A PHYSIOLOGICO–PATHOLOGICAL STUDY OF A CASE OF HEART–BLOCK OCCURRING IN A DOG AS A RESULT OF NATURAL CAUSES.*

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P L A T E S 1–7.

In the course of an investigation upon the action of strophanthus on the heart in complete auriculo-ventricular dissociation, it was the good fortune of the writer to find a dog with heart-block. This condition, which can be recognized readily by registering the movements graphically or the electrical variations of auricles and ventricles, has been studied experimentally on the mammalian heart by a number of investigators, notably by Humblet (1), Hering (2), and Erlanger (3). In accordance with the results obtained by these observers, it is generally believed that an injury to the auriculo-ventricular bundle will interfere with the free passage of the excitation wave which, in man, is normally conducted from auricle to ventricle within the narrow limits of 0.15 to 0.2 of a second.

The interference with the passage of the excitation wave varies directly with the extent of injury to the bundle.¹ This can be demonstrated easily by means of Erlanger’s clamp with which it is possible to produce, by gradual compression of the bundle, all grades of interference with a-v conduction, from a prolongation of the a-v interval, to a dropping out of one ventricular contraction in 10, 9, 8, 7, 6, 5, etc., auricular contractions until only every second or third excitation wave is able to force the block and excite the ventricle to contraction (2:1 and 3:1 rhythm). Finally, a condition of complete block is obtained in which auricles and ventricles

* Received for publication, April 12, 1912.

¹ The term injury is used here in a broad sense, not necessarily implying a destruction, either partial or complete, of essential elements, but including in its meaning an impairment of functional activity.
beat independently of each other and with entirely different rhythms.

Following these physiological researches, numerous observations of auriculo-ventricular dissociation were made on man by clinicians. A fair number of these clinical cases came to autopsy and in almost all of them a lesion of some essential part of the conducting system was found. The results of clinico-pathological studies, however, are not so uniform as those yielded by physiological experiment. A perusal of the somewhat extensive literature on the subject leaves the impression that the relationship existing between lesions of the auriculo-ventricular bundle and auriculo-ventricular dissociation is still ill defined. It is obvious, therefore, that the elucidation of this problem requires further work along the lines suggested by the best of the physiological and pathological studies already made.

The unique case here reported is of especial interest because it was possible to apply in its study the direct methods of the physiological laboratory.

**Physiological Part.**

*Technique of the Experiment.*—The dog, a female weighing 7,550 grams, was in the kennel for four days previous to the experiment. There was nothing abnormal in its actions, and though not under constant observation, it was never seen in any apoplectic form seizures such as are common in cases of heart-block in man, and in dogs with an experimental lesion of the a-v bundle of some duration (Erlander (4)). The animal was rather remarkable for its quietness, resting in a normal position the greater part of the time. No observations were made on the pulse before the experiment.

The dog received four cubic centimeters of a 2 per cent. solution of morphin sulphate hypodermically and twenty minutes later was fully anesthetized by means of ether. Both vagi were then exposed in the neck and ligatures passed under them; a small cannula filled with sodium carbonate solution was tied in a crural vein and later connected with a burette containing a solution of strophanthin (0.025 per cent.) in physiological saline. The chest was opened in the usual way, under artificial respiration; care was taken during the entire experiment to secure thorough ventilation of the lungs, as
a defective ventilation is capable of causing serious impairment of a-v conduction (5). The pericardium was slit open and the edges stitched to the sides of the opening in the chest wall. The right auricular appendage and the right ventricle were connected to tambours and their movements registered on the Hürthle kymograph. A time marker giving tenths of seconds and a signal magnet, in circuit with the primary coil of an inductorium, were placed beneath the levers of the recording tambours. All levers wrote on the same perpendicular line.

In the series of experiments to which this one belongs, a record of the heart's action was first obtained; that strength of rapidly repeated induced currents which would be sufficient to cause complete arrest of the whole heart was determined, and finally an attempt was made to crush completely the auriculo-ventricular bundle by means of Erlanger's clamp. This attempt was generally successful. In this particular instance, however, owing to a timely recognition of the abnormal action of the heart, the clamp was not applied.

On first opening the chest, the heart was observed to beat less frequently than is usually the case in dogs under morphin-ether anesthesia; there was also some arrhythmia, the beats having a tendency to occur in groups of two; the second beat was not an extrasystole. The auricles were beating so feebly that distinct pulsations could not be discerned. As stimulation of the vagus is often followed in a short time by more vigorous auricular contractions, this nerve was stimulated three times (from 1 to 5 seconds) at intervals of a few seconds. Although the current was a moderately strong one, the ventricles did not stop, neither were they appreciably slowed. The auricles, however, soon after vagus stimulation, gave contractions which were strong enough to be clearly recorded (beginning of figure 1); the degree of arrhythmia decreased also. It became then quite obvious that the low frequency noted in the ventricle was also present in the auricle, and that the contractions of the two chambers bore their normal time relation. The inference could therefore be drawn that the abnormal infrequency of the heart's action was due to overaction of the vagus.

Effect of Cutting the Right Vagus.—In order to test this hypothesis, the right vagus was cut, whereupon the auricular contrac-
Case of Heart-Block Occurring in a Dog.

tions more than doubled their former frequency (from 42.21 they rose to 99.83 per minute); at the same time they became quite regular and increased noticeably in force. The rate of the ventricles, however, remained unchanged, but their arrhythmia became a little more accentuated. Simultaneously with the increase in auricular rate there appeared, therefore, a dissociation of the action of auricles and ventricles (figure 1).

Two possibilities offer themselves in explanation of this phenomenon. The a-v dissociation might be due to an anatomical interference with the conductivity at the auriculo-ventricular junction, an interference which became manifest only upon an increased auricular rate and coincident decrease in the strength of the individual auricular impulses; or it might be due to the unopposed action of the left vagus nerve.

This second possibility is suggested by the recent observations of Cohn (6) and of Robinson and Draper (7). These observers found that in a number of instances, stimulation of the right vagus was followed by stoppage of the entire heart, while stimulation of the left vagus had but slight effect upon the auricles, although the ventricles were more or less inhibited, so that various grades of heart-block occurred. They infer, therefore, that the right vagus acts principally upon the chronotropic property of the heart muscle, while the left vagus influences principally its dromotropic property. Differences in the action of the two vagi are phenomena well known to physiologists; as far as the writer is aware, however, there has been no systematic study made regarding the percentage of cases in which the specific differences mentioned above may be found.

It is at least doubtful whether this case can be explained upon these premises; if the a-v dissociation were due to the unopposed action of a hypertonic left vagus, stimulation of the peripheral end of the right vagus with maximal induced shocks would certainly inhibit the whole heart completely, but as we shall see later, such stimulation was without effect upon the ventricles. The writer is therefore forced to the conclusion that the interference with a-v conduction was due to an anatomical block at the junctional tissues and not to hyperfunction of the unopposed left vagus. Such hyperfunction would, at any rate, be extremely rare, for, out of a fairly
large number of observations (incidental to class demonstrations) in which the right vagus alone was cut, this is the only instance in which a-v dissociation occurred. The reasons for the absence of a-v dissociation previous to section of the right vagus, in spite of the existence of an anatomical block, are given below.

The degree of block seems, on first inspection, to be slight; the tracings (figures 1, 2, and 3) show auriculo-ventricular rhythms varying from 1:1 to 2:1 and 3:1. A measurement of a number of a-v intervals gives figures ranging from 0.1 to 0.33 of a second; on the other hand, it happens sometimes that auricles and ventricles begin their contraction simultaneously.

A diagnosis of partial a-v block could be made were it not that a number of factors point to a conclusion which is, in all probability, more correct; namely, that the block is relatively complete. When the block is partial a sudden increase in auricular frequency is accompanied by ventricular stoppage which is then followed by a higher degree of block than existed before the rise in auricular rate. Such a phenomenon does not occur in absolutely complete block, but it may occur in relatively complete block.

Erlanger (8), who studied the reaction of the ventricle to increased auricular frequency in various degrees of a-v block, suggests that the rise in the rate of auricular contractions is accompanied by a diminution in the strength of the impulses transmitted to the ventricles. The sudden withholding of adequate impulses to the ventricles in partial block brings the ventricles to a standstill until they have developed their individual rhythm or until their irritability has reached such a height that they respond to a weak stimulus. In absolutely complete block, a rise in auricular frequency is not followed by stoppage of the ventricles for the reason that the ventricles have become entirely independent of the auricular impulses for their contraction, and have fully developed their own rhythmicity.

It is evident from this brief statement of Erlanger's findings that the duration of ventricular stoppage in partial block will depend on two factors, provided the frequent auricular impulses remain of uniform strength; viz., (1) the degree of irritability of the ventricular muscle, and (2) the nearness of the ventricular contractions to that rate characteristic of their inherent rhythm.
Case of Heart-Block Occurring in a Dog.

The degree of irritability of this dog's heart cannot be stated with certainty in the absence of a special inquiry into this property of the heart muscle; there is, however, no reason for believing it to be abnormal. The ventricle will be nearest the full development of its inherent rhythm when the partial block is of high grade, and particularly of that grade which Erlanger designates as relatively complete block. Whether ventricular stoppage occurs or not when the auricles are accelerated, will depend on the length of the ventricular cycle which in turn depends generally on the degree of a-v block. The longer the ventricular cycle, the nearer will be the full development of the idioventricular rhythm. The measurement of a number of ventricular cycles before section of the right vagus gives durations varying from 1.2 to 1.8 seconds; the longest cycle immediately following section of the vagus occupies 2 seconds. This cannot be regarded as a stoppage of the ventricles, as a number of cycles which occurred later and were independent of auricular impulses, had a duration of 1.8 to 2.1 seconds.

We may therefore consider the a-v block, here, to be of a very high grade though not absolutely complete. When the auricles are beating at a low rate and the excitation wave is presumably of high intensity, each auricular beat is followed by a ventricular contraction; in other words, the impulse is able to force the block; moreover, the conduction time is normal (0.1 of a second, first part of figure 1). On the other hand, when the auricles are beating at a high rate with a corresponding decrease in the intensity of the excitation wave, several auricular impulses fail to excite the ventricles to contraction. The rhythms that ensue vary considerably. There may be seen 1:1, 2:1, 3:1 rhythms and complete block, recurring very irregularly. The conduction time, when the block appears to be partial, varies from 0.1 to 0.33 of a second (second part of figure 1). Owing to the fact that auricular impulses force the block irregularly, the ventricles exhibit an aperiodic form of arrhythmia.

The Effect of Stimulation of the Peripheral End of the Cut

*This last figure would indicate an abnormally long conduction time; it is possible that what appears under such circumstances to be a true a-v rhythm is nothing more than a coincidence.
Vagus.—Erlanger (9) has shown that the duration of ventricular stoppage which follows tetanic stimulation of the vagus with maximal stimuli decreases as the degree of a-v block increases. When the block is complete, little or no slowing of the ventricles results. This slowing occurs some little time after the cessation of vagus stimulation; viz., in five to seven seconds in Erlanger's experience.

In my experiment the peripheral end of the right vagus was stimulated with maximal tetanizing shocks. Of five observations, four were made early in the experiment, while the last one was made during the rise of ventricular frequency which followed the injection of strophanthin. In all these tests except the last, the auricles came immediately to a complete standstill when stimulation began. Direct inspection of the auricles did not reveal the presence of the least contraction in these chambers. Furthermore, their stoppage continued for some time after the cessation of stimulation. The auricles, following complete inhibition, did not return immediately to their former rate, but after the first beat, two, three, or more auricular cycles took place with durations greater than the average. The first auricular contraction, on recovery, was much higher than the average.

There can be no doubt, therefore, that the stimuli sent into the vagus were of maximal strength, and yet such stimulation was practically without effect on the ventricles. An examination of table I shows that during the stimulation no slowing is present; and after stimulation has ceased, the slowing that occurs is insignificant and is found in the second or third beat following. At this time the auricles have practically recovered. A measurement of ventricular cycles beyond those shown in the table has failed to reveal any further slowing. There is a slight difference, therefore, between these results and those of Erlanger, who found that the maximal slowing of the ventricles did not occur until six to eleven ventricular beats had taken place following the beginning of stimulation. This difference is but one of degree and may be due to the fact that the duration of stimulation of the vagus in Erlanger's experiments was much greater than in those here reported.

There can be no doubt that when the a-v block is complete, or at least of very high grade, it is impossible to produce a decided
inhibition of the ventricles by vagus stimulation (figures 2, 3, and 4, and table I). A number of experiments performed on other dogs with complete a-v block, produced by crushing the a-v bundle, gave the same results. Erlanger's conclusion, therefore, that the vagus exerts little or no direct chronotropic influence on the ventricles would seem to be justifiable.

On the supposition that inhibitory impulses pass from auricles to ventricles along the same route as the a-v bundle, it does not appear from Erlanger's experiments that the structure concerned in this action is capable of regenerating, unless it be assumed that the character and intensity of the experimental lesion produced by this author precluded the possibility of regeneration. By electrical stimulation of the ventricles to a frequency higher than the rate of the independent ventricle simultaneously with vagus stimulation, Erlanger and Hirschfelder (12) have demonstrated that it is not the slow rate of the ventricles that causes them to manifest little or no inhibition.

The usual results of vagus stimulation in a-v block were likewise obtained by Erlanger (13) during the acceleration of the ventricles that followed the intravenous injection of digitalin. These findings are confirmed here by the result that followed vagus stimulation during the notable acceleration seen after the intravenous injection of strophanthin. At this time the auricles were beating at the rate of 148.88 and the ventricles at the rate of 153.41 per minute. Stimulation of the vagus brought the auricles (after one contraction following the onset of stimulation) to a complete standstill lasting 3.4 seconds. The duration of stimulation of the vagus was 1.4 seconds. In spite of this apparent increase in susceptibility of the heart muscle to vagal inhibition, no corresponding effect was observed in the ventricles. There was a disappearance of extrasystoles for a short period, but no distinct slowing (table I and figure 4).

In a recent article by Fredericq (10), this statement, as well as those that follow as a corollary, is disputed. This investigator shows that complete block may be produced by appropriate pressure upon the a-v bundle without interfering with the usual inhibitory action of the vagus upon the ventricles; greater pressure abolishes the latter effect. Garrey (11) obtained similar results for the turtle's heart at the sino-auricular junction.
## TABLE I.

*The Effect of Stimulation of the Peripheral End of the Vagus Nerve.*

<table>
<thead>
<tr>
<th>Before stimulation.</th>
<th>During stimulation.</th>
<th>After stimulation.</th>
<th>Duration of muscular stoppage.</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5, 0.7, 0.7, 0.6, 0.6</td>
<td>1.8, 1.7, 1.8</td>
<td>0</td>
<td>1.8</td>
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<tr>
<td>0.6, 0.6, 0.6, 0.6</td>
<td>1.7</td>
<td>0</td>
<td>1.8</td>
</tr>
<tr>
<td>Thirteen cycles of 0.6 sec. each</td>
<td>1.7</td>
<td>0</td>
<td>1.8</td>
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<tr>
<td>Eleven cycles of 0.6 sec. each</td>
<td>1.8, 1.8, 0.8, 1.8</td>
<td>0</td>
<td>1.8</td>
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<tr>
<td>Nine cycles of 0.6 sec. each</td>
<td>1.9, 1.3, 1.8</td>
<td>0</td>
<td>1.9, 1.9</td>
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<tr>
<td>Twelve cycles of 0.4 sec. each</td>
<td>0.45, 0.3, 0.45, 0.5, 0.3, 0.35, 0.3</td>
<td>0.45, 0.3</td>
<td>0.4</td>
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Case of Heart-Block Occurring in a Dog.

The Reaction of the Heart to Strophanthin.—The pharmacodynamics of cardiac drugs, particularly of those of the digitalis series, has received a great deal of attention, both from pharmacologists and from experimental therapeutists. Thus it has been established that the action of strophanthus on the cardio-inhibitory apparatus is practically identical with that of digitalis. This fact, however, is not so generally accepted as one might suppose, and numerous clinicians adhere still to the belief that the inhibition of the heart obtained under the administration of strophanthus is due to a direct action of the drug on the cardiac muscle and not to a stimulation of the cardio-inhibitory apparatus. We have in the condition of complete a-v dissociation a simple means of demonstrating that this belief is based on erroneous premises, since, as we have seen, the ventricles are under such conditions practically free from vagal influence. On the other hand, the auricles remaining under the control of the vagus, any effect which the drug may exert upon the inhibitory apparatus will become apparent in the behavior of the auricles. It will be possible, therefore, to determine simultaneously any effect which the drug may have upon the cardio-inhibitory apparatus on the one hand, and upon the heart muscle on the other hand, by observing the action of the auricles in the first case, and that of the ventricles in the second case.

The preparation used was strophanthin (Merck's crystalline). A solution of the strength of 0.025 per cent. was made in physiological saline. This solution was injected from a burette into a crural vein, as explained under the technique. Each dose was one cubic centimeter and the time interval between each injection varied from four to seven minutes.

The first effect of strophanthin was to cause a decrease in the rate of the auricles and ventricles. The lowering in frequency of both auricles and ventricles is not due, however, to the same cause. The auricles are inhibited through the stimulating action of strophanthin on the cardio-inhibitory center. This fact can be determined readily by injecting by the same method a single dose of the same preparation or of the tincture of strophanthus into a dog with an intact heart. The auricles slow gradually until complete inhibition is established. This inhibition disappears on section of both
vagi, or following the injection of atropin (Gottlieb and Magnus (14), Kochmann (15), Liagre (16)). During the complete arrest of the auricles, the ventricles beat at the rate characteristic of their own rhythm.

The decrease in auricular frequency became manifest after the first injection of strophanthin; during this time the auricles beat rhythmically (figure 5). With the advent of stronger inhibition following the second injection, the auricles beat arrhythmically, the arrhythmia being occasioned by the irregular occurrence of pauses (figure 6) which became progressively longer following the third injection; the height of the auricular contractions decreased with the lowering in their frequency.

As mentioned before, the ventricular rate was likewise diminished. This slowing of the ventricles, however, cannot be due to any chronotropic influence of the vagus on these chambers since direct stimulation of the peripheral end of the cut vagus was practically without effect on the ventricular rate. There is, however, simultaneously with the decrease in ventricular frequency, a decrease in the conductivity across the a-v bundle. In other words, the vagus under the action of strophanthin, exercised a well defined negative dromotropic influence on the junctional tissues. This is shown by the fact that with the decrease in ventricular rate the ventricles became rhythmical and by the further observation that the a-v block from being relatively complete became absolutely complete. Auricles and ventricles beat with entirely independent rhythms (figure 5).

It is true that the ventricular rate fell as low as 27.49 per minute, a rate of idioventricular contraction which is abnormally low for the dog's heart; but it is necessary to take into consideration here the special circumstance that in this animal the ventricular rate was at no time very high, in fact the average ventricular rate, preceding the administration of strophanthin and exclusive of the periods during which the vagus was stimulated, was 38.32 per minute. The duration of those ventricular cycles which were apparently not disturbed by auricular impulses varied from 1.8 to 2.1 seconds; under these conditions the idioventricular rate varied from 33.33 to 28.57 per minute, figures which are practically
Case of Heart-Block Occurring in a Dog.

the same as those found under the first phase of the action of strophanthin, viz., from 32.72 to 27.49 per minute (table II). The conclusion is therefore justifiable that if strophanthus exerts any direct inhibitory action on the heart muscle, it is so slight as to be negligible.

The action of strophanthin on the cardio-inhibitory mechanism was soon overshadowed by a rise of the irritability of the cardiac muscle, so that in spite of the fact that the vagus was likewise in a state of heightened irritability, as shown by the effect of faradic stimulation, the auricular and ventricular rates increased. Coincidently with the rise in the frequency of the auricular contractions the auricles became regular again, but there was no increase in the force of their beats (figure 8). Previous to the increase in ventricular rate, the conductivity across the a-v bundle improved so that, with an anatomical block which was not quite complete, the ventricles became again irregular from the occasional arrival of an adequate excitation wave from the auricle.

The rise in ventricular irritability manifested itself at first by the occurrence of an occasional extrasystole; later by the appearance in groups of a number of beats succeeding each other rapidly (figure 7). Shortly afterwards the ventricular acceleration became well established and rose progressively to a high degree; simultaneously, the height of the contractions increased. The rise in the irritability of the heart muscle occurred after the fourth injection (one milligram of strophanthin).

The auricular rate before the fifth injection was 132 per minute; that of the ventricles, 157.24 per minute: the auricular contractions were irregular and weak but quite distinct, while the ventricular contractions were regular and vigorous. Following the fifth and sixth injections, the auricular rate rose to 164.37 per minute, and afterwards declined rather rapidly to complete arrest preceded by group beating (figure 9). The auricles stopped approximately four minutes before the ventricles. If atropin be injected into the jugular vein immediately after auricular stoppage, the auricular contractions may return; shortly afterward they again stop, this time not to contract again. The auricular stoppage under excessive doses of strophanthin is therefore due primarily to a
Two stimulations of vagus immediately after section of rt. vagus.

Continuation.

Immediately after section of rt. vagus.

Stimulation of peripheral end of rt. vagus.

Continuation.

Continuation.

Continuation.

Immediately after section of rt. vagus.

Stimulation of vagus.

Immediately after section of rt. vagus.

Immediately after.

Continuation.

Immediately after.

During second injection.

Immediately after.

During third injection.

Immediately after.

During fourth injection.

Continuation.

During fifth injection.

Immediately after.

Continuation.

Stimulation of vagus.

Immediately after.

Immediately after.

During sixth injection.

Immediately after.

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return of vagal inhibition, and secondarily to a loss of irritability through the poisonous action of the drug on the cardiac muscle.

A careful analysis of this and other similar experiments leads to the inference that the increase in the tone of the cardio-inhibitory apparatus under the influence of strophanthus lasts practically the entire time that the auricle is beating. The increased activity of the cardio-inhibitory mechanism is unable to make itself felt during the notable rise of irritability of the heart muscle which follows moderately large doses of the drug. As soon as the irritability declines sufficiently, however, vagal inhibition is manifested by complete stoppage of the auricles. During this stage, lasting but a short time, the intravenous injection of atropin is followed by a return of the auricular beats. The auricular irritability continues to decline rapidly until all auricular contractions cease permanently. Curiously enough, while the auricles are the more irritable parts of the mammalian heart and the right auricle is the ultimus moriens under normal conditions, these chambers are nevertheless, the first to succumb to the toxic action of strophanthus. The ventricular contractions following the fifth and sixth injections became irregular owing to the occurrence of extrasystoles; the ventricular frequency rose to 190.02 per minute to decline in a short time to 174.19 per minute. From this relatively high frequency the ventricles passed suddenly into fibrillary contractions and stopped in the dias-
tolic position.

The quantity of strophanthin necessary to bring about the death of the heart was therefore 1.5 milligrams. As the animal weighed 7.550 grams, the lethal dose was 0.1986 of a milligram per kilo of body weight. This dose is smaller than the one given by Étienne (17), who determined that the minimal fatal dose of strophanthin (Merck) in the dog is 0.25 of a milligram per kilo when administered intravenously. His animals were neither anesthetized nor operated upon, circumstances which doubtless played an important part in their resistance to the drug.

PATHOLOGICAL PART.

The Gross Appearance of the Heart.—Immediately after the complete arrest of the heart, this organ was removed, its chambers
were opened, and the clots that had formed in the right auricle washed out. The following is taken from the protocols.

Heart.—Color and size normal. Weight 60.5 grams.

Right Side of Heart.—The posterior (septal) leaflet of the tricuspid valve is considerably thickened at its free edge; this thickening is smooth, firm, elastic, and semitransparent (resembling myxomatous tissue). Immediately above the attached portion of this valve and five millimeters from the opening of the coronary sinus, the auricular septal musculature shows an oval patch which is grayish in color and is traversed in all directions by fine dark red lines resembling enlarged capillaries. This patch measures three by five millimeters and its long axis runs parallel with the auriculo-ventricular margin. The pars membranacea septi is immediately in front of this patch (figure 10).

Left Side of Heart.—The same semitransparent gelatinous thickening seen at the edge of the septal tricuspid leaflet is found also in the angle between the posterior (non-coronary) leaflet and the right anterior leaflet of the aorta; it therefore overlies the pars membranacea septi, forming there a distinct nodule. The same thickening spreads along the entire length of the attachment of the posterior aortic leaflet as well as along the right (or posterior) attached margin of the right anterior leaflet (figure 11). The rest of the heart shows nothing noteworthy.

The vagi throughout their course in the neck showed no abnormality. The medulla was likewise normal in appearance.

The proportion of heart weight to body weight is 0.00801. The average proportional weight of the normal dog's heart according to Stewart (18) is 0.00721, and in the case of a female in his series with a body weight of 7,700 grams the proportional weight was 0.00746. We may therefore conclude that little or no hyper trophy was present.

Microscopic Examination of the Septum.—The entire heart was placed in 10 per cent. formalin for fifteen days. A block of tissue was then cut from the septum as follows: the interauricular septum was cut parallel with the auriculo-ventricular junction ten millimeters above it; another cut parallel with this one was made through the interventricular septum twenty millimeters below the auriculo-
ventricular junction. These two cuts were joined anteriorly by one at right angles with them and five millimeters in front of the pars membranacea septi, and posteriorly by another cut parallel to the one just mentioned and three millimeters posterior to the opening of the coronary sinus (figure 12).

This block of tissue was dehydrated in ascending strengths of alcohol and, after thorough infiltration, was embedded in celloidin. The block was oriented in such a manner that the sections were cut in a frontal plane, so that each section included a part of the interauricular septum and adjoining structures (e.g., the wall of the aorta), the auriculo-ventricular junctional tissues and the interventricular septum. The sections began anteriorly to the pars membranacea septi and were continued backward well beyond the opening of the coronary sinus.

The sections were cut twenty-five microns thick and were mounted serially. At first every fifth one was mounted, but later, as those parts of the tissue which are of interest were reached, three out of every five were selected, so that from among 900 sections obtained from the entire block, 480 were mounted. The sections were stained with Mayer’s acid hemalum and Van Gieson’s stain.

Before any part of the a-v bundle appeared, portions of the right limb and, later, of the left limb were found on the corresponding sides of the ventricular septum. The muscle fibers of both limbs were normal and the neighboring tissues presented nothing unusual. The succeeding sections showed a gradual rise in the position of the limbs of the bundle along the sides of the ventricular septum, so that ultimately they could be seen on each side of the lower border of the pars membranacea septi. Here, there appeared under the endocardium a tissue occurring in spherical or ovoid masses and consisting of ill defined fibers arranged more or less concentrically, giving to these masses the appearance of whorls. The fibers take a faint yellow stain except at the periphery of the mass, where in many sections they take a pink color. The nuclei are spindle-shaped. The same tissue can be seen at the free end of the septal tricuspid leaflet and at the base of the aortic leaflets in situations corresponding to those of the semitransparent swellings described in the gross appearance of the heart.
Case of Heart-Block Occurring in a Dog.

This tissue is, in all likelihood, newly developed connective tissue. The concentric arrangement of its fibers suggests that it is developed from the walls of the blood-vessels and that it might be elastic connective tissue. A few sections stained with Weigert’s elastic stain, however, gave negative results.

This tissue is seen in all succeeding sections. It invades now the right, now the left side of the membranous septum; it comes in contact in several places with the fibers of the bundle, which then exhibit evidences of pressure, but nowhere does it interrupt the main body of the bundle. A few foci of round cell infiltration are seen at various points on the surface of the bundle; these, however, are not numerous nor conspicuous.

There is a large amount of adipose tissue above the entire course of the bundle (figure 16). The extensive distribution of this adipose tissue corresponds to the area covered by the oval, grayish patch seen in the gross specimen above the attached margin of the septal tricuspid leaflet. A comparison of similar sections obtained from a normal dog’s heart shows that the adipose tissue has replaced a great part of the bundle fibers and of the ordinary auricular musculature. In some places the fibers of the bundle are separated by the adipose tissue into groups of various sizes (figures 13 and 15). The muscular connection between auricle and bundle (at the node of Tawara) takes place by a relatively narrow strand only, and but a short distance from the opening of the coronary sinus.

The anatomical pathway for the propagation of the excitation wave from auricle to ventricles was not completely interrupted at any point of its course. Indeed, it had, for a short distance at least, an almost normal appearance (figure 14). Along the greater part of the course of the bundle considerable pressure was evidently exerted upon its elements by the numerous whorls of new connective tissue already described. While such pressure led to structural alterations of the muscle fibers in but a few places, it is quite possible that this was the cause of the interference with the function of the conducting system exhibited in the action of the heart. A further impediment to the free action of this system was found in the relatively narrow connection between the auricular muscle and the node, as well as in the attenuation of the main bundle observed along its course.
Review of the Pathology of Heart-Block.—Most of the cases of heart-block found in the literature have been cases exhibiting the Adams-Stokes syndrome. Such cases were described by Morgagni (19) in 1761 and by Spens (20) in 1792 long before the contributions of Adams (21) in 1827 and of Stokes (22) in 1846 appeared. The number of cases published before the description of the auriculo-ventricular bundle by His (23) and others, and the subsequent study of its function, is relatively small. But even before a knowledge was gained of the part played by heart-block in the causation of the Adams-Stokes syndrome, the condition of the heart had been studied at autopsy, and Stokes, in particular, sought to establish a definite relationship between affections of the myocardium and the syndrome with which his name is associated.

A statistical study of the pathology of heart-block falls naturally into two distinct periods; viz., a period preceding the general recognition of heart-block, and one following it. There is, it is true, a period of transition during which the influence of certain opinions regarding the underlying pathology of the Adams-Stokes syndrome continued to be felt while our present conception of it was gradually spreading. This transitional period is naturally difficult to delimit and, moreover, were it possible to do this it would serve no useful purpose. For this reason, the year of His’s communication (1899) has been chosen arbitrarily as the date dividing the old period from the new.

The old period is of interest chiefly from an historical point of view. From this period I have been able to collect but fifteen cases that contain more or less definite information concerning the heart (table III). Even in these old cases it is possible to pick out nine with lesions occupying such positions as to constitute presumptive evidence of implication of the auriculo-ventricular bundle.4

The number of cases studied clinically and post mortem since 1899 testifies to the interest of the medical profession in this curious malady. I have collected sixty-three of these cases.

The object of collecting these cases was to determine to what extent the clear cut results of physiological experimentation were corroborated by disease of the auriculo-ventricular conducting sys-

4 These cases are indicated in the table by an asterisk.
**Case of Heart-Block Occurring in a Dog.**

### Table III

<table>
<thead>
<tr>
<th>Year</th>
<th>Author</th>
<th>Pathologic condition</th>
<th>Year</th>
<th>Author</th>
<th>Pathologic condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1885</td>
<td>Gibbings (32)</td>
<td>Heart and coronary arteries normal.</td>
<td>1887</td>
<td>Frey (32)</td>
<td>Not given.</td>
</tr>
<tr>
<td>1892</td>
<td>Sendlor (33) (Devic's case.)</td>
<td>Heart enlarged and fatty. Tumor (fibroma) the size of a walnut and of cartilaginous hardness 1 cm. below opening of pulmonary artery.</td>
<td>1893</td>
<td>Dumas (34) (Devic's case.)</td>
<td>Hypertrophy of heart. Lesion, the size of a large hazelnut, in the posterosuperior portion of interventricular septum.</td>
</tr>
<tr>
<td>1895</td>
<td>Rendu (35)</td>
<td>Gumma of interventricular septum extending from base of aortic cusps to anterior papillary muscles and implicating large mitral leaflet. The tumor was surrounded by a zone of interstitial fibrosis.</td>
<td>1895</td>
<td>Not given.</td>
<td></td>
</tr>
</tbody>
</table>

**Gross.**

**Microscopic.**

This statistical investigation has been somewhat disappointing owing to the incompleteness in many instances of the data necessary for such comparison. An analysis of table IV shows, for instance, that in sixteen cases in which a lesion in the path of the a-v bundle was demonstrable macroscopically, no microscopic examination of the septum was undertaken. In these cases the de-
struction, either partial or complete, of the a-v conducting system or of any part of it, must remain a matter of conjecture. On the other hand, of forty-one cases in which the septum was examined microscopically, seventeen are without definite information regarding the degree of auriculo-ventricular block existing during life. Thus, out of what seems at first to be ample material, there remain but twenty-four cases which can be used for the matter under consideration. These cases show that a complete transverse lesion of the main body of the conducting system (node and bundle proper) is invariably followed by complete heart-block.

The only exception to this rule is the well known case of Heineke, Müller, and Hösslin (68), in which, despite the complete replacement of the a-v bundle by fibrous tissue, the block was partial; during the last weeks of the patient's life the block, however, became apparently complete. Whether the complete destruction of the bundle took place during the last six weeks of the patient's life can only be surmised. The authors have suggested that a slow destruction of the bundle may be accompanied by the formation of other muscular pathways for the conduction of the excitation process. Or it may be that preformed muscular pathways under such circumstances assume this new function. The smooth muscle of the sub-endocardium and of the blood-vessels have been mentioned in this connection by Monrad-Krohn (84).

A second group of cases includes lesions varying widely in their severity. There seems to be in this group no definite relationship between the extent of the anatomical change and the character of the heart's action. The a-v block may be partial or complete, or a partial block may become complete; again, a partial block may disappear, the heart's action becoming normal. Finally there have been reported, within recent years, cases that exhibit in periodical recurrence normal a-v sequence, partial block, and complete block. Two such cases have come to autopsy; one was reported by Pribram and Kahn (79) and the other by Cohn, Holmes, and Lewis (83) (table IV).

A third group, also of recent origin and consisting at present of five observations, concerns cases of auriculo-ventricular dissociation

\[^5\text{Histological examination by Koch (86).}\]
Case of Heart-Block Occurring in a Dog.

in which alterations in the bundle were absent or insignificant. In the first of these the block was probably complete (Fahr\textsuperscript{a} (52)); in the second the block was complete (Krumbhaar (76)); in the third the degree of a-v dissociation is not given (Monrad-Krohn (84)); in the fourth, the block was partial (Mollard, Dumas, and Rebattu (85)); while in the fifth, the block was probably complete (Price and Mackenzie (87)).

It is unfortunate that, in none of these cases, apparently were the limbs of the bundle followed to their termination; viz., the points of fusion of the Purkinje fibers with the ventricular muscle proper. This is a matter of importance, and one which was correctly estimated by Fahr and by Monrad-Krohn when they refused to attach any great value to their own similar observations.

Evidently the number of well studied cases is insufficient to permit of any positive conclusion. The more general application of graphic methods in clinical investigations promises to furnish, in the near future, more accurate information upon the character of the heart's action, and in a greater percentage of cases than has been obtained heretofore. The post-mortem examination of the heart must be just as thorough as its ante-mortem study; it is particularly important that the whole conducting system shall be examined. An examination of the node, main bundle, and the beginning of the latter's limbs, is not sufficient; it should include besides the parts mentioned the junction of the auricular fibers with the node and the junction of the Purkinje branches with the ventricular muscle. Two cases point to the wisdom of this course; one is that of Armstrong and Mönckeberg (82) in which the lesion destroyed the connecting fibers between auricle and node, and the other, not so well defined, is that of Koch (80) (Pribram and Kahn (79)) in which a diffuse subendocardial induration seemed to have interrupted the branches of the left limb, especially at the base of the papillary muscles.

SUMMARY.

What is believed to be the first known case of heart-block arising

\textsuperscript{a}This is the first case of Deneke, in which Fahr reported negative findings. Subsequently Fahr rejected as unjustified his first conclusion, that permanent heart-block could occur without lesion of the conducting system.
in a dog as a result of an ingenerate pathological lesion is here reported.

The auriculo-ventricular dissociation was of that degree known as relatively complete block and became apparent on section of the right vagus nerve.

Stimulation of the peripheral end of the cut vagus failed to inhibit the ventricles, although complete inhibition of the auricles occurred. The same results were obtained during the ventricular acceleration produced by strophanthin, so that the failure of the vagus to inhibit the ventricles is not due to the latter's infrequent action, but more probably to a normal lack of direct chronotropic influence upon the ventricular muscle. These findings are similar to those obtained by Erlanger in experimental heart-block.

To small repeated doses of strophanthin injected intravenously the heart reacted as follows: (a) irregular slowing of the auricles and conversion of the relatively complete into an absolutely complete a-v block; (b) a rise in the irritability of the cardiac muscle manifested by a rapidly progressing auricular and ventricular frequency, the ventricular frequency surpassing ultimately the auricular frequency; (c) complete arrest of the auricles, the ventricles continuing at their high rate; (d) sudden fibrillation of the ventricles and shortly afterwards arrest in diastole.

There were found post mortem myxomatous-like thickenings at the free edge of the septal tricuspid leaflet and at the attached margin of the posterior aortic leaflet and along part of the right anterior aortic leaflet. There was also a grayish patch on the right side of the auricular septum above the auriculo-ventricular junction.

The thickenings at the edge of the valves consisted of dense, circumscribed masses of what appeared to be new connective tissue. The same tissue was found pressing against the bundle along the greater part of the latter's course. There was considerable fatty infiltration of the auricular musculature immediately above the bundle and, to a slight extent, of the bundle itself. The fibers of communication between the auricular muscle and the node of Tawara were relatively few as compared with those of the normal heart.

A review of the pathology of heart-block is appended, showing
the present status of the question concerning the relationship existing between disease of the a-v conducting system and the various grades of heart-block.

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George Bachmann.
Case of Heart-Block Occurring in a Dog.

EXPLANATION OF PLATES.

PLATE I.

In all the tracings, the upper curve is a record of the auricular movements; the lower curve that of the ventricular movements; upstrokes represent contractions. The time record gives tenths of seconds. The lowest line is that of the signal magnet.

Fig. 1. The first part of the tracing shows the action of the heart with vagi intact. The arrow marks the moment at which the right vagus was cut.

Figs. 2 and 3. Stoppage of the auricles on stimulation of the peripheral end of the right vagus. The ventricles are apparently not influenced.

Fig. 4. Effect of stimulation of the peripheral end of the right vagus during the cardiac acceleration that follows the administration of strophanthin. The auricles are completely inhibited; the only effect on the ventricles is a momentary disappearance of the extrasystoles.
Fig. 5. First effect of strophanthin. The transformation of a relatively complete, into an absolutely complete block by abolishing all a-v conduction. The ventricles beat regularly.

Fig. 6. Further action of strophanthin. Irregular inhibition of the auricles by stimulation of the cardio-inhibitory center. The ventricles continue to beat regularly at their own rhythm.

Fig. 7. Further action of strophanthin. The auricular rate is increased. The lower record shows the beginning of the increase in ventricular rate.

Fig. 8. Further action of strophanthin. The increase in auricular and ventricular rates is well established.

Fig. 9. Further action of strophanthin. Group beating of the auricles. The ventricular rate is notably increased. The vigor of the contractions is greater than at any other time during the experiment.
FIG. 15.
Plate 3.

Fig. 10. Right side of the septum (natural size). Note the swelling at the free margin of the septal tricuspid leaflet and the grayish patch with distended capillaries above the attached margin of the same leaflet. The light area in front of the patch indicates the position of the pars membranacea septi.

Fig. 11. Left side of the septum (natural size). Note the swelling at the attached portion of the right anterior and of the posterior aortic leaflets. The nodule at the angle between these leaflets overlies the point of division of the a-v bundle. The left limb of the bundle shows as a light band apparently continued into the false tendon running into the papillary muscle.

Fig. 12. Diagram of the right side of the septum showing the size and position of the block of tissue examined in serial sections. The numbered vertical lines indicate the position of the sections here illustrated. It will be seen that two of these include the pars membranacea septi (in dotted outline); the other two are in the region of the main body of the bundle.

Plates 4-7.

Figs. 13, 14, 15, 16. Camera lucida drawings of sections 215, 333, 438, and 493, respectively. Their position in the septum is indicated in figure 12.

a = auricular muscle; v = ventricular muscle; f = fibrous septum; b = a-v bundle; r1 = right limb; l = left limb; n = new fibrous tissue (myxomatous?); d = right side of fibrous septum; s = left side of fibrous septum; c = aortic cusp; t = tricuspid leaflet; w = aortic wall.