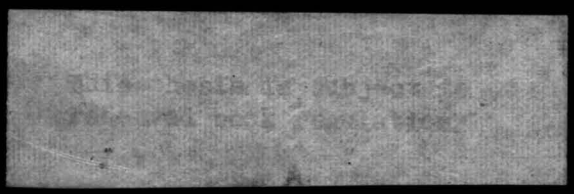

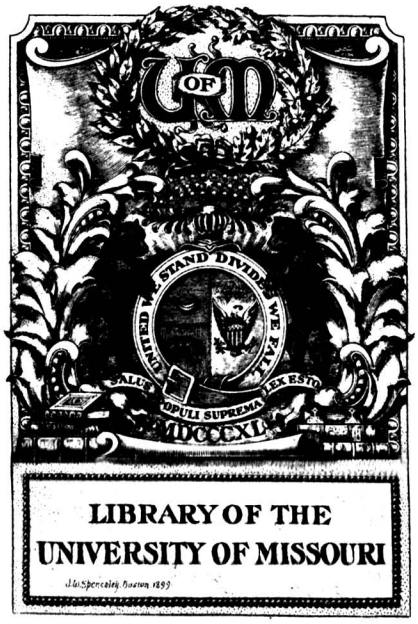

SOME FACTORS ON THE INNERVATION OF THE HEART WITH SPECIAL REFERENCE TO THE CARDIAC ACCELERATOR MECHANISM OF THE HEART OF THE TURTLE *EMYDOIDEA BLANDINGI*

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C O N T E N T S .

PART I

PART II.

PART III.

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A REVIEW OF THE LITERATURE

The Extra-cardiac Accelerator Nerves

The first suggestion of an accelerator nervous mechanism for the heart was given by Legallois[1] in 1812. He found in the dog and cat that stimulation of the cord by its sudden destruction produced an increase in the force of the beat. Von Bezold[2] used a better stimulating and recording apparatus than did Legallois and again raised the question of cardiac nerves other than the vagi. He did not, however discover the pathway of the augmentory impulses from the cord to the heart.

Ludwig and Thiry[3] sharply attacked the work of Von Bezold. They found that after destroying with a galvano-cautery all the nerves connecting the heart with the spinal cord and then stimulating the spinal cord electric-

ally, they got the same rise in blood pressure as did Von Bezold and which he ascribed to the action of the augmentary cardiac nerves.

The work of these men still left the question of cardiac accelerators undecided. In 1866 E. Von Cyon and Ludwig[4] discovered the depressor nerve and the vaso-constrictor action of the splanchnics. Using these discoveries as guides to further researches upon the heart they sectioned the vagi, the depressors, the cervical sympathetics and the splanchnics. Stimulation of the cord divided at the level of the atlas now gave an increase in the heart rate without any change in blood pressure. They proved that this acceleration was only produced so long as the sympathetic trunk remained intact. After extirpation of the inferior cervical ganglia and the superior thoracic ganglia on both sides there was no augmentation produced. By these experiments they clearly proved the existence of the cardiac accelerator nerves and their pathway to the heart. Von Cyon and Ludwig definitely stated the action of the accelerator nerves upon the heart in the following summary:- The accelerator nerves are not the motor nerves of the heart ending in its muscle, because (1) excitation of them does not produce tetanus of the heart. (2) Likewise they do not augment the work of the heart. Indeed we have

shown that the excursions of the column of mercury of the manometer falls while the number of beats are increased. (3) The heart possesses within itself the motor ganglia. (4) Curare does not paralyze the accelerator nerves. (5) The accelerator nerves are more than vaso-motor nerves to the heart, for an occlusion of the vessels does not produce acceleration of the beats. (6) These nerves do not join the ganglionic cells of the heart.

Finally they define the work of the accelerators as follows:- Their action consists in changeing the time factor of the work of the heart. They are therefore the antagonists of the vagi in the sense that stimulation of the latter increases the intensity of the beats of the heart while stimulation of the accelerators increases the beats of the heart and diminishes their extent.[5]

The cardiac accelerator center is supposed to lie in the medulla in the region of the Calamus scriptorius. The nerve cells, the axones of which form the efferent rami communicantes, lie in the gray matter of the spinal cord. The accelerator branches emerge from the cord in the anterior roots of the second, third and fourth spinal nerves. Some authors are of the opinion that they emerge to a certain extent in the first and fifth spinal nerves or even in the lower cervical nerves. Passing from the stellate ganglion these fibers run by way of the annulus

of Vieussens to the cardiac plexus. Boehm[6] was able to demonstrate in the cat a nerve which ran directly from the stellate ganglion to the cardiac plexus to which he gave the name "Nervus Accelerator Cordis."

However one must not assume that the annulus of Vieussens contains accelerator fibers only. Roy and Adami[7] report fibers passing from the stellate ganglion, excitation of which causes weakening of the force of the auricular and ventricular contractions. Fredericq[8] also presents evidence that stimulation of the annulus under certain conditions produces slowing. He cites Dogiel[9] as having found the same.

The action of the cardiac accelerator nerves may in general be classed as two fold:- (1) To produce an increase in the heart rate, and, (2) to increase the strength of the beat. These actions may be seperate or may occur together. As to the terminology in describing these two functions there seems to be much confusion. The terms <u>acceleration</u> and <u>augmentation</u> have been used somewhat interchangeably in the literature. But the term acceleration ought to be taken to mean only increase in the heart rate, while augmentation should be taken to mean increase in the strength of the heart contraction. Stimulation of the sympathetic cardiac nerves may produce either one or both of these effects. The action of the

cardiac accelerator nerves is looked upon as being exactly the opposite of the action of the vagi. In general authors agree as to this point, though some have found variations in the action of the sympathetics.

Roy and Adami[10] find that the sympathetics play only a passive role in the determination of the heart rate. They consider that they serve only as a check upon the activity of the inhibitors and in this way are able to increase the rate of the heart. Reid Hunt[11] on the other hand finds that stimulation of the cardiac sympathetics produces marked acceleration even when the vagi have been cut. He considers that the accelerators are always in tonic activity. Roy and Adami consider that they are not always in tonic activity and that the only direct effect that the sympathetics have upon the heart is to increase the contraction volume. This factor is in direct opposition to the vagus effect. The accelerator nerves can be stimulated both directly and reflexly. However these nerves do not show nearly as great an effect when the heart is beating fast as when it is beating slowly. To this statement Hunt seems to agree. Hunt also finds that section of the accelerators may produce an effect upon the conduction of the contraction impulse from the auricle to the ventricle. Hunt says that this is not a vagus effect since in the cases where it appeared the

vagi were cut and there was no change in blood pressure. He thinks that it is only found in those hearts which are in very poor condition. Stimulation of the accelerator nerves brought the heart back to the normal rate and beat again.

A third important influence of the sympathetic is its regulation of the auricular tonus. Bottazzi,[12,13] Fano and Badano[14] and Oimuma[15] are the chief contributors along this line. They find that stimulation of the vagus raises the tonus. The two nerves work in opposition to each other in this case as in all others.

To this point I have considered only the possibility of accelerator fibers reaching the heart by way of the sympathetics. Certain authors mention the possibility of the vagus containing accelerator fibers. Dale, Laidlaw and Symonds[16] found after the giving of nicotine that under certain conditions cardiac acceleration was obtained. It was found that slowing of one or two beats of the heart was produced by stimulation of the vagus. But on cessation of the stimulus there was a marked slowing. If the vagus was stimulated again before the heart had returned to its normal rate marked acceleration was produced. If this was repeated four or five times there appeared periods of acceleration during the stimulation and periods of marked inhibition upon cessation of the stimulus. This is just

the reverse of the usual effect. The authors are of the opinion that this effect is due to masked accelerator fibers in the vagus. However they leave the question open as to whether the above interpretation is correct or whether possibly it is due to reversed action of the vagus. This condition was found best in the cat and ferret, weakly present in the dog and not at all in the rabbit.

Nöel Paton[17] found that the vagus of the duck contained fibers which produced augmentation of the heart beat. The author is of the opinion that the vagus is distributed to both auricles and ventricles. It is also probable that the augmentors are limited to the auricles, a factor which probably explains the failure of the avian ventricle to respond to adrenaline.

Edward Weber[18] discovered the inhibitory function of the vagus by experiments on fishes and other cold-blooded animals. However Gaskell[19] was the first to emphasize comparative physiology in this line of work. He found in the frog that stimulation of the vagus produced sometimes an acceleration which was hard to account for. This irregularity he later showed to be due to the fact that in this animal the cardiac accelerators join the vagus near its origin and that he was stimulating the combined vago-sympathetic.[20] Gaskell[21] also investigated the cardiac accelerator nervous mechanism of the hearts of

several species of reptiles among which were the alligator, crocodile and turtle. He chose the alligator as a type as he thought this animal would have the most elaborate sympathetic nervous system. He found in the region where the vertebral artery enters the vertebral canal that there is a large ganglion which in many respects in analagous to the ganglion stellatum in mammals. This he proposes to call the "ganglion cardiacum." From this ganglion strong cardiac branches run toward the heart. Stimulation of these branches produced strong augmentation and acceleration of the heart. In Testudo Graeca he found that cardiac branches arose from the ganglion fusiforme, which is analagous to the ganglion cardiacum in the alligator and which Bottazzi[22] in Emys Europea calls ganglion cervicale inferius. Stimulation of this ganglion or the sympathetic chain in the neighborhood of this ganglion produced marked acceleration. Mills found that the sea turtle possesses accelerator cardiac nerves the course of which was similar to that of the cardiac accelerator nerves in mammals. In experiments upon Pseudemys rugosa, Mills[23] found that stimulation of branches from the middle cervical ganglion produced acceleration as did the stimulation of the main sympathetic stem between the lower cervical ganglion and the ganglion cardiacus basale. Stimulation of the sympathetic stem between the middle and the

inferior cervical ganglia produced no very appreciable results.

INTRA-CARDIAC INNERVATION AND CONDUCTION

The presence of ganglia in the heart itself was discovered by Remak[34] in the heart of the calf. This group of ganglion cells is situated in the wall of the sinus venosus. A group of cells was discovered by Ludwig[35] in the interauricular septum of the frog's heart and a third group by Bidder in the base of the interauricular septum, in the wall of the auriculo-ventricular orifice and in the base of the ventricle. Intracardiac ganglion cells have been described by various investivators as scattered throughout the ventricle. However they are much fewer in number if not absent in the apex of the heart.

Friedlander[36] states that he has found ganglion cells in all parts of the heart. For the most part they are found between the pericardium and the heart muscle itself. On the other hand Schweigger-Seidel[37] finds numerous nervous networks containing nuclei in all parts of the ventricle. Howell[38] states that the fibers of the vagus end around those ganglis whose neurones are distributed to the heart muscle. However it is very doubt-

ful if any of the vagus fibers find their way to the ventricle. Gaskell[39] mentions the fact that in the crocodile the ventricular contractions seem to be uninfluenced by stimulation of the vagus. In another article upon the heart of the tortoise he states the same belief.[30] The rate and force of the ventricular contractions are affected by the vagus through the mediation of the auricle and not by action upon the ventricular muscle direct. He finds that the vagus exercised two kinds of influence upon the heart:- (a) chronotropic, (b) inotropic. He proves that both vagi run into a large number of ganglion cells in the sinus and from thence to the auriculo-ventricular groove. After leaving the sinus the right nerve gives off a free branch which runs to the collection of ganglion cells in the auriculo-ventricular groove. Section of this nerve produces no effect upon the rate or the force of the heart. Stimulation of the peripheral end, i.e. the end in connection with the auriculo-ventricular groove, produces a reduction in the force of the auricular contractions but no change in rate. Stimulation of the right vagus after section of this nerve, which Gaskell calls the coronary nerve produces a diminution in rate and an increase in the contractions due to the slow rate. He finds that stimulation of the central end of this nerve causes a diminution in force of the auricular

contractions. This seems to give to the ventricle some regulative control over the auricles. Gaskell also mentions that there is some evidence for the belief that the ventricle may also affect the rate, but he is not so sure of this. Garrey[31] states that in Pseudemys elegans and Pseudemys rugosa the vagal inhibitory fibers do not reach the ventricle. For this reason he believes that the vagus can control the ventricle only through the mediation of the auricle. He finds that a moderate pressure exerted upon the sino-auricular junction produces a condition of arrhythmia or block but does not do away with the inhibitory action of the vagus.[32] In a later paper he points out that in many cases stimulation of the vagi so lowers the conductivity of the cardiac tissue that a condition of block is produced. Fredericq[33] finds that after section of the bundle of His in mammals the ventricle is not slowed by vagus stimulation. There is also produced arrhythmia. Garrey's work confirms the work of Bayliss and Starling,[34] that stimulation of the vagus lowered the conductivity of the cardiac tissue. Cullis and Tribe[35] working upon the perfused heart of mammals in situ, found that after section of the atrio-ventricular bundle, the vagi produced no effect upon the ventricular rate. Perfusion of pilocarpine and muscarine through the heart while in this condition, gives none of the normal

slowing and inhibitory action upon the ventricles. Release of the auricle from the toxic action of the above named drugs by the action of atropine, produces no change in the ventricle. They are of the opinion that the vagus fibers do not reach the ventricle and their action upon it is an indirect one. Leetham[36] using strips of dogs ventricle perfused with pilocarpine and muscarine came to the same conclusions.

I have been able to find but little literature upon the relation of the accelerator apparatus to the intra-cardiac nerve complex. Cullis and Tribe[37] state that perfusion of adrenaline caused marked acceleration and augmentation of the ventricle. From this they argue that the ventricle is well supplied with sympathetic, i.e. accelerator and augmentor nerve fibers. As this result was gotten after section of the atrio-ventricular bundle they came to the conclusion that the sympathetic nerves enter the ventricle by some other path.

Many experimenters have found by means of pressure or by cutting the auriculo-ventricular junction that the ventricle set up a rhythm all its own. Stannius[38] was the first to demonstrate this fact using the frog's heart. Tigerstedt[39] by means of the "atriotom" cut through the atrio-ventricular junction of the mammalian heart and found that coordination was lost between auricle and ventricle.

What is the mechanism through which cardiac coordination takes place? Gaskell[40] working with the heart of the turdle concluded that conduction was myogenic in nature. Külbs and Lange[41] Laurens[42] and Henri Fredericq[43] working upon the heart of the lizard, Lacerta ocellata, found that the conduction was muscular in nature. Imchanitzky[44] reported that ligation of nerves situated in the posterior face of the heart of the lizard produced arrhythmia. The above named authors were unable to confirm this work of Imchanitzky's. In the mammalian heart it has been found that the coordination of the auricle and the ventricle, is brought about through the atrioventricular bundle. Hering[45] found that cutting of this bundle produced disassociation of the auricle and ventricle. In the work reported by Cullis and Dixon,[46] and Cullis and Tribe,[47] upon sectioning the bundle, they have found that complete arrhythmia is produced between the auricles and ventricles. Cullis and Dixon emphasize the fact that in order to produce complete arrhythmia the bundle must be cut before it branches. Meakins[48] and Erlanger[49] were able to produce heart block by pressure upon the atrio-ventricular bundle. It seems to be agreed that it is through this mechanism that the auricles and ventricles are coordinated. As it has been shown by Kent[50] that this bundle is modified cardiac muscle, the conception that conduction between auricle and ventricle, as was held by Gaskell, Fredericq and

Laurens et al, for the cold blooded animals still holds good in the case of the warm blooded ones. Erlanger[51] after crushing the atrio-ventricular bundle and allowing the animal to recover found that functional union was not reestablished. He concluded that the cardiac impulse was conducted through muscle fibers, rather than through nerve fibers located in the cardiac tissue.

THE NODAL TISSUE AS THE PACEMAKER OF THE HEART

Since the time of Galen[52] it has been known that the vagi were not the motor nerves of the heart. Since then many theories have arisen explaining the cause of the heart beat. At present physiologists are divided into two camps . One of these holds that the heart beat is due to nerve cells placed in the sinus region of the heart. Haller[53] and Legallois[54] are the ones whose names stand out clearest in regard to this theory. In 1881-83 Gaskell[55,56] brought forward evidence showing that the beat of the heart was due to the intrinsic rhythmic power of the cardiac muscle. This theory has since been further developed by Gaskell and Englemann (Howell). It is needless to go into all the evidence pro and con of the heart beat. Be the cause of its beat neurogenic or myogenic, the question at issue in this paper is how and to what extent is the heart controlled by the vagi and sympathetics?

In 1906 Tawara[57] announced the discovery of a node of specialized tissue, the atrio-ventricular node upon the right side of the heart at the base of the interauricular septum. The following year Keith and Flack[58] discovered the Keith-Flack node on the sino auricular node in the region of the sulcus terminalis at the level of the junction of the superior Verra Cava with the right auricle. Since that time considerable work has been done to show its relation to the heart beat.

Jaeger[59] used the method of scorching the node and got no change in rhythm. Moorhouse,[60] using the method os excision of the node does not think that the sino-auricular node is specific as regards regulating the heart beat. The majority however come to a dif erent conclusion. Flack[61] by excision and pinching the node came to the conclusion that the heart beat is slowed but the heart is not stopped. This is not agreed to by Cohn, Kessel and Mason.[63] They found that upon excision of the node stoppage of the heart resulted, followed later by a slower rate. However Flack could make the same objection to this that he did to the work of Cullis and Dixon, viz that the heart was under artificial perfusion.

Flack found that excision of the auriculo-ventricular node resulted in arrhythmia. In a previous article he reports the results of the application of cold,

and of electricity?[63] The rhythm of the heart is dominated by these agents. Application of muscarine to this node caused a slowing, with a release from this drug's action when atropine was applied. Wybauw[64] comes to the same conclusion and considers that dur ng vagal stimulation the pacemaker is moved from this node but is in the innediate neighborhood. However, the more complex mechanism found in the mammalian heart is not fully developed for the simpler types of the heart, as for example in the heart of the turtle, for thwich we have experimental data. Garrey[65] using the suspension method found that the caval veins went into contraction before the simus. This is in opposition to the older observers who considered the cardiac cycle as beginning with a contraction of the sinus followed by the auricles and next the ventricles. He finds that the right vein sets the pace and that it is about two and one-half times as fast as the left. This work was later contradicted by Eyster and Meek.[66] Using a string galvanometer they found that primary negativity (i,e. tissue which is about to go into contraction), is shown first by the sinus then in succession by the right vein, right auricle, various parts of the auriculo-ventricular ring, ventricular base and finally by the ventricular apex. In a series[67,68] of articles they have definitely proved that the sino-auricular node in mammals is responsible for the initation of the cardiac cycle.

Lewis[69] using the same method located the pacemaker in the same region. Flack considers that it is through the innervation of this spot in the heart, by the vagus and sympathetic nerves particularly the ones on the right side, that the rhythm is affected. Schlomovitz, Eyster and Meek[70] came to this conclusion as far as the vagus is concerned. They consider that the vagi act by depressing the activity of the tissue which is acting as the seat of impulse formation, viz the nodal tissue. It has been mentioned before that if this nodal tissue be excised, crushed or cooled that the heart takes on a slower rhythm. This rhythm is due to the fact, as Erlanger[71] and Porter[72] pointed out that the property of rhythmicity is not confined to any one part of the heart but is better developed in the region of the sino-auricular node, and by the law of " all or none" is able to dominate the rate of the heart beat.

SUMMARY OF THE LITERATURE AND THE STATEMENT OF THE PROBLEM

We see from the preceding review of the literature that the work that has been done on the physiology of the heart of the turtle has been rather small in amount. The chief contributor in Europe has been Gaskell. His work was done chiefly upon the European land tortoise, Testudo

graeca. Bottazzi has found augmentation and acceleration upon stimulation of the sympathetic chain of Emys europea in the region of the fusiform ganglion. Mills in this country has investigated the problem of cardiac accelerators in Pseudemys rugosa. He described accelerator branches coming off from the sympathetic in the same region as did Bottazzi and Gaskell. However it has been repeatedly noted that in common species of turtle used in this laboratory that no certain evidence could be obtained whether or not these turtles possessed an accelerator mechanism. From time to time the suspicion has been raised as to whether or not accelerator cardiac nerves are to be found but it has never been affirmed or denied. With this question in view this research has been undertaken to determine whether the turtle, Emydoidea blandingi, posses a cardiac accelerator mechanism and if so to determine its course.

MATERIALS AND METHODS

The species of turtles used in this series of experiments was the one most available in this territory for general laboratory use, the mud turtle Emydoidea blandingi. It is distributed from New York to Wisconsin, and ours were obtained from northern Indiana.

The method of preparation of the turtle for experiment varied somewhat according to the point under test. In a majority of cases the turtle was killed simply by crushing the cord in the neck in such a way that the vagi would not be injured and thus cause a disturbance from this source. The plastron was in most cases removed immediately. In a few it was trephined over the heart so as to expose that organ as little as possible to the influence of the air. In those cases where it was necessary to expose the sympathetic chain of the thoracic region a longitudinal saw-cut was made in the carapace about four cm. from the midline and somewhat toward the anterior end. After the removal of the plastron, two breaks were made in the carapace, one at each end of the saw mark. By this means a segment of the carapace was removed. This gave easier access in the dissection of the sympathetics. In certain experiments curare sufficient to produce complete motor paralysis was given. The curareized turtles were

treated in two ways. One way was to decapitate and bleed for the purpose of producing a bloodless preparation. The other method was to follow curare by ligation of both carotid arteries and to prevent bleeding to any extent.

The method for taking records of the heart beat was Englemann's suspension method. In the case of the ventricle when auricular tracings were made one of two methods was used, either the suspension method or by an air transmission cardiograph.

The suspension method was in brief to attach the apex of the ventricle to a light lever by thread and a small wire hook. The lever was carefully counter balanced by a light weight and provided with a flexible tip. Kymograph records were taken. The air transmission cardiograph was the form demonstrated before the American Physiological Society at the last mid-winter meeting. It is a modified air tambour that records the movement of the muscle between the points of attachment only. It used air transmission. The heart was kept moist by means of blood serum, peritoneal fluid or Ringer's solution.

The nerves were prepared for stimulation by careful dissection, care being taken to avoid injury by streching or pinching. Stimulation of these nerves was made with ordinary platimum stimulating electrodes. The method of stimulation of the spinal cord will be taken up later in con-

nection with the particular point with which we are dealing.

The current for stimulating was obtained from a Harvard inductorium driven by a single dry cell .

EXPERIMENTAL RESULTS

The problem as it has been stated, has been to find whether this turtle Emydoidea blandingi possesses an accelerator cardiac apparatus. To determine this, all nerve structures connected with the aympathetic nervous system which under any possibility might contain accelerator fibers were dissected out and stimulated.

The experimental work was begun upon the thoracic sympathetic chain. The method of preparation was as follows:- As the ganglia of the sympathetic chain are bound closely with the thoracic spinal nerves, these nerves were cut central to the ganglia and likewise peripherally. The spinal nerve segment with the attached sympathetic ganglion was then stimulated with various strengths of the induction current. In the experiments upon each animal, stimulation was begun upon the more caudal of the sympathetic ganglia to be stimulated. The ganglia upon the other spinal nerves were then tested in order toward the head. Stimulations were made upon the sympathetic ganglia at the level of the fifth, fourth, third, and second spinal nerves respectively. The strengths of the stimuli employed were such that the weakest used was just perceptible when the electrodes were applied to the tongue. The stimuli were increased in intensity in this and all the following

experiments by one centimeter shifts of the secondary at a time until the current was strong enough to induce possible injury to the nerve.

As the method of procedure and the results obtained were very much alike upon stimulation of the sympathetic chain ganglia on the fifth, fourth, third and second spinal nerves, they will be considered together. The data for the stimulation of these nerves were computed as follows:- the rate in beats per minute and the amplitude of contractions on the chart measured in millimeters of all the effective stimuli upon each particular structure were averaged for the animal and this average is used in the table. A grand average was then made of all the different individual turtles. These averages show very slight change in either rate or amplitude, a change which is easily within the limit of error. If there had been any outflow of accelerator fibers in any of these spinal nerve roots or below stimulation of the sympathetic chain would have provoked acceleration of the heart beat. For the results of the stimulation of the nerve roots mentioned above see Tables I, II, III, and IV.

In the region of the first, second and third dorsal ganglia there is a rather curious arrangement of the connectives in many of the animals. Instead of the second dorsal sympathetic ganglion being connected in sequence between the third and first as usual there was no con-

nection between the first and second at all. The continuity of the chain was maintained however by a strand connecting the third thoracic ganglion with the first, thus leaving possible ascending fibers from the second ganglion to pass down to the third, thence up to the first by this exceptional pathway.

Stimulation of this third-first connecting strand resulted as is shown by Table V. The average of the tests made upon two animals shows no change in rate or amplitude, which is significant. It is apparent that no accelerator fibers run in this strand. This result was hardly to be expected when we consider the fact that the stimulations of the isolated thoracic roots of the series of thoracic nerves show no accelerator fibers. No new fibers have entered the sympathetic chain that could ordinarily reach this strand.

Above the point of the last stimulation the sympathetic connects the ganglion on the first thoracic nerve with a large ganglion. This ganglion will be considered as the inferior cervical ganglion. The ganglion fusiforme of which Gaskell and Gadow[73] speak, is probably a ganglion on the sympathetic chain between the inferior cervical ganglion and the first thoracic. It is in this region that Gaskell and Gadow and Mills[74] mention having found accelerator cardiac branches. No trace of nerve

fibers were to be found here by the most careful search. Stimulation of the first thoracic - inferior cervical commisure gave only an exceedingly slight increase in rate. In experiments on five animals only two showed increase in rate. This however was only transitory and can be considered as being within the limit of variation of the heart's rate. For the results of the stimulation of the above named connective see Table VI.

Seven animals were used for testing the inferior cervical ganglion pathway. Mills mentions having found fine branches coming off from this ganglion. Bottazzi[75] finds accelerator cardiac branches from this ganglion. Gaskell and Gadow as far as I am able to tell, found accelerator cardiac branches from this region in Testudo graeca. However, they describe seperate ganglia in this region which are evidentally fused with the inferior cervical ganglion in Emydoidea blandingi. In Eymdoidea blandingi no cardiac branches were detected. The average of the stimulations made upon various turtles as shown by Table VII show a normal rate of 25.9 beats per minute, during the stimulus. 25.7 beats per minute, and after 24.7 beats per minute. The amplitude decreased from 26.5 mm. normal, to 26.1.mm. during the stimulus and 25.5 mm. after. This shows that there was no appreciable change in either rate or amplitude. The only conclusion that can be drawn

from these results is that there are no accelerator fibers in the inferior cervical ganglion.

The connecting strand between the middle and inferior cervical ganglia was tested in twenty-one turtles. The results obtained from stimulation of the strand between the middle and inferior cervical ganglia were all negative. The average of Table VIII shows a slight decrease in rate and amplitude which can be considered as negligible. We could not consistently look for any change from stimulation of the connecting strand between the inferior and middle cervical ganglia since no new fibers could have joined it above the inferior cervical ganglion.

In a few cases I was able to isolate small nerves running from the middle cervical ganglion along with the vagus toward the heart. Only in a very few turtles could this be done. When present these nerves were dissected out and stimulated. Bottazzi and Mills describe accelerator branches coming from this ganglion. However, Table IX shows practically no change at all from their stimulation in Emydoidea blandingi.

All the possible nerve tracts and ganglia from the thoracic spinal nerves to the middle cervical ganglia that usually carry cardiac nerves were stimulated but have not revealed accelerator function. There still remains the cervical sympathetic and vagal pathways.

These though unlikely channels for accelerator fibers were stimulated about four cm. above the middle cervical ganglion. Before stimulation of the vagus trunk atropine was given in order to eliminate its inhibitory function. After elimination of the inhibitory function by means of atropine, stimulation of the vagus trunk produced no change in either rate or amplitude. Stimulation of the cervical sympathetic likewise was ineffective in producing accelerator change as is shown by Table X.

We have repeatedly stimulated all structures in which accelerator fibers are usually found and have gotten no evidence of acceleration or augmentation of the heart beat. As a last resort the method of Legallois[76] was used on the theory that any pathway that escaped detection would be caught up by direct stumulation of the spinal cord. The cardiac accelerator center lies in the medulla in the region of the calamus scriptorius. Upon stimulating the spinal cord any descending accelerator fibers would be stimulated before they emerge in the spinal nerves. The preparation of the animals was as follows:- Five to ten minims of curare was given which was sufficient to produce skeletal muscle paralysis. After complete loss of nervous control of the muscles had been obtained, the carotid arteries on both sides were quickly dissected out and ligated as close to the body as could be done easily. The

animal was then decapitated between these ligatures and the head by means of a sharp chisel. The plastron was removed quickly and carefully so as not to injure any underlying structures. A large smooth glass rod was slipped down the oesophagus and under the heart. The rod was fixed in a clamp on a stand so that any slight mechanical movements of the turtle would not affect the heart. The turtle was stimulated by means of two platinum electrodes in one of two ways, both of which produced essentially the same reuslts. The electrodes which were long thin platinum wires were slipped carefully down the vertebral canal on either side of the cord so that no injury was produced and no short circuit obtained. The other method was to dissect off one of the cervical vertebrae leaving part of the cord exposed. Hooks made in the electrodes were then slipped over the cord, seperated by four or five millimeters and bent so as to make good contact with the cord but not tight enough to produce injury to the cord. The pericardum was cut so that any muscular movements of the turtle would produce no mechanical traction on the heart. The heart itself was suspended and its movements recorded in the usual manner. The cord was then stimulated with varying strengths. Stimulation in some cases produced no results either in change in amplitude or heart rate. In other animals however, in which the

blood vessels retained considérable blood, stimulation of the cord produced a marked increase in amplitude and a slight increase in rate. In a few tests the change in amplitude was enormous. Experiment number 35 is a particularally good example to show this change. The following average of the effective stimulations on this animal shows a great change in amplitude. Measurements of rate and amplitude were taken just before, during stimulation, immediately after and 6-10 minutes later.

Rate per minute			
Normal	During Stim.	Immediately After Stim.	6-10 Minutes After Stim.
35.7	35.9	36.3	36.2
Amplitude in mm.			
37.6	48.1	49.7	40.3

The augmentation produced at first sight was considered to be due to stimulation of augmentory nerves as Bottazzi[77] has suggested for cardiac tone. The very slow return to mormal, as for example in Exp. 35, argues very strongly for a true accelerator effect. The return to the normal rate and amplitude is in fact slow after stimulation of true accelerator nerves. Yet the phenomenon was not constant. It could not always be obtained from successive turtles tested. Certain relatively bloodless turtles did not show acceleration and suspicion was aroused that the effect was brought on by vaso-motor changes that varied the resistance against which the heart worked. To

test whether this conception was correct or not the spinal cord was stimulated in a series of bloodless animals the aorta being opened to exclude change in resistance. The average of this series is shown by Table XIV. This table is divided into two parts, sections (a) and (b). Section (a) embraces all turtles which were bled and then stimulated. No further tests were made on them. Section (b) in this table, embraces those turtles which were stimulated first with the blood retained in the vascular system and then one of the aortae cut so as to render the preparation bloodless. Stimulation of the spinal cord was then made of which section (b) in this table shows the results. The grand averages of each of these two sections are as follows:-

	Rate per Minute			Amplitude in mm.		
Section	Normal	During Stim.	After Stim.	Normal	During Stim.	After Stim.
(a)	34.9	35.6	35.8	29.7	27.6	26.9
(b)	26.0	25.6	26.0	30.6	29.7	27.9

In none was there increase in amplitude or rate sufficient to be conclusive of acceleration.

In another series of turtles the spinal cord was stimulated while the vascular system was full of blood. In practically all the animals in this group stimulations

of the cord produced an increase in amplitude and but very little change in rate as is shown by Table XIII, of which the following is the grand average.

Rate per Minute			Amplitude in mm.		
Normal	During Stim.	After Stim.	Normal	During Stim.	After Stim.
27.2	28.0	28.4	31.8	32.9	31.5

If now the mechanical effects on the heart from the rise of blood pressure during cord stimulation are eliminated the picture changes. This was accomplished as follows:- One of the aortae was cut so as to drain the arterial system of blood, and the cord was again stimulated at various strengths. The stimulation now caused absolutely no increase in rate or amplitude. Table XIV, section (b) shows the results of these experiments of which the following is the grand average:-

Rate per Minute			Amplitude in mm.		
Normal	During Stim,	After Stim.	Normal	During Stim.	After Stim.
26.0	25.6	26.0	30.6	39.7	27.9

In order that an average might be made of those stimulations of the spinal cord which produced an appreciable rise in amplitude uninfluenced by those stimulations which were ineffective, a table was made of those

results alone. The stimuli which produced an appreciable rise in amplitude were averaged for each turtle. These were collected in a table to themselves, which comprises Table XV, the average of which is as follows:-

Rate per Minute

Normal	During Stim.	Immediately After Stim.	3-1- Minutes After Stim.
28,9	29.2	29.8	29.7

Amplitude in mm.

30.4	35.4	36.6	30.7

Of all the turtles comprising this table only one, number 33, was bled. This one exception to the rule was a turtle in which the plastron was not removed and the heart was reached by trephining the plastron. The neck was well drawn in and it is probable that bleeding was incomplete.

The outstanding feature of these two series of experiments upon the bled and unbled specimens is the fact that in those animals which had not been bled and whose vascular systems were full of blood, stimulation of the spinal cord produced a great increase in the amplitude of the heart's contractions. This increase in the amplitude of the contractions I consider to be due to two factors:-
(a) Possible better nutritional conditions of the myocardium.
(b) Increased resistance to the blood flow thus causing

a rise of hemostatic pressure which required greater tension of the heart to overcome it, and as a result mechanically stimulating the heart to greater amplitude of contraction.

DISCUSSION AND SUMMARY

The experimental results which I have obtained from the direct stimulation of various parts of the sympathetic chain have resulted in but very little change in the heart rate or amplitude. In those parts of the sympathetic chain from which Gaskell and Mills describe accelerator cardiac branches arising I was unable to find any at all in Emydoidea blandingi. These facts argue very strongly for the assumption that there are no accelerator fibers for this particular species of animal.

The stimulation of the spinal cord was undertaken for the purpose of detecting possible accelerator fibers before their emergence in the spinal nerve roots. The stimulatinn of the spinal cord called out a change in the amplitude of the beat which however was due to vaso-motor changes that caused an increase in the blood pressure. This blood pressure change in turn stimulated the heart to greater activity of amplitude of contraction and to a slight increase in rate. That these effects are wholly secondary

was proven by the method of bleeding the blood vessels thus eliminating blood pressure change. The stimulation of the cord therefore resulted in no change of the rate of the heart or its amplitude induced by cardiac accelerator nerves.

The conclusions which I have drawn from these findings are as follows:-

1. The turtle Emydoidea blandingi possesses no accelerator cardiac outflow through the usual sympathetic pathway as has been described by Gaskell and Mills for other species.

2. Stimulation of the sympathetic connecting strand between the inferior and middle cervical ganglia produced no cardiac acceleration.

3. Stimulation of the small nerves from the middle cervical ganglion which were running toward the heart produced no cardiac acceleration.

4. No cardiac accelerators can be demonstrated by stimulation of the spinal cord thus disproving the usual assumption that they are present.

5. Stimulation of the spinal cord resulted in vasomotor changes which caused a rise in blood pressure, thus secondarily causing the amplitude of the heart to be increased and to a lesser degree the heart rate.

EXPLANATION OF TABLES

For each animal the figures given are the average of all stimulations of effective strength. The grand average is given at the end of each table or sections thereof.

TABLE I.

Tabulated results of stimulation of the Sympathetic chain ganglion on the fifth dorsal nerve.

Turtle No.	Rate per Minute			Amplitude in mm.		
	Normal	During Stim.	After Stim.	Normal	During Stim.	After Stim.
3	38.0	38.5	37.3	37.6	37.5	36.9
4	18.0	18.0	18.0	32.0	30.8	30.6
5	23.6	23.5	23.6	16.5	16.2	15.6
Average	23.2	23.3	22.9	28.7	28.1	27.7

TABLE II.

Tabulated results of stimulation of the Sympathetic chain ganglion on the fourth dorsal nerve.

Turtle No.	Rate per Minute			Amplitude in mm.		
	Normal	During Stim.	After Stim.	Normal	During Stim.	After Stim.
3	29.5	29.5	30.0	33.3	33.6	32.9
4	18.6	18.0	18.7	25.0	24.8	24.7
5	24.5	24.5	24.7	14.5	14.1	14.0
6	19.2	19.1	19.1	33.3	32.5	32.3
7	21.8	21.6	21.7	26.9	26.9	25.7
Average	22.7	22.5	22.8	26.6	26.4	25.9

TABLE III.

Tabulated results of stimulation of the Sympathetic chain ganglion on the third dorsal nerve.

Turtle No.	Rate per Minute			Amplitude in mm.		
	Normal	During Stim.	After Stim.	Normal	During Stim.	After Stim.
4	18.8	18.8	18.4	18.9	18.9	21.3
5	25.5	26.0	25.7	11.4	11.2	10.8
6	20.1	19.7	20.2	28.1	27.6	26.6
7	20.2	20.0	19.7	22.7	23.4	23.5
Average	21.1	21.1	21.0	20.3	20.3	20.5

TABLE IV.

Tabulated results of stimulation of the Sympathetic chain ganglion on the second dorsal nerve.

Turtle No.	Rate per Minute			Amplitude in mm.		
	Normal	During Stim.	After Stim.	Normal	During Stim.	After Stim.
4	18.5	18.3	18.7	15.5	15.7	15.3
5	26.0	25.6	26.0	7.8	7.5	7.5
6	21.4	21.6	21.6	28.2	28.5	21.0
7	20.0	19.0	19.6	21.9	21.8	21.4
8	32.4	32.2	31.9	36.5	37.3	40.9
Average	23.6	23.3	23.6	20.8	18.9	21.2

TABLE V.

Tabulated results of stimulation of the strand connecting the sympathetic chain ganglia on the third and first dorsal nerves.

Turtle No.	Rate per Minute			Amplitude in mm.		
	Normal	During Stim.	After Stim.	Normal	During Stim.	After Stim.
8	30.8	30.6	30.6	32.6	32.5	33.0
14	31.0	30.8	31.5	13.6	13.0	11.6
Average	30.9	30.7	31.1	32.1	32.7	32.3

TABLE VI.

Tabulated results of stimulation of the commisural strand between the ganglion on the first dorsal nerve and the inferior cervical ganglion.

Turtle No.	Rate per Minute			Amplitude in mm.		
	Normal	During Stim.	After Stim.	Normal	During Stim.	After Stim.
9	28.6	28.6	28.4	26.8	26.3	25.6
10	27.0	27.4	27.4	35.4	35.6	35.7
11	15.3	16.4	16.4	36.8	36.0	37.4
12	20.8	20.2	21.2	27.4	27.0	27.3
13	19.0	19.0	19.0	35.0	34.5	35.0
Average	22.1	22.8	22.5	32.3	31.9	32.2

TABLE VII.

Tabulated results of stimulation of the inferior cervical ganglion.

Turtle No.	Rate per Minute			Amplitude in mm.		
	Normal	During Stim.	After Stim.	Normal	During Stim.	After Stim.
7	27.3	26.6	27.0	30.6	29.3	31.0
9	27.9	27.6	27.5	19.9	19.9	19.6
11	15.3	14.4	14.9	34.7	34.8	34.6
14	31.0	30.8	31.5	13.6	13.0	11.8
15	32.4	32.8	33.5	33.6	33.1	30.0
16	24.5	24.7	24.5	30.3	29.6	29.6
17	23.4	23.6	23.8	23.3	23.0	22.4
Average	25.9	25.7	24.7	26.5	26.1	25.5

TABLE VIII.

Tabulated results of stimulation of the sympathetic connecting strand between the middle and the inferior cervical ganglia.

Turtle No.	Rate per Minute			Amplitude in mm.		
	Normal	During Stim.	After Stim.	Normal	During Stim.	After Stim.
8	30.3	30.3	30.3	25.3	24.3	24.6
9	26.0	25.4	26.2	15.4	15.2	14.6
10	28.5	28.7	26.6	24.9	24.6	23.5
11	16.9	16.4	16.8	32.1	31.9	31.9
12	20.8	21.2	21.4	24.9	24.6	24.2
13	20.1	20.0	20.1	34.6	34.1	33.6
14	31.4	30.8	31.4	6.6	7.0	6.2
15	33.6	34.2	33.5	21.2	20.4	20.0
16	25.7	25.8	25.8	19.3	18.9	18.2
17	23.5	23.7	24.5	17.9	17.5	17.8
18	27.2	27.6	28.5	33.3	32.7	31.5
19	22.7	22.0	22.7	18.9	19.7	18.5
20	27.3	27.2	27.9	17.2	17.3	16.9
25	21.5	21.4	21.7	31.0	27.5	29.0
26	19.1	18.8	19.2	29.2	29.3	29.0
27	36.8	36.7	36.4	28.7	28.5	27.5
28	27.0	26.9	27.0	15.0	15.0	13.1
29	25.1	29.0	28.7	18.3	15.7	18.7
30	31.2	31.3	31.4	26.0	25.5	25.4
42	23.2	23.5	23.5	33.8	33.8	34.0
43	14.0	14.2	13.6	29.5	30.5	30.5
Average	25.3	24.8	25.1	24.9	23.1	23.3

TABLE IX.

Tabulated results of stimulation of a small nerve from the middle cervical ganglion running toward the heart.

Turtle No.	Rate per Minute			Amplitude in mm.		
	Normal	During Stim.	After Stim.	Normal	During Stim.	After Stim.
11	15.2	15.7	15.7	29.0	30.0	28.9
42	26.6	27.4	27.0	31.6	31.3	31.0
30	30.4	29.8	30.4			
Average	24.1	24.4	24.4	30.3	30.6	29.5

TABLE X.

Tabulated results of stimulation of the cervical sympathetic, (uncut).

Turtle No.	Rate per Minute			Amplitude in mm.		
	Normal	During Stim.	After Stim.	Normal	During Stim.	After Stim.
11	16.1	16.1	16.0	30.8	30.8	30.9
12	20.0	19.9	19.9	17.9	19.8	17.7
13	21.6	21.7	21.1	29.8	30.0	29.4
14	30.0	30.2	30.5	6.4	6.5	6.5
15	35.1	35.3				
18	30.0	29.1	28.0	19.8	19.9	19.4
19	23.5	23.6	26.5	14.1	14.4	13.0
20	29.5	30.0	29.6	11.6	12.1	11.9
21	22.9	23.0	28.5	29.7	29.5	29.5
22	20.8	30.6	31.3	20.9	21.2	20.6
23	30.0	29.4	29.6	19.8	19.5	19.5
24	24.0	23.8	24.0	25.6	26.5	22.8
25	22.0	21.7	22.0	22.4	22.1	21.7
26	19.9	20.2	19.9	28.2	28.6	28.2
28	24.6	24.3	24.5	10.6	10.4	9.3
29	29.0 28.5	29.3 28.3	29.0 28.4	24.0 16.8	23.0 16.3	23.0: 17.0:
30	30.5	30.8	30.3	23.0	28.3	22.5
42	29.8	29.5	30.2	29.7	30.4	33.6
Average	25.6	25.5	25.9	21.7	21.7	20.9

TABLE XI.

Tabulated results of stimulation of the cut cervical sympathetic.
(Cephalic end)

Turtle No.	Rate per Minute			Amplitude in mm.		
	Normal	During Stim.	After Stim.	Normal	During Stim.	After Stim.
12	18.1	13.2	16.7	16.7	16.6	16.6
14	31.0	30.5	30.5	4.5	4.5	4.5
Average	24.5	21.8	23.6	10.6	10.5	10.5

TABLE XII.

Tabulated results of stimulation of the cut cervical sympathetic.
(Abdominal end)

Turtle No.	Rate per Minute			Amplitude in mm.		
	Normal	During Stim.	After Stim.	Normal	During Stim.	After Stim.
12	18.1	18.4	18.0	17.3	16.6	16.0
14	30.5	32.0	31.0	4.7	4.5	4.5
Average	24.3	25.2	24.5	11.0	10.5	20.2

TABLE XIII.

Tabulated results of stimulation of the spinal cord.

(unbled turtles)

Turtle No.	Rate per Minute			Amplitude in mm.		
	Normal	During Stim.	After Stim.	Normal	During Stim.	After Stim.
35	33.6	34.2	35.1	37.1	42.1	41.7
36	30.0	29.8	30.3	19.7	21.3	20.3
37	31.3	31.1	31.6	26.6	25.6	25.7
38	22.4	22.2	21.6	28.3	29.3	28.1
39	27.6	27.0	27.6	44.3	43.6	43.5
40	36.2	36.0	37.0	27.6	26.5	26.1
41	28.3	28.2	27.8	29.4	29.2	28.5
44	23.2	23.6.	23.9	34.9	36.9	35.0
45	24.6	24.6	24.3	34.0	34.1	34.8
46	17.6	18.1	18.4	34.2	37.3	36.4
47	27.3	27.3	27.8	33.6	31.8	32.4
48	34.0	34.0	35.0	32.3	37.8	36.0
Average	27.2	28.0	28.4	31.8	32.9	31.5

TABLE XIV.

Tabulated results of stimulation of the spinal cord. (bled turtles)

Section (a)

Turtles which were bled and the spinal cord stimulated. No further experiments performed on them.

Turtle No.	Rate per Minute			Amplitude in mm.		
	Normal	During Stim.	After Stim.	Normal	During Stim.	After. Stim.
31	26.6	26.6	26.7			
32	29.5	30.4	30.3	16.3	16.2	15.4
33	40.4	41.2	41.7	27.2	31.2	30.1
34	35.0	35.3	35.4	36.0	35.5	35.2
Average	34.9	35.6	35.8	29.7	27.6	26.9

Section (b)

Turtles with blood retained in the vascular system and the spinal cord stimulated. Later the vascular system was drained of blood and the spinal cord stimulated ~~of which~~ the following are the results.

Turtle No.	Rate per Minute			Amplitude in mm.		
	Normal	During Stim.	After Stim.	Normal	During Stim.	After Stim.
44	25.5	25.0	25.5	30.0	32.0	30.0
45.	24.0	23.6	24.0	30.6	27.0	25.2
46	18.6	18.3	18.4	32.5	30.0	27.5
47	28.0	28.0	28.0	34.5	33.0	31.5
48	34.0	34.0	34.0	25.7	26.5	25.5
Average	26.0	25.6	26.0	30.6	29.7	27.9

TABLE XV.

Tabulated results of experiments in which the stimulation of the spinal cord resulted in some change in the amplitude irrespective of whether they had been bled or not.

Turtle No.	Rate per Minute			
	Normal	During	Immediately After Stim.	3-10 Minutes After Stim.
33	39.4	39.7	41.6	41.2
35	34.3	35.7	36.1	36.5
36	29.8	29.9	30.6	30.5
38	23.0	22.7	22.7	22.9
44	24.3	24.6	25.0	24.6
46.	17.5	18.1	18.3	18.5
48	34.0	34.0	34.7	34.0
Average	28.9	29.2	29.8	29.7

Turtle No.	Amplitude in mm.			
	Normal	During Stim.	Immediately After Stim.	3-10 Minutes After Stim.
33	23.5	29.5	33.7	27.7
35	37.6	48.0	49.7	34.7
36	19.4	22.5	21.2	20.0
38	31.2	33.0	33.7	30.5
44	35.3	40.0	40.5	36.3
46.	33.5	37.5	39.0	32.7
48	32.3	37.8	38.6	33.3
Average	30.4	35.4	36.6	30.7

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