit., p. 104.

perhaps in its usual sense, but rather in a sense similar to that of Heidenhain when he divides the nerves supplying the sub-maxillary gland into secretory and trophic."

The Mode of Action of the Vagus on the Heart.

The exact manner in which the terminal fibres of the vagus are brought into relation with the cardiac muscle is unknown. The effects produced by vagus stimulation, and by the action of certain poisons, have led some physiologists to believe that the arrangement is an extremely complicated one; and in order to explain these results, they have theorised that there existed an inhibitory mechanism within the heart itself, the action of which is strengthened (brought into play) by impressions carried to it by the terminal branches of the vagus, and which in its turn acts upon, i.e. inhibits the ganglionic apparatus more immediately concerned in the production of the rhythmical movements of the heart, i.e. the automatic nerve mechanism.

"The facts and arguments which they have advanced in support of the view that the vagus does not act directly upon the cardiac muscle, but that it acts through some intermediate nerve apparatus are as follows:—

"1. The latent period, which elapses between electrical stimulation of the vagus and the production of its inhibitory action on the heart is twenty times longer than that which elapses between the electrical stimulation of an ordinary motor nerve, and the contraction of its muscle, viz. $\frac{1}{3}$ th and $\frac{1}{100}$ th part of a second respectively.

"2. A very much stronger current is required to produce inhibition of the heart through the vagus, than is required to produce spasm of a voluntary muscle, when its motor nerve is stimulated.

"3. If the action of the heart be arrested by stimulation of the vagus, the rhythmical contractions after a time return, although the stimulation of the vagus be continually kept up, a fact which may be explained either by supposing that the inhibitory fibres of the vagus become gradually exhausted by the prolonged stimulation, or that the accumulation of nerve force in the automatic ganglia becomes after a time too great to be held back, and that an explosion and muscular contraction consequently take place.

"4. Continued stimulation of one vagus annuls or prejudices the action of the other.

"5. 'The effects of vagus inhibition are perhaps more marked when the electrodes are placed on the boundary line between the sinus venosus and the auricle, than over the vagus trunk itself.'—*Foster*.

"6. If during the complete relaxation which results from powerful stimulation of the vagus, the muscular tissue be mechanically irritated, it is still found to contract.

"While the existence of an intermediate (intra-cardiac) in-

hibitory mechanism between the terminal fibres of the vagus and the automatic nerve apparatus they think is proved by the following circumstances:—

"1. When the electrodes are placed on the boundary line between the sinus venosus and the auricles, more powerful inhibition is produced than when they are applied to the vagus itself.

"2. After the administration of urari, stimulation of the vagus no longer produces inhibition of the heart, but stimulation in the region of the sinus venosus will still do so.

"3. After the administration of atropia, neither stimulation of the vagus nor of the sinus produces any inhibitory effect. It is therefore concluded that atropia paralyzes the intra-cardiac inhibitory apparatus itself.

"4. Muscarin and jaborandi in full doses produce exactly the same effect which is produced by powerful vagus stimulation, viz., complete arrest during diastole, an effect which is not prevented by the previous administration of urari, which, as we have seen paralyzes the terminal fibres of the vagus, but does not touch the inter-cardiac inhibitory mechanism; but which is prevented by the previous administration of atropia which paralyzes the intra-cardiac inhibitory mechanism. Hence it is concluded that muscarin and jaborandi stimulate the intra-cardiac inhibitory mechanism."

Dr. Gaskell's view as to the mode of action of the vagus is different. He has shown that the action of the vagus on the cardiac muscle is in many respects identical with the action of a weak interrupted current. He believes that the nerve acts directly upon the muscular fibre itself, and he argues that the action of atropin, muscarin, and some of the other cardiac poisons to which I have referred above, can be consistently explained upon this view.¹

¹ "Both atropin and muscarin," he says, "produce the effects above mentioned, by directly modifying the various functions of the cardiac muscle, and in proportion to the stability of the effect so produced is the possibility of a modification of that effect by the direct stimulation of the muscle or by the action of the cardiac nerves. It is partly because the atropin acts on the muscular tissues in such a way as to keep the various muscular powers fixed in a relatively high state of activity, that the cardiac nerves are unable any longer to depress those powers. It is because atropin is able to restore the rhythmical power of the muscle, that stimulation of the vagus and of the sinus is no longer able to produce inhibition; it is because the atropized muscle contracts with the very first stimulus at its full strength, that neither the cardiac nerves nor the interrupted current is any longer able to diminish these contractions; it is because atropin repairs the conducting power that stimulation of the vagus is no longer able to prevent the contraction wave passing from the sinus into the auricles." Again, "atropin not only prevents the action of the vagus nerves by its direct influence on the cardiac muscle, but also by its action on the intra-cardiac nerves themselves, and perhaps especially on their ganglionic nerve cells. Muscarin, on the other hand, influences the muscular tissues, leaving the nervous action intact, at all events, until a very large dose

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

"In this paper as well as in my previous paper, all the facts have tended strongly to prove that the vagus acts in the same manner upon the rhythm of the heart, and upon the force of its contractions, so that if separate inhibitory and accelerator nerve

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has been given. . . . Atropin then not only influences the muscular tissue, but also the nervous structures of the heart in such a way that neither the direct action of the interrupted current nor stimulation of the vagus nerves are any longer able to produce their usual effects upon the various functions of the cardiac muscles.

"The views put forward in this paper," he says, "necessitate a revision of the opinions at present held in respect to the action of a large number of cardiac poisons. The difference between the action of curare and atropin is one of the main arguments in favour of the existence of an inhibitory centre capable of being paralysed by atropin, but not by curare. Both poisons prevent the inhibitory action of the vagus nerve; but while after curare inhibition can still be caused by the direct stimulation of the venous sinus; after atropin this is no longer possible. The inhibition caused by muscarin can be removed by atropin, but not by curare. These facts do not, in my opinion, in the slightest degree prove the existence of an inhibitory centre; they simply confirm the well-known fact that curare is essentially a poison which affects nervous and not muscular stimulus, and give another proof of the affinity of the cardiac muscle and nerve to the ordinary striated muscle and nerve. Thus curare prevents the inhibitory action of the vagus, because it paralyses some part or other of the nerve endings. It does not prevent the inhibition caused by the direct stimulation of the venous sinus, because, unlike atropin, it does not act upon the muscular tissue of the sinus, and therefore cannot prevent the inhibitory action of the current applied directly to that muscle. For the same reason it is unable to influence the inhibitory action of a muscular poison like muscarin."—"Journal of Physiology," vol. iv., No. 2, pp. 114-116.

fibres exist for the one, separate depressor and augmentator fibres must exist for the other. If, therefore, it can be shown that such diminution and augmentation of the rhythm of the contractions are due not to different influences reaching the muscle, but to the same influence affecting the muscle when its conditions are different, then it is, to say the least, highly probable that slowing and acceleration are also due, not to different nerve fibres, but to the action of the same nerve fibre under different circumstances. In the frog, as I have previously pointed out, such a complete gradation exists between a primary excessive diminution of the contractions and a primary augmentation in consequence of nerve stimulation, as to render the hypothesis that such curves depend upon the simultaneous stimulation of two antagonistic nerve fibres very improbable. I have now proved in addition, that a weak interrupted current applied to the smallest strip of cardiac muscle produces the same two opposite effects, and that here the depressing effect may be removed and the augmenting alone remain, when the condition of the muscle is altered by the application of atropin. In order, therefore, to still hold to the view of specific nerve fibres acting in opposite directions upon the force of the contractions, it is necessary to assume, not only that those nerve fibres possess opposite qualities up to their very termination in the muscle, but that even when the muscle itself is stimulated, the relative action of these two sets of nerves still holds its ground. In addition, atropin would have to be considered as acting upon these two sets of nerve endings, and not upon the muscle, paralysing the depressor nerve endings before those of the augmentor nerves. The experiments of Luchsinger and Szpilman, which lead them to the conclusion that atropin has a special action upon unstriated muscular fibre, those of Bowditch, already referred to, and my own, all point to the conclusion that atropin affects the cardiac muscle directly in consequence of its affinity to unstriated muscle fibre. The whole evidence goes to show that the vagus is a constructive and not a destructive nerve, that the initial depression of function is not of the nature of exhaustion, but is preliminary to a greater functional activity. The phenomenon presented by the muscular tissue of the frog and tortoise under the influence of an induced current, is of exactly the same nature as that seen in the muscle of the snail's heart (as pointed out by Foster and Dew-Smith) when a constant or weak interrupted current is sent through it. In both cases augmentation of function occurs as well as depression; in the one case the evidence is as strong in favour of special inhibitory and accelerator nerves as in the other. Clearly, in the case of the snail, it is simply impossible, as Foster has said, to explain such results by the presence of accelerator and inhibitory fibres in every strip of muscular tissue, when, as a matter of fact, cardiac nerves of any kind whatever have not been proved to exist. Clearly also, whatever explanation will ultimately be found for the action of the current upon the muscular tissue of the snail's heart, will also explain the same phenomena in the heart of the frog and tortoise. The problem which demands

solution is essentially, Why is the condition of the muscle ultimately improved in every one of its functions by the direct application to it of a continuous stimulus, which is not strong enough to produce motor effects? and why is it that improvement of function is preceded in many cases by a diminution of function? When these two questions have received a satisfactory answer, it will no longer be strange that the vagus produces throughout two opposing effects, and the action of atropin will become clear; then the relationship between trophic and motor action will be understood, and the true functions of the ganglion cells found in connection with nerve fibres will be indicated. At present it can only be said that the vagus is the trophic nerve of the cardiac muscle, its action resembling that of a stimulus too weak to produce motor effects, and therefore it is possible that the function of the ganglion cells, in the course of the nerve, is to convert an otherwise motor into a trophic nerve."¹

"This argument," Dr. Gaskell writes me, is based upon experiments upon cold blooded animals, how far it applies to the warm blooded I (Dr. Gaskell) do not yet know. Eichhorst and Tander conclude that the vagus in the warm blooded contains trophic fibres."

The action of the sympathetic upon the heart is even less clearly understood than the action of the pneumogastric, but it is believed that there exists in the medulla oblongata (or possibly above it), a centre, stimulation of which produces increased frequency of the heart's beat, and it is supposed that this accelerator, or cardiac-motor centre, as it is sometimes called, may be stimulated, i.e. the frequency of the heart's beat may be increased either by direct or reflex stimuli. The influences which throw this centre into action have not been very accurately ascertained, but it is probable that emotion excites the heart through the agency of the accelerator nerves; while diminished blood pressure within the cranium is supposed to stimulate them.

Impulses generated in this centre, the action of which, be it observed, is supposed to be intermittent (and in this respect to differ from the action of the cardio-inhibitory centre, which is supposed to be constant), appear to pass down the lateral column of the cord to the lower end of the cervical region, whence they pass through the nervi communicantes, to the (?) middle and inferior cervical ganglia of the sympathetic, and thence to the heart.

"According to Prof. Michael Foster the accelerator nerves frequently pass along the nerves accompanying the vertebral

¹ It may appear to some that I have entered into undue physiological detail in dealing with this subject, but it must be remembered that the mode of action of drugs is of the greatest interest in connection with the therapeutics of the heart. Further, I am fully convinced that it is only by attention to these minute physiological details that the physician can hope to make much advance in cardiac pathology, a subject on which our knowledge of the ordinary details of morbid anatomy is already so far advanced.

artery, and reach the heart through the last cervical and first dorsal ganglia."¹

It is supposed from the long latent period which elapses between stimulation of the accelerator and the production of its specific action on the heart, that its fibres terminate in an intermediate ganglionic apparatus similar to that which I have already described in speaking of the termination of the pneumogastric.

Now, although the pneumogastric acts as inhibitor, and the sympathetic as accelerator, it must not be supposed that their action is directly antagonistic. That such is not the case seems abundantly proved by physiological observation. Physiologists have shown, says Dr. M. Foster, that "if during maximum stimulation of the accelerator nerves, the vagus be stimulated even with minimum currents, inhibition is produced with the same readiness as if the accelerator nerves were not acting. Vagus stimulation does not annul, but appears simply to suspend, during its continuance, the manifestation of the accelerator action."²

The Relationship between the Heart and the minute Blood-vessels.

In order to conclude the description of the innervation of the heart, I must shortly direct attention to the intimate relationship which exists between the heart on the one hand and the peripheral blood vessels on the other, and to the beautiful self-adjusting mechanism by which alterations in the one are of necessity followed by corresponding changes in the other.

We have already seen the fundamental importance of looking at the heart both as a mechanical pump and as a vital organ; and another point which I must now insist upon—and it is hardly of less importance whether we are studying the heart from a physiological, a pathological, or a clinical point of view,—is *the necessity of taking an all-round view*, so to speak, *of the circulation*. Indeed it is essential to remember that the heart is only a part of the vascular mechanism, and that the condition of the circulation, and consequently the condition of the heart (for the organ naturally adapts itself to the amount and kind of work which it has to perform) depend in no small degree upon the condition of the peripheral resistance, which is in its turn mainly due to the obstruction which the blood meets with, in passing through the minute arteries.

In conditions of health, the minute arteries are always more or less constricted in consequence of a permanent contraction of their middle or muscular coats, and it is to this 'tonic' contraction that the peripheral resistance is in great part due. [The peripheral resistance depends also upon the facility with which the blood passes through the capillary system of vessels; and

¹ The middle and lower cervical ganglia in man appear to correspond to the lower cervical and first dorsal ganglia in the rabbit, through which accelerator impulses have been proved to pass, as shown in Fig. 2.

² 'Text Book of Physiology,' p. 175.

since the blood flow through the capillaries may be influenced by alterations in (a) the conditions of the capillary walls, (b) the condition of the tissues outside the capillary walls, and (c) the composition of the blood itself, all of these factors must be taken into consideration as causes of peripheral resistance, and of variations in the blood pressure. In conditions of disease variations in the blood pressure may result from alterations in the "capillary resistance," but these variations are, in my opinion, never so great, either in conditions of health or disease, as those which are due to alterations in the condition of the muscular coat of the minute arteries.]

The degree of constriction is constantly undergoing variations even in health, and is subject to marked alterations in some diseased conditions; hence the amount of resistance which the heart has to overcome in forcing the blood into the capillaries, is constantly changing; and to meet sudden variations of this description a delicate self-adjusting nervous mechanism is provided. But in order that this part of our subject may be properly understood, I must now describe the mechanism by means of which the arterial "tone" is regulated.

There seems good reason to believe:—

(1) That the tonic constriction of the muscular coats of the minute arteries is (immediately) due to the presence of a peripheral neuro-muscular or (purely) muscular apparatus, which may be thrown into action by local stimuli, the most important of which is the blood pressure.

"The peripheral mechanism concerned in this maintenance of arterial 'tone' probably bears a close resemblance to the peripheral mechanism concerned in the production of the rhythmical movements of the heart.

"Ganglionic masses can be demonstrated in the walls of many of the minute blood-vessels, and it has been by some authorities supposed that the blood pressure produces stimulation of the muscular coats of these vessels in a reflex manner (see Fig. 17); but in many vessels (e.g. those in the skin and muscle) no such ganglionic masses have as yet been demonstrated, and in their case we must conclude that the contraction of their muscular coats is due to direct stimulation of the muscular fibre itself, or of the terminal vaso-motor filaments which are distributed to it.

"The view, which supposes that the muscular fibre is itself stimulated by the blood-pressure, is probably the correct one."

(2) That the action of this peripheral neuro-muscular or purely muscular mechanism is, under ordinary circumstances, maintained and regulated by impulses which are being *constantly* sent to it from centres (vaso-constrictor centres) in the medulla and spinal cord, through the vaso-motor nerves; and that the action of these vaso-constrictor centres may be increased or diminished both by direct stimulation or in a reflex manner. In other words, the calibre of the minute arteries, and therefore the peripheral

resistance, may be increased or diminished by central and peripheral causes (stimuli).

"The vaso-motor (i.e. vaso-constrictor) centre of the medulla, which is probably bilateral, is situated immediately above the calamus scriptorius, and extends for some distance into the pons (to 1 or 2 mm. below the corpora quadrigemina). The conducting fibres proceeding from it are believed to pass through the lateral columns of the spinal cord, and to proceed to the blood-vessels chiefly through the sympathetic system of nerves. The vaso-motor centre of the medulla probably regulates the vascular system of the abdomen, the arteries of the skin and muscles being probably mainly supplied by vaso-constrictor fibres proceeding from the vaso-motor centres in the spinal cord. The exact position of these spinal centres is not ascertained.

"The action of the vaso-motor (i.e. vaso-constrictor) centres, which it will be remembered is supposed to be constant, may probably be intensified by:—

"(a) Increased blood pressure within the cranium, and local irritative lesions of the medulla.

"(b) Impressions proceeding from the cerebrum.

"(c) Impressions proceeding from the periphery. It has been experimentally proved that irritation of any afferent (sensory) nerve, such as the sciatic, will produce constriction of the minute blood vessels (especially those of the abdomen) and increased blood pressure, presumably by reflexly stimulating the vaso-motor centre in the medulla."

(3) That the action of the peripheral neuro-muscular mechanism may be inhibited by nervous impulses passing to it from certain centres in the medulla, and (?) spinal cord, through the vaso-dilator nerves; and that the action of the vaso-dilator centres, which is not constant, may be called into play by central and reflex stimulation.

The calibre of the minute arteries may therefore be increased, and the blood-pressure lowered either by inhibition of the vaso-constrictor, or by stimulation of the vaso-dilator centres in the medulla and (?) spinal cord.¹

"It is not absolutely certain that a distinct and separate vaso-dilator centre exists; some authorities in fact believe that the same centre may at one time evoke vaso-constrictor and at another vaso-dilator impulses; but it seems tolerably well ascertained that there are distinct fibres for the conduction of these two sets of impressions, and for theoretical and teaching purposes it is convenient to describe and represent a distinct vaso-dilator centre.

¹ It must be remembered that the inhibitory action of the vaso-dilators on a peripheral neuro-muscular or muscular mechanism, is theoretical, and it is not definitely proved. "It is quite possible," as Foster says, "that dilation may be brought about in different ways, in different cases, and so also with constriction."

—'A Text Book of Physiology,' p. 211.

"The exact course of the vaso-dilator conductors in the cord is yet undetermined, but it seems probable that they pass down in some part of the lateral columns, and reach the blood vessels chiefly through the cerebro-spinal (and not through the sympathetic) nerves.

"The vaso-dilator centre in the medulla is chiefly, if not exclusively, connected with the vessels of the abdominal viscera; and it is most readily thrown into action by stimuli passing to the medulla through the *depressor* nerve, and by impressions passing from the abdominal viscera through the splanchnics."¹

Now, as I have previously stated, a very striking diminution of blood pressure results from stimulation of the superior cardiac branch of the vagus or *depressor* nerve, as it has therefore been called. It is obvious, therefore, that there is an important connection between the heart and the vaso-dilator centre in the medulla, by means of which the heart and peripheral blood vessels are brought into such close physiological connection, that changes at one end of the circulation, so to speak, are at once attended by compensatory changes at the other. If, for example, the arterial blood pressure is from any cause suddenly increased, a sudden strain is necessarily thrown upon the left ventricle, and it might easily happen that the resistance in front was too great for the force of the pump. Under such circumstances paralytic distention of the left ventricle and death would follow, if it were not for the fact that the undue distention of the cavity and the effort which the heart is making to overcome the resistance, produce irritation of the terminal fibres of its sensitive nerve (the superior cardiac or depressor nerve), in consequence of which a powerful stimulus is sent to the vaso-dilator centre in the medulla, with the result that a sudden dilatation, of the capacious blood-vessels of the abdomen, occurs, and that there is a rapid fall of the blood pressure. The peripheral resistance is in this manner immediately diminished, and paralytic distention of the left ventricle prevented.

It has likewise been thought that the vaso-dilator and vaso-constrictor centres are also connected with the cardio-inhibiting centre in the medulla; and some physiologists have supposed that reflex inhibition of the heart might be produced by the stimulation of the sensitive nerve of the heart (superior cardiac nerve), which presumably occurs in conditions of over-distention of the organ.

¹ This description of the action of the vaso-motor mechanism is not complete. It must of course be remembered, that local variations in the blood supply are being constantly required by the ever-varying needs of particular times and organs, and that as Prof. M. Foster says, "the great use of the whole vaso-motor system is not to maintain a general arterial tone, but to modify according to the needs of the economy the condition of this or that vascular area" ('A Text Book of Physiology,' p. 213). But in studying cardiac affections the changes in the action of the heart, which are induced by local variations of this description, may, for practical purposes, be safely ignored. Hence I have limited my description to those alterations of the vaso-motor mechanism which are sufficiently general to produce definite changes in the action of the heart.

The recent experiments, however, of Ludwig and Luchsinger, and of Sewall and Donaldson, seem to prove that this is not the case, and that increased blood pressure within the heart, as a whole, generally weakens the inhibitory influence of the vagus. The last two observers, however, conclude "that changes of intra-cardiac pressure, *when experienced by the ventricle alone*" (no italics in the original), "are without effect on the cardio-inhibitory function of the vagus."¹ Possibly, therefore, when the ventricles only are over-distended, some reflex inhibition may occur; but even if it does occur, it certainly must be temporary and slight, for the main effect of stimulation of the sensitive nerve of the heart is reflex stimulation of the vaso-dilator centre, and consequent diminution of blood pressure throughout the body; and diminished blood pressure, as we have previously seen, tends to lessen rather than to increase, the inhibitory action of the vagus.

¹ Journal of Physiology, vol. iii., p. 363.