THE INTERPRETATION OF THE NORMAL ELECTROCARDIOGRAM. A CRITICAL AND EXPERIMENTAL STUDY *

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INTRODUCTION

Waller,¹ in 1888, was the first to demonstrate that the action currents arising from the heart muscle during its contraction were conducted out to the peripheral tissues in sufficient strength to be detected by leading off from the limbs to an electrometer. It was not, however, until the improvement and adaptation to physiological work of the thread galvanometer by Einthoven,² in 1903, that any considerable interest in this matter was aroused. In the nine years since Einthoven's first publication, a very large and rapidly increasing literature on the subject of the electrocardiogram has appeared, and great interest has developed as a result of its evident clinical and physiological importance. Notwithstanding the great amount of work that has been done, the various workers in this field are by no means agreed as to the interpretation of the normal electrocardiogram, and as a result, the interpretation of those departures from the normal that occur in cardiac disease, as well as the significance of the normal electrocardiographic curve in reference to the normal course of the cardiac impulse over the heart, has been largely influenced by the point of view held by the individual investigator.

Up to the present time the usefulness of the electrocardiogram from the clinical standpoint has been principally evident in the analysis of two classes of abnormal cardiac conditions; first, the heart arrhythmias, including under this the disturbances arising from depressed conductivity as well as those arising from ectopic impulse formation; and second, the condition and activity of the auricles (auricular hypertrophy, auricular fibrillation, etc.). In these two classes of conditions the electrocardiogram has only certain technical advantages over the venous and esophageal pulse tracings.

In a third group of cases however, of great importance clinically and to which in its present development at least the venous pulse is not applicable as a means of study, namely, the functional activity of the

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1. Waller: *Philosoph. Tr. Royal Soc.* 1888, 178B, 215.

2. Einthoven: *Ann. der Physik.*, 1903, xii, 1056.

ventricles, the electrocardiogram has yielded results which are to a considerable degree interpreted differently by different investigators. This is mainly due, it would seem, to the marked differences in interpretation of that portion of the normal electrocardiogram which represents ventricular activity (the Q, R, S and T waves of Einthoven). It is the purpose of the present paper to present certain facts from the literature and certain experimental observations of our own, which, while bearing on the interpretation of the electrocardiogram as a whole, have particular reference to the ventricular portion.

HISTORICAL REVIEW

An attempt at a complete review of the development of the electrocardiogram and the immense amount of clinical and experimental work of this subject would be beyond the scope of this paper. Reference will be made only to articles which bear directly or indirectly on the interpretation of its features as applied to the course of the cardiac impulse and the contraction of the different parts of the heart. An extensive review of the literature up to 1910 is given in the monograph of Kraus and Nicolai.³

The normal electrocardiogram, as described by Einthoven,⁴ shows always at least three waves, all usually in the same direction. If the leads to the galvanometer are so arranged that a movement upward of the thread on the record occurs with relative negativity of the electrode in contact with that portion of the body more directly connected with the base of the heart, all of these three waves are in the upward direction. The three waves, according to the nomenclature of Einthoven, are designated P, R and T. With certain leads, T may be directed downward, and this wave may change its direction independently of the other waves in apparently normal beating hearts. Aside from these waves, two downward-directed waves may occur. The first of these (the Q wave of Einthoven) immediately precedes the R. It is quite infrequent and is regarded by Kraus and Nicolai³ as abnormal. The second downward wave (the S wave of Einthoven) follows at once on the R. It is present in the electrocardiograms from adults in about one-third of all cases. In electrocardiograms from children it is always present and its frequency and size decrease with age (Kraus and Nicolai⁵). Finally, there are two parts of the curve which are described as having a horizontal course indicating equal potential of base and apex of the heart, one between the P and Q (or R) waves, the other between the R (or S) and T waves.

3. Kraus and Nicolai: *Das Elektrokardiogram des Gesunden und Kranken Menschen*, Leipzig, 1910.

4. Einthoven: *Arch. internat. de physiol.*, 1906, iv, 132; *Arch. f. d. ges. Physiol.*, 1908, exxii, 517.

5. Kraus and Nicolai: *Berl. klin. Wehnschr.*, 1907, lxiv, 765 and 811.

In his first publication, Einthoven ascribed the P and Q waves to the contraction of the auricles, the R, S and T waves to ventricular systole. Later work by Einthoven and others has shown that only the P wave of the normal electrocardiogram can be ascribed to the auricle. The P wave is the only wave present when the auricle alone contracts (Einthoven, Kraus and Nicolai). It is enlarged in auricular hypertrophy and absent in the absence of auricular contraction. The work of Samojloff⁶ and of Kraus and Nicolai³ tend to show that the P wave of the electrocardiogram is the first part of a diphasic variation which is evident in its entirety when the leads to the galvanometer are from the exposed auricle and not from the surface of the body.

In the interpretation of the group of waves which precede or accompany the first part of ventricular systole (Q, R and S), the views which have had widest acceptance are those of Einthoven and of Kraus and Nicolai. According to Einthoven,⁴ the horizontal portion of the electrocardiogram following the auricular wave (P) and lying between this wave and the first ventricular wave, represents the time necessary for the impulse to pass through the His bundle and its various ramifications, where physiological connection is made with the ventricular musculature. During this time the galvanometer shows no movement, because both auricles and ventricles are at rest and the contraction wave through the connecting bundle is so weak as to cause practically no difference in potential. Einthoven evidently regards the passage of the impulse through the bundle to be associated with a weak contraction.⁷ The next movement of the galvanometer thread does not occur, therefore, until the impulse has reached the ventricular musculature. The extensive branchings and connections of the auriculo-ventricular bundle, as shown by the work of Tawara,⁸ ensure that the excitation passing downward from the auricles reaches the ventricle, not merely at the base or apex, but over a large surface of ventricular musculature. With the passage of the excitation into the ventricle the complex Q R S occurs. If the impulse first reaches the portions of the ventricles lying toward the apex, the apex of the heart shows relative negativity to the base, and the downward directed Q wave occurs. If other portions of the ventricles lying nearer the base (particularly the right ventricular base) first receive the

6. Samojloff: Beitr. z. Physiol. u. Pathol., Festschr. f. Hermann, 1908, p. 171; Samml. anat. u. physiol. Vortr. u. Aufsätze. Hrgb. von Gaupp und Nagel, 1909, 1-5.

7. "Während dieser Zeit schreibt das Saitenbild des galvanometers eine horizontale Linie. Vorkammern und Kammern befinden sich in Ruhe, und die durch das Verbindungsbündel fortschreitende Kontraktionswelle ist an und für sich zu schwach um bei der für die Registrierung eines zweckmässigen Elektrokardiograms erforderlichen starken Spannung einen merkbaren Ausschlag des Galvanometers zu erzielen."

8. Tawara: Das Reizleitungssystem des Säugetierherzens, Jena, 1906.

impulse, the Q wave is absent. The R wave represents the spread of the excitation to and the contraction of the right ventricle and more basal lying regions. When S is present, it is an expression of the fact that the left ventricle and more apical regions of the heart soon show a predominant activity over the base and the apex thus becomes relatively electronegative to the base.

The second point of view, developed by Kraus and Nicolai,⁹ rests on the well-known division of the ventricular musculature into the papillary system, the circular musculature (Treibwerk) and the outer spiral fibers (Nicolai⁹), the first two being in connection by the so-called intramural fibers. Following the contraction of the auricles the impulse passes over the His bundle and those structures functionally connected with it. The slow conduction in the bundle explains the long interval between the P and R (or S) waves, and no action current of any importance occurs at this time because of the small size of the muscular mass. After this interval the basal portions of the papillary system normally first receive the excitation and as an expression of this the curve rises sharply to form the R wave. The excitation now spreads toward the apex and the R wave ends. This spread of the excitation is largely in a linear direction and explains the large size of the R wave.

The potential differences arising under these circumstances are all in the same direction and are cumulative, while when many muscle masses passing in different directions are the seat of an excitation, the potential differences may to a considerable extent or entirely neutralize one another. The Q wave, when present, is an expression of the fact that the excitation passes in the Purkinje conducting system quite far toward the apex before it reaches the papillary muscles proper. This causes relative apical negativity for a short period. The papillary system includes the papillary muscles proper and the internal longitudinal fibers of the ventricles. Through the auriculo-ventricular conducting system and its ramifications the impulse is distributed to all parts of the papillary system. Normally, the excitation reaches first that part of the papillary system lying toward the base and the true papillary muscles. The base of the ventricle thus shows relative negativity, and the R wave results without a preceding Q wave. The work of Hering¹⁰ tends to show that the true papillary muscles are the first part of the ventricle to enter into contraction. Since these arise toward the apex of the ventricle, they do not form a part of the basal portion of the papillary system and this would seem to be opposed to the view of Kraus and Nicolai. Rehfish¹¹ notes, however, that

9. Nicolai: *Verhandl. d. physiol. Gesellsch. zu Berlin*, Nov. 22, 1907; *Zentralbl. f. Physiol.*, 1907, xxi, 678; *Handbuch der Physiologie des Menschen*, Hrgb. von Nagel, 1909, i, 805.

10. Hering: *Arch. f. d. ges. Physiol.*, 1909, cxxvi, 225.

11. Rehfish: *Deutsch. med. Wehnschr.*, 1910, xxxvi, 977 and 1035.

the basal portion of the papillary system is more or less firmly fixed by attachments to the aortic cartilage and the auriculoventricular ring, and while this part probably receives the first branches from the His bundle and normally is the first part of the ventricle to receive the excitation, the first part to show movement of sufficient degree to be graphically recorded may well be the true papillary muscles. The basal portions of the papillary system may thus enter first into excitation, but due to the anatomical arrangement, show no visible contraction. Kraus and Nicolai thus conceive of the excitation as spreading out through the His bundle and its ramifications to various parts of the internal longitudinal fibers and papillary muscles of the ventricles. Normally, it affects the basal portions first, and hence the first ventricular wave (R) is directed upward. When the excitation reaches the parts of the papillary system lying more toward the apex of the ventricles, the true papillary muscles receive the impulse at their base and it spreads from base to apex of these muscles, a course opposite in direction to that from base to apex of the ventricle as a whole. This causes a downward-directed wave (Q), a wave stated by Kraus and Nicolai to be absent from the strictly normal electrocardiogram. In such an event, however, the activity of the base soon becomes predominant and the R wave occurs. The R wave is completed when the excitation spreads out from the papillary system through the intramural fibers to the circular fibers (*Treibwerk*) of the ventricles. If the excitation in its spread from the base reaches the apical parts of the papillary system before this occurs, as is usually the case, a short period develops in which there is relative negativity at the apex. This is expressed as the S wave. If, on the other hand, the spread through the intramural fibers occurs before or simultaneously with the excitation reaching the apical parts of the papillary system, the S wave is absent.

It will be seen that considered broadly, the views of Einthoven and of Nicolai in reference to the cause of the Q, R and S waves of the electrocardiogram agree quite closely. No distinction is made in either between the spread of excitation and contraction of the muscle, and it would seem that it is really contraction of the different regions which causes the development of the electrocardiogram. Einthoven even suggested, as we have seen, that the spread of the impulse through the auriculoventricular bundle is associated with a weak contraction. According to both views, this passage through the bundle and conductive system of the heart produces no wave in the electrocardiogram. It is only when the larger muscle masses of the ventricle are affected that any noticeable differences in potential arise. The two views differ mainly as to exactly what muscular masses of the ventricles in their activity produce these differences in potential. Einthoven lays stress particularly on the right ventricular base in the production of the R wave, while Nicolai goes into more detail in reference to the different layers of muscle of the ventricles.

Passing now to the remaining portions of the electrocardiogram, the horizontal part lying between the R (or S) wave, and the T wave, and the T wave itself, both Einthoven and Nicolai explain the former on a general and simultaneous contraction of the musculature of both ventricles, the action currents arising therefrom neutralizing one another so **that no difference in potential between base and apex** is present. Nicolai lays particular stress on the contraction of the circular fibers (*Treibwerk*). The development of the T wave is explained by Einthoven by the right ventricle (particularly the basal part) remaining in contraction longer than the remainder of the heart, causing the development of a late negativity of the base. This view is founded on the experimental work of Bayliss and Starling,¹² concerning the course of the excitation over the mammalian ventricle. These investigators concluded that in the exposed dog's heart the impulse passed from base to apex, and the indication of terminal basal negativity in the electrocardiogram (recorded by the capillary electrometer from the exposed heart) was to be explained by the base remaining in negativity after the negativity had subsided at the apex and not to a return of the excitation to the base. If under abnormal conditions the contraction ceases in each ventricle simultaneously, as Einthoven supposes to occur in myocardial insufficiency, the T wave is entirely absent. Kraus and Nicolai, on the other hand, explain the T wave as due to a late return of negativity to the base of the heart, a region of the base lying especially around the aorta and pulmonary artery being the last portion of the ventricles to enter into contraction. This view of the course of the impulse was first suggested by Gotch¹³ in 1907, and elaborated in more detail in 1909. Gotch conceives the contraction of the ventricle as beginning around the venous orifices, at the base of the ventricle, and spreading to the apex and thence to the arterial bases of the ventricles, following in its course the direction of the primitive cardiac tube. This work will be considered more fully in a detailed discussion as to the course of the T wave later in this paper.

Of other views that have been advanced to explain the normal electrocardiogram, we may next consider the interpretation of Eppinger and Rothberger.¹⁴ As we have seen, both Einthoven and Nicolai explain the electrocardiographic curve as a resultant of the play of antagonistic forces of electric potential between base and apex. Eppinger and Rothberger object to Einthoven's assumption that the relatively weak right ventricle can be regarded as representing, so far as the electrocardiogram is concerned, the cardiac base, and playing the predominant rôle in the production of the normal curve, while the left ventricle with its massive

12. Bayliss and Starling: Internat. Monatssehr. f. Anat. u. Physiol., 1892, ix, 256 and 276.

13. Gotch: Proc. Royal Soc., 1907, 79B, 323; Heart, 1909, i, 235.

14. Eppinger and Rothberger: Wien. klin. Wchnschr., 1909, xxii, 1091.

basal region, is actually regarded as the cardiac apex in this scheme. Eppinger and Rothberger understand Nicolai to regard the R wave as an expression of the spread of the stimulus, to conduction of the impulse in contrast to actual contraction, and cite several facts which they regard as opposed to such an interpretation. They state that if R is referred to conduction alone the interval from P to the end of R, which under these circumstances would represent As-Vs conduction, is actually larger than this conduction period. They find it difficult to understand why the R wave is not always diphasic in such conduction in a linear direction between two points and why the conduction of the excitation produces such a marked effect (R wave) in the terminal connections of the conductive system while it produces no effect in its passage through the bundle and its branches. They believe that the observations of Kahn on the time relation between the R wave and the rise of intraventricular pressure do not support, as they have been supposed to do, Nicolai's interpretation. Kahn, in a series of papers, has studied the time relations between the waves of the electrocardiogram and various features that occur in the cardiac cycle. He found by simultaneous records of the intraventricular pressure, the carotid pulse and the electrocardiogram, that the R wave begins before the pressure in the ventricle rises and is completed during the period of tension, having ended by the time the outflow period begins.¹⁵ Since, according to Nicolai, the R wave is due to the activity of the papillary system, it must occur before that part of the heart musculature which causes a reduction of the internal capacity of the heart becomes active, and this, as we see, Kahn finds to be the case. Similar relations have been found by Kahn to hold between the beginning of the first heart sound and the R wave.¹⁶ Eppinger and Rothberger criticize those facts as applied in support of Nicolai's view, in that they believe that the electrical change actually in all cases precedes the mechanical change to which it corresponds, and call attention to the fact that Kahn's curves show that the P wave of the electrocardiogram also precedes the rise in the pressure curve of the right auricle. Furthermore, they state that the contraction of the musculature must reach a certain point before rise of intraventricular pressure begins. They cite the experiment of Kahn in which he found that in artificial stimulation of the ventricle in *vagus* standstill the action current began .075 seconds before the rise of intraventricular pressure. Here the contractile substance was directly stimulated and yet the mechanical definitely followed the electrical response. Kahn,¹⁷ in reply to these objections, shows by a series of experiments on the dog's heart that while the electrical latent period of the heart (the time from incidence of stimulus to electrical

15. Kahn: *Arch. f. d. ges. Physiol.*, 1909, cxxvi, 197.

16. Kahn: *Arch. f. d. ges. Physiol.*, 1909, cxxix, 291.

17. Kahn: *Arch. f. d. ges. Physiol.*, 1910, cxxxii, 209.

change) comprises a considerable period of time (.02 to .03 seconds), the difference between the electrical and mechanical response is extremely short, not more than .002 seconds. Kahn concludes from this that the mechanical contraction of that part of the heart, the electrical expression of which goes to form the R wave, must occur not later than .002 of a second after this wave begins. He repeats his original conclusion as to the relation of the R wave to activity in the ventricle and shows that the mechanical activity of the anterior wall of the right ventricle begins after completion of the R wave. The time relations of the rise in pressure in the left ventricle, the first heart sound and the mechanical activity of the wall of the right ventricle to the beginning and length of the R wave of the electrocardiogram confirms the view that the R wave is to be referred to the activity of the papillary system. Kahn further states that he has never committed himself to the view that the R wave is purely a conduction phenomenon, but has merely insisted that the activity of the circular fibers (*Treibwerk*) occurs only after the completion of the R wave and has nothing to do with the production of this wave. Rehfish¹¹ calls attention to the fact that Eppinger and Rothberger have really misinterpreted Nicolai's statement in reference to the R wave. Nicolai does not state that the R is a pure conduction wave, but that it arises from conduction in and contraction of one of the muscle layers of the heart, namely, the papillary system. It is extremely difficult to obtain from Nicolai's statements the relative parts he regards conduction and contraction to play, if indeed he has in mind any sharp distinction between the two.

Having found serious objections to the two prevalent theories concerning the interpretation of the electrocardiogram, Eppinger and Rothberger present another point of view founded on a long series of experiments in which they attempted to render functionless different layers of the heart muscle by freezing with ethyl chlorid or by the injection of mercuric chlorid or silver nitrate. The results from these experiments lead them to the conclusion that it is not the play of antagonistic electric potentials at the base and apex of the ventricles that produce the electrocardiogram, but that the curve is the resultant of the action currents arising from the longitudinal and circular muscle system of the heart. Activity of the longitudinal musculature causes the galvanometer to give an upstroke (when connected so that the R is directed upward), while activity of the circular fibers neutralizes this or actually produces a downward movement. In other words, the production of the electrocardiogram does not depend on the resultant of electric conditions developed at base and apex of the ventricles from activity of the muscle in these regions, as assumed in the theories of Einthoven and of Kraus and Nicolai, but whether the curve is up or down depends on whether negativity pre-

dominates in the longitudinal or circular fibers of the heart. This conclusion is founded on the following experimental results:

1. Freezing the surface of the ventricles with a spray of ethyl chlorid produces no change in the R wave. This is true for both ventricles and for base and apex. The R wave must arise, therefore, from some deeper structure than the outer longitudinal layer. The T wave becomes smaller or negative on freezing any part of the surface of the left ventricle or the surface of the apex of the right ventricle. Freezing the surface of the base of the right ventricle, on the other hand, increases the T wave (in a positive direction). Section shows that the effect of freezing does not extend at the greatest to a depth of more than 1 millimeter.

2. Injury to the deeper layers of the left ventricle by injection of mercuric chlorid or silver nitrate caused in certain cases increase in the height of R, abolition of S, if present, loss of the level period between R and T, increase of the height and duration of T, and finally fusion of R and T to form a large monophasic upward directed curve. This effect, regarded as typical, was observed in thirteen out of twenty-five cases. In some cases no effect occurred from the injury; in others, there was merely an increase of T and a tendency to fusion with R. The results were the same whether the injections were made into the base or the apex of the ventricle. Injury to the anterior and posterior papillary muscles produced no effect.

3. Injury to the deeper layers of the right ventricle cause in typical cases the appearance, or increase if already present, of the S wave and increase of the T wave. The S and T continue to increase, the R wave becomes reduced and finally disappears and the curve assumes the form characteristic of an extra-systole of the left ventricle. That it is not, however, an extra-systole of the left ventricle is shown by the presence of a P wave. In some cases the R is reduced, the T increased and S is unaffected, but usually the essential change is the appearance or increase of an already present S wave. It is suggested that the different effects observed may be due to differences in the seat of injury, particularly as to whether the auricular or pulmonic regions are affected, but the experiments are not sufficient to demonstrate this.

4. Injury to the interventricular septum causes the same effect as injury to the deep layers of the left ventricle, unless the lesion reaches the muscles lying just beneath the endocardium, when the result is the same as that following injury to the right ventricle.

Eppinger and Rothberger cite the anatomical researches of Krehl and others as showing that while the middle or circular layer of fibers (*Treibwerk*) of the right ventricle is very poorly developed, it forms the greater mass of musculature of the left ventricle. The longitudinal fibers, on the other hand, are well developed in both ventricles. They believe, therefore, that any effect produced by injury to the deeper layers of the

left ventricle can be referred mainly at least, to the circular fibers. Injury to these causes an increase in the whole electrocardiogram in an upward direction, while injury to the right ventricle or internal longitudinal layers of the septum or left ventricle causes the opposite effect. The antagonistic forces at work in the production of the electrocardiogram may thus be regarded as the circular and longitudinal muscular systems. The former in its activity tends to cause the electrocardiographic curve to descend, the latter acts in the opposite direction. The normal electrocardiogram represents the resultant of these two. When one set of fibers is injured, the action of the other preponderates and a corresponding change in the curve occurs.

Eppinger and Rothberger's detailed explanation of the electrocardiogram is as follows: The R wave is an expression of the unopposed action of the internal longitudinal fibers and corresponds therefore to the onset of systole of the ventricles. The remainder of the electrocardiogram is the resultant of the action of two forces. The activity of the circular fibers may predominate for a short time to form an S wave. The level part of the curve between S (or R) and T represents a complete antagonism of the two systems. They make no definite statements in reference to the formation of the T wave. The observation of Einthoven that in man hypertrophy of the left ventricle is frequently associated with a negative R, while in hypertrophy of the right ventricle the R is increased in a positive direction, seemed to support his view that the base of the heart, so far as concerns the production of the electrocardiogram, is represented by the right ventricle and it is the activity of this which normally causes the R wave. Eppinger and Rothberger note that the same fact may be well explained on their interpretation, since in left ventricular hypertrophy the increase is almost entirely in the circular fibers, while in right ventricular hypertrophy it is the longitudinal system which is increased.

In a later paper, Eppinger and Rothberger¹⁸ study the effect on the electrocardiogram of dogs of cutting away the whole of either the right or the left ventricle. Complete removal of the left ventricle causes the normal electrocardiogram to be replaced by a large upward-directed monophasic curve, which persists until stoppage of the heart (usually in about five minutes). The first effect of removal of the right ventricle is a reduction of the R and a great increase in the S wave, but before complete stoppage of the heart the curve assumes a fairly close resemblance to the normal electrocardiogram. The R wave is small, the T very large. It would appear, therefore, that the left ventricle alone can give an approximately normal electrocardiogram, while the right ventricle alone cannot. Since the left ventricle contains both longitudinal and

18. Eppinger and Rothberger: *Zentralbl. f. Physiol.*, 1911, xxiv, 1053.

circular musculature, while the right ventricle contains very few if any circular fibers, these results seem to bear out the interpretation based on their earlier work.

Eppinger and Rothberger thus assign all the waves of the electrocardiogram, more definitely perhaps than either Einthoven or Nicolai, to muscular contraction. The accuracy of their experiments and the value of the conclusions derived from them would seem to depend largely on the exactness of localization of the methods employed for producing loss of function in the different muscle layers. The injury done was apparently determined as far as possible by post-mortem examinations. It must be noted that the experimental results were by no means uniform and many departures from the results they regarded as typical occurred. These may be perhaps explained, as they suggest, by injury to more than one layer. The heart of the frog and tortoise, as shown by Samojloff,¹⁹ Straub,²⁰ and Gotch,¹³ gives an electrocardiogram in every way similar to that of the mammal. We have been unable to find in the literature any full description of the muscular layers of the cold-blooded heart or any study as to the possible differentiation into longitudinal and circular fibers. It is impossible, therefore, to say at present whether the similarity of the electrocardiogram of cold-blooded animals and mammals is opposed to the theory of Eppinger and Rothberger. They suggest that this similarity is best explained on a similar anatomical arrangement of the cardiac musculature in the cold-blooded animal and the mammal.

From results obtained by the action of digitalis on the dog's heart *in situ*, Selenin²¹ interprets the electrocardiogram as the resultant of the interference of the electrical waves arising from the right and left ventricles respectively. The ground elements are the diphasic waves of the two ventricles, such as occur in characteristic and unmodified form in extra-systoles of these chambers. An extra-systole of the right ventricle produces a diphasic electrocardiogram in which the first movement (R) is upward, the second (T) downward. The R is large, the T relatively small. An extra systole of the left ventricle, on the other hand, causes a diphasic curve in which the first movement is downward, while the T is positive. The R in this case is smaller than the T. Combining these two curves one may obtain a curve similar to the normal electrocardiogram of the two ventricles. The upward R of the right ventricle more than neutralizes the downward R of the left; therefore the normal R is positive in direction, but smaller than the R of a right ventricular extra-systole. The positive T of the left ventricle is also larger than the negative T of the right ventricle, so the T wave of the normal electrocardiogram is usually in an upward direction. Selenin explains the effect of

19. Samojloff: Arch. f. d. ges. Physiol., 1910, cxxxv, 417.

20. Straub: Ztschr. f. Biol., 1910, liii, 523.

21. Selenin: Arch. f. d. ges. Physiol., 1912, cxliii, 137.

digitalis as causing a preponderance in action of the left ventricle and quotes from the literature in support of the view that digitalis acts mainly on the left ventricle. In the therapeutic stage of action of the drug the P and R are not essentially changed, while the T is increased. As the toxic stages develop the R wave becomes reduced, the T much increased and finally the curve resembles that caused by an extra-systole of the left ventricle. The R almost entirely disappears, it is followed by a large downward-directed wave (S) and a large positive T. The S wave is explained by Selenin by an absence of complete synchronism of the electrical curves of the two ventricles, the S wave really representing the first phase of the diphasic curve of the left ventricle.

Opposed to Selenin's view may be mentioned the observation of Eppinger and Rothberger,²² that the left ventricle alone may give an approximately normal electrocardiogram, while the right ventricle alone cannot. Eppinger and Rothberger²² have furthermore shown that when the branch of the His bundle going to either ventricle is cut, the electrocardiogram assumes the form characteristic of an extra-systole of the ventricle still retaining its connection with the bundle. Both ventricles continue to contract and yet the electrocardiogram is profoundly modified. The development of the so-called atypical electrocardiogram characteristic of extra-systoles would seem to depend, therefore, rather on an abnormal entrance of the impulse into the ventricle. Instead of the excitation being conducted to the ventricle over its normal route from the auricle, the His bundle and its branches, it originates at the part of the ventricular muscle stimulated, or in Eppinger and Rothberger's experiments, spreads from the other ventricle. When one ventricle is stimulated, both, of course, contract, and there is no evidence that the one not directly stimulated contracts less strongly than the one stimulated. To support Selenin's view, it would seem necessary to show that the left ventricle contracting alone or the right ventricle contracting alone would give curves, which, on combining, would form the usual electrocardiographic curve as a resultant.

In marked contrast to the preceding views as to the interpretation of the electrocardiogram, is the theory of Hoffmann.²³ From a critical review of the literature, certain observations in man and experimental work on animals, Hoffmann came to the conclusion that the normal electrocardiogram represents two distinct activities in the heart occurring during its systole, namely, conduction of the excitation and contraction of the muscle. Each activity, according to this interpretation, is associated with the development of electrical energy, and so far as the ventricle is concerned, the Q R S complex is caused by the passage of

22. Eppinger and Rothberger: *Zentralbl. f. Physiol.*, 1911, xxiv, 1055; *Ztschr. f. klin. Med.*, 1910, lxx, 1.

23. Hoffmann, A.: *Arch. f. d. ges. Physiol.*, 1910, cxxxiii, 552.

the wave of excitation over the conducting system of the ventricle, while the remaining portion of the ventricular electrocardiogram (level period and T wave) results from the electrical energy liberated by the contracting ventricle. That a possible separation of these two phenomena in the genesis of the electrocardiogram must be considered seems to have been first suggested by Judin.²⁴ The curve of electrical response of a frog's skeletal muscle (gastrocnemius) shows, according to Judin, a rapid and large wave preceding and a much slower and less intense change accompanying the contraction of the muscle. Judin evidently realized the importance of this observation in reference to the analysis of the electrocardiogram, but so far as we know he has not attempted this in detail. In the article referred to the following statement occurs:

Dem Aussehen nach erinnert diese Kurve sehr an den Teil des Elektrokardiograms, der sich auf die Ventrikel bezieht. Daraus folgt, das ehe eine Erklärung des Elektrokardiograms gegeben wird, es geboten erscheint, Klarheit in die Frage von den Aktionsströmen des Muskels überhaupt zu bringen, da diese Frage nicht so einfach ist, wie man dies bis jetzt gewöhnlich annimmt.

Hoffmann shows by a review of the literature and by his own experimental work that the R and T waves frequently vary independently of each other, and believes that the R wave cannot be considered as representative of contraction of the ventricular muscle, since it does not, as has been assumed, especially by Einthoven, show any relation in its size to the extent of this contraction. He calls attention to the fact that in the so-called atypical electrocardiogram (electrocardiogram of extrasystoles or ectopic impulse formation²⁵) the R wave is much larger than the normal, while in many cases at least the mechanical systole is much weaker than normal. Many observations, on the other hand, indicate that the size of the T wave, frequently, at least, varies directly with the size of contraction.

The T wave is increased during and after muscular work (Einthoven,⁴ Müller and Nicolai²⁶); it is first increased and then decreased by the action of heart poisons (Kraus and Nicolai³), before death it becomes small or disappears (Kraus and Nicolai), and it is small or negative after excessive hemorrhage and in chloroform narcosis (Einthoven⁴). Hoffmann's own experiments speak strongly for the view of direct association between the contraction and the T wave. He recorded the electrocardiogram from frog hearts simultaneously with suspension curves of the ventricle and showed that when the heart is brought to a complete standstill by the application of muscarin, an electrocardiogram is still evident.

24. Judin: *Zentralbl. f. Physiol.*, 1908, xxii, 365.

25. Hering has introduced the term *nomotopic* to indicate a normal impulse originating in the normal pacemaker of the sinus region. All impulses originating outside of this area are *ectopic*.

25. Hering: *Arch. f. d. ges. Physiol.*, 1910, cxxvii, 466.

26. Muller and Nicolai: *Zentralbl. f. Physiol.*, 1908, xxii, No. 2.

This electrocardiogram from the non-beating heart differs from the normal merely in the absence of a T wave; the R wave is not reduced in size. As the beats return following the removal of the muscarin effect by the application of atropin, the R wave becomes no greater, although the extent of contraction increases rapidly. The T wave, however, reappears, and gradually increases as the size of the beat returns to normal. In the frog's heart during *treppe* the R wave does not increase as the extent of contractions increase. Application of distilled water to the heart produces weaker and weaker systoles and finally cessation of contraction without decrease in the R wave, but with decrease and disappearance of the T wave. These results show a striking lack of correspondence between the extent of contraction and the R wave and prove that the production of the electrocardiogram is in part unconnected with contraction of the cardiac muscle. The abolition of contraction with maintained conductivity does not entirely abolish the electrocardiogram. The group R (Q, R, S) is to be ascribed, not to contraction of the muscle, but to conduction of the cardiac impulse. Under normal condition the impulse wave, or wave of excitation, is followed by the contraction wave. Under certain experimental conditions, as described above, this does not occur and the change in the electrocardiogram that results is confined solely to the T wave. Hoffmann further notes that in the frog's heart the T wave falls toward the end of systole, and when the length of systole is changed by cooling or warming the heart the T wave separates or approaches R to hold its place always toward the end of systole. The T wave is thus closely associated with contraction and particularly the latter part of the curve. Hoffmann agrees with Einthoven and with Kraus and Nicolai in explaining the level part of the electrocardiographic curve between R and T as due to simultaneous contraction of all parts of the heart and the action currents arising from this neutralizing one another so that no difference in the potential of base and apex occurs. His interpretation of the T wave is essentially that of Einthoven in that it is referred to the cessation of contraction in certain regions of the ventricle while contraction continues in other regions. With reference to each wave of the electrocardiogram the interpretation in detail is as follows: The P wave is the expression of the spread of the impulse over the auricle. The following level part of the curve between P and R represents the contraction of the auricle and the passage of the impulse through the His bundle to the ventricle. The contraction of the auricle is presumably too weak to give any noticeable differences in potential, and hence no auricular T wave is normally present. The conduction through the His bundle is very slow and this explains why it produces no effect on the electrocardiogram. He cites the work of Grützner, Mackenzie, Kuhe and Biedermann, in showing the absence of electrical change in slowly contracting smooth muscle. The impulse is distributed

first to the papillary muscles. If the parts lying near the apex first receive the impulse from the branches of the bundle, a Q wave occurs. When the excitation reaches the base the R wave occurs. It then rapidly passes to the apex, causing the development of the S wave. By the end of this period the whole musculature of the heart has received the wave of excitation. Now contraction sets in and for a certain period no further change occurs in the electrocardiogram, because all of the heart muscle is active. After a time contraction begins to wane in certain regions and persists undiminished in others and thus gives rise to a difference in potential between base and apex and the T wave is produced.

The essential characteristic of Hoffmann's interpretation and the point in which it differs from all views in reference to the formation of the electrocardiogram is thus the sharp differentiation between the rôle played in its production by conduction of the excitation on the one hand and the contraction of the muscle on the other. As expressed by Hoffmann, the electrocardiogram is to be regarded as a curve of excitation plus the end of a contraction curve.

Considering now in more detail the interpretation of the T wave, the various views that have been more or less definitely expressed may be divided into four groups: (1) The T wave is not really indicative of any potential change arising from activity of the cardiac muscle, but is due to changes in the position of the heart during its contraction, resulting in disturbance of the null point of the galvanometer. 2. The T wave is the result of the contraction of the musculature of certain regions or certain layers of the heart just as the R wave is the expression of the contraction of other regions. 3. The T wave is not a special feature associated with the contraction of musculature from any particular region of the heart, but is a phenomenon associated with contraction of cardiac muscle in general. 4. Some factor or factors enter into its formation other than simple contraction of the muscle.

The first mentioned view has been suggested by Ussoff.²⁷ As a result of contraction of the ventricle the long axis increases and a change of the line of isopotential in relation to the leads to the galvanometer results. Normally, this change in position results from activity of the left ventricle and the T wave is positive. If the right ventricle contracts more strongly than the left the T wave is negative. If the whole heart contracts weakly, as occurs in dilatation, the form change is slight or absent, and the T wave is likewise small or absent. Most authors have attempted to interpret the T wave according to the second mentioned view. Probably the interpretation that has been most widely accepted is that developed by Gotch.¹³ In this the T wave is referred to a late contraction of the musculature of the ventricles surrounding the base

27. Ussoff: Quoted from Rehfish (Note 11).

of the aorta and pulmonary artery. Gotch attempts to bring the course of the cardiac impulse into relation with the phylogenetic development of the heart from the primitive cardiac tube, and conceives the impulse in the fully developed mammalian organ as entering the auricular end of the ventricle, thence passing to the apex and finally terminating at the arterial base (aortic and pulmonic bases). Bayliss and Starling¹² had previously worked on the course of the impulse over the mammalian ventricle by the method later used by Gotch and had concluded that the late basal negativity (as shown by the T wave of the electrocardiogram) was due, not to return of negativity from the apex to the base, but resulted from the fact that the negativity at the base outlasted that at the apex. They conceived the contraction wave as beginning at the base and passing to and terminating at the apex, while Gotch differentiates between the auricular and arterial bases and supposes the wave of contraction to pass from the first to the apex and thence to the aortic and pulmonic base. Gotch worked on the exposed heart of the tortoise and rabbit with the electrodes placed directly on the surface of the heart and connected with a capillary electrometer. With one electrode in contact with a considerable part of the base of the ventricle, including the muscle lying around the base of the aorta, the other in contact with the apex, he obtained a curve from the tortoise's heart resembling the normal ventricular electrocardiogram with a pronounced T wave. The late negativity of the base (T wave) was not obtained when the basal contact was limited to the lateral regions of the ventricular base, while a localized contact on that part of the base from which the aorta arises gave a curve resembling that obtained when the contact included the basal region as a whole. It seemed clear, therefore, that the portion of the base which is responsible for this late negativity is the region lying at the base of the aorta. The base of the ventricle is thus the seat of two potential changes which occur at different times in ventricular systole, one early, the other late. The second change, that which gives rise to the T wave, is only manifest when the contact of the basal electrode includes that portion of ventricular musculature lying at the root of the aorta. If it is true that the impulse passes as a wave from the auriculoventricular junction to the apex and then returns to the neighborhood of the aorta, the former should show evidence of negativity before the aortic region, and this he found actually to be the case. When one electrode was placed in contact with the lateral parts of the ventricular base and the other with the base of the aorta, the curve obtained was diphasic; the auricular base was first negative and after a period of equipotential, relative negativity developed at the aortic region. The experiments on the exposed heart of the rabbit confirmed this interpretation. Gotch, furthermore, found that in the frog, tortoise and rabbit, an increase in the contraction of the aortic region of the ventricle produced by a rise of blood-pressure is associated with an

increase in the size of the T wave. In the rabbit's heart a weakening of the beat of the ventricle from any cause results in a decrease, or if pronounced, a total disappearance of the T wave. In a strongly-beating rabbit's ventricle shifting the basal electrode away from the aortic (or pulmonic) region results likewise in a reduction of the T wave.

Nicolai, as we have seen, explains the T wave by a return of negativity to the base and hence agrees with the interpretation first proposed by Gotch. Einthoven, on the other hand, inclines to the conception developed by Bayliss and Starling, that the terminal basal negativity does not represent a return, but a continuation of negativity of this region after it has disappeared at the apex. Eppinger and Rothberger make no very definite statements in reference to the cause of the T wave. They note that since freezing the superficial layer of the ventricular muscle affects only the T wave, while injury to the deeper layers produces none or only a slight effect on this wave, it probably does not arise from activity of the deeper layers. In their description of the effects of injury to the deeper muscles they, however, describe quite marked effects on the T wave.

The third point of view mentioned above, namely, that the T wave is not to be referred to any special region or layer of musculature, but is an essential feature accompanying the contraction of cardiac muscle in general, is the central idea in Hoffmann's interpretation of the electrocardiogram. Hoffmann, as we have seen, differentiates sharply between the electrical effect produced by conduction, on the one hand, and contraction on the other. The first is represented in the ventricular electrocardiogram by the group R (Q, R, S), the second by T. Early in systole, when the whole cardiac muscle is in contraction, no T wave normally develops because the various action currents produced neutralize one another so that no difference in potential between base and apex is present. Such difference in potential only arises when some portion of the heart (normally the apical regions) begin to pass out of contraction, while others (normally the basal regions) remain strongly contracted. While thus it is really one particular region of the heart, the ventricular base, which is mainly concerned in the production of the T wave, by this point of view as expressed, any contracting cardiac muscle, no matter from what region of the heart, should give a T wave if the change in potential thereby induced is unopposed by simultaneous changes developed in other regions of the heart.

Finally, the view that some other factor besides simple contraction of heart muscle plays a rôle in the formation of the T wave has been suggested by Samojloff and by Straub. Samojloff,¹⁹ working on the frog's heart, came to the conclusion that the T wave is composed of two components, one representing conduction of the excitation, the other contraction of the muscle. He found in extra-systoles of the frog's ventricle

that while the direction of the R wave changed, depending on whether the extra-systole arose from base or apex stimulation, that the T wave always retained the direction present in the normal beat. However, the size of the T wave varied in these two cases. When the T wave in an extra-systole is in the same direction as the R, it is smaller than in a normal beat, while when the T is in opposite direction to the R, it is larger than the normal. This can be explained if the T wave is regarded as representing the second part of a diphasic curve of conduction, plus a contraction curve, in which the latter element always predominates. The part of the T representing conduction is always opposite to the R, representing as it does, the second part of a diphasic change. When the second component of the T (representing contraction) is opposite in direction to this, these two subtract from each other and the T is small. When they are both in the same direction the two components are added and the T wave is larger than normal. It will be noted that in each case the second component of the T (that representing contraction) predominates. Straub²⁰ places the T wave at the beginning of diastole in the frog's heart and suggests that it may be in some way connected with assimilatory processes in the muscle. He showed that warming the ventricle increases its size (in a positive direction), while cooling causes it to become small or negative.

The T wave, as has been noted by most writers, is by far the most variable feature of the electrocardiogram. While in the normal curve from man it is nearly always in the same direction as the R wave, in the frog, tortoise and in mammals used in experimental work a downward-directed (negative) T wave is not at all uncommon in an apparently normal heart beat. Many observations have been made in an attempt to determine the factor or factors that underlie the variations in size of the T wave and the majority perhaps point to the conclusion that a close correspondence exists between the extent of ventricular contraction and the size of this wave. The work of Hoffmann in this connection and the literature he cites has already been referred to. Rehfish,²⁸ in an extensive as determined by orthodiagraphic methods. The highest positive T waves comes essentially to this conclusion. In an analysis of 350 clinical cases the size of the T wave was compared with the arterial blood-pressure as measured by the v. Recklinghausen tonometer and the size of the heart as determined by orthodiagraphic methods. The highest positive T waves were present in cases of moderate blood-pressure (111 to 130 mm. systolic pressure), and in which there was no great enlargement of the heart, but in which the x-ray examination showed particularly strong heart movement. The most pronounced examples of this type were cases of well-developed hypertrophy with no evidence of broken compensation, espe-

28. Rehfish: *Ztschr. f. exper. Pathol. u. Therap.*, 1911, ix, 716.

cially well marked in cases of pure cardiac neuroses. In pronounced heart weakness or in dilatation and in very small hearts with low blood-pressure, the contractions of the heart, as shown by the fluoroscope, are small, and these are always associated with a small T wave. In greatly enlarged hearts with very high blood-pressure (180 to 250 mm. systolic) the T wave is small or negative in the majority of cases. The R wave shows a tendency to increase in size with increase in blood-pressure and increase in size of heart, but the change is not so marked as occurs in the case of the T wave. Pribram and Kahn²⁹ conclude from a study of over 300 pathological cases that while variations in the size of the T wave in apparently similar cases is quite common, in general T is strongly positive in forcibly contracting hearts, while it is small or absent in very weak hearts. While they find that frequently the R wave is modified in right and left ventricular hypertrophy in the way described by Einthoven, many exceptions occur. Samojloff¹⁹ found that in the electrocardiogram of the frog's heart the first systole following the compensatory pause of an extra-systole produced by stimulation of the ventricle ("post extra-systolic systole") shows a larger T than normal, while the R wave is unchanged in size. The T wave of the second normal systole following an extra-systole is, however, smaller than that of succeeding systoles. Langendorff³⁰ and Bottazzi³¹ have shown that the first post extra-systolic systole is larger, the second smaller, than the average systole. In the electrocardiogram these changes in size of systole are marked solely by changes in size of the T wave. Moreover, in the extra-systole itself the T wave is smaller than normal and this difference is more pronounced the earlier the extra-systole follows a normal systole. As is well known, the earlier an extrasystole falls in the preceding cycle the smaller the contraction. The size of the extra-systolic contraction is thus directly connected with the size of the T wave. That the T wave frequently varies independently of the R and seems to depend as to degree of its development largely on the extent of contraction of the heart, is further indicated by studies on the action of certain poisons on the heart and on the influence of the extrinsic cardiac nerves.

The action of drugs of the digitalis series has been studied by Nicolai and Simons,³² by Straub,³³ and more recently by Selenin.²¹ The last-named investigator worked on dogs with hearts *in situ* and found that in the stage of therapeutic action of digitalis the P and R waves were not essentially changed from the normal, while the T wave was increased in size. Nicolai and Simons describe in man an increase in size of the T

29. Pribram and Kahn: *Deutsch. Arch. f. klin. Med.*, 1910, xcix, 479.

30. Langendorff: *Arch. f. d. ges. Physiol.*, 1898, lxx, 473.

31. Botazzi: *Zentralbl. f. Physiol.*, 1896, x, 401.

32. Nicolai and Simons: *Med. Klin.*, 1909, v.

33. Straub: *Ztschr. f. Biol.*, 1909, liii, 106.

wave without essential change in the R as a result of therapeutic doses of digitalis. Straub describes similar effects from strophanthin in cats and rabbits at the beginning of the toxic stage of action. Further action causes a negative T. Epinephrin (adrenalin) causes the T to become large and negative. The increase of the T is the characteristic effect of the action of digitalis on the frog's heart, according to Straub.³⁰ Hering,³⁴ in studying the *pulsus alternans* produced by the intravenous injection of glyoxylic acid, found that the most common change in the electrocardiogram produced by the ventricular alternation is in the T wave; the R wave is never alone affected and is always less changed than the T. In a previous paper, Hering³⁵ had shown that the essential feature in the alternation produced by glyoxylic acid in the mammal's heart is not a hyposystole (diminished contraction) of the whole ventricle, but a partial asystole. Certain parts of the ventricle do not enter into contraction at all in the alternating small beats. The view that *pulsus alternans* is a hyposystole seems to have been first suggested by Gaskell,³⁶ and to have been confirmed for the frog's heart by Trendelenburg,³⁷ and by Muskens.³⁸ Hering could find no relation between the portion of the ventricle affected and the change in the T wave and concludes that the T wave is produced by every part of the musculature which may be in activity toward the end of systole and is not to be referred to any special region of the ventricles. Kahn and Starkenstein³⁹ confirm Hering in that they find in *pulsus alternans* produced by glyoxylic acid that the T wave varies considerably in size in the large and small beats, while the R wave is little affected.

The effect on the electrocardiogram of section and stimulation of the extrinsic cardiac nerves has been studied in detail by Rothberger and Winterberg.⁴⁰ Increased accelerator influence as a result of vagus section causes increase in P. R is unchanged or smaller and T is much increased. Stimulation of the right stellate ganglion with vagi intact causes a similar change. Stimulation of the left stellate ganglion causes P to become small; R becomes diphasic with pronounced S wave; T usually becomes strongly negative. Increase of vagal effect by section of accelerators causes P and T to undergo marked decrease, while R is increased. They conclude that the effect of increased accelerator influence is the result of a localized strengthening of the contraction, a "partial hyper-systole." In reference to the anatomical distribution of the right and left accelerator fibers they believe that stimulation of the left accelerator

34. Hering: Ztschr. f. exper. Pathol. u. Therap., 1909, vii, 363.

35. Hering: München. med. Wchnschr., 1908, lv, 1417.

36. Gaskell: Philosoph. Tr., 1882, clxxiii, 993.

37. Trendelenburg: Arch. f. (Anat. u.) Physiol., 1903, p. 271.

38. Muskens: Jour. Physiol., 1907, xxxvi, 104.

39. Kahn and Starkenstein: Arch. f. d. ges. Physiol., 1910, cxxxiii, 579.

40. Rothberger and Winterberg: Arch. f. d. ges. Physiol., 1910, cxxxv, 506.

causes negativity of the T wave due to increased strength of contraction of the left ventricle, while increase of the T in a positive direction from stimulation of the right accelerator is due to increased contraction of the right ventricle.

The rôle that different parts of the ventricle play in the genesis of the T wave has been studied in an interesting series of experiments by Henle.⁴¹ Hering and Biedermann had shown that as a result of the application of a constant electric current to the frog's heart the region of the ventricle under the anode remains uncontracted while the current is passing. If the current is very strong the effect may spread to the entire ventricle, but by using a current of moderate strength a well localized effect may be obtained. For a short time following the cessation of a current which has been passing for some time, the region around the anode contracts more strongly in each systole than the remaining parts of the heart, while the region surrounding the cathode shows diminished activity. These effects likewise involve larger areas the stronger the current employed. If the current is not too strong it is possible to obtain a localized region which contracts to a less or to a greater degree than the remaining ventricular muscle. Henle applied this method to the study of the effects produced by these localized regions of depressed or augmented activity on the electrocardiogram from the heart of frogs and mammals (dogs). Since the passage of a current through the heart would affect the electrocardiogram, he utilized the effects produced on the heart which follow the withdrawal of the current, namely, an augmentation surrounding the anodal and a depression surrounding the cathodal region. One electrode, which can be made either anodal or cathodal, is placed on the heart; the other serves as an indifferent electrode connected with some portion of the body surface. By the use of a commutator a galvanic current is passed through the heart for a period of fifteen to twenty seconds and then by reversal of the key connection is made with the galvanometer and the electrocardiogram obtained from the surface of the heart (base and apex of the ventricle) for the next few beats. With the anode on the base or the cathode on the apex of the heart, the effect on the electrocardiogram in the next few beats following the cessation of the current was an increase in size of the T wave over the normal. The T wave is thus increased in a positive direction when the base contracts stronger or the apex weaker than normal. With the anode on the apex or the cathode on the base the T wave is small; in the first two or three beats following the withdrawal of the current it may be negative. The R wave is practically unaffected. As a result of the current probably the activity of only the superficial layer of the heart muscle is affected, and since this affects only the T wave it is suggested

41. Henle: *Ztschr. f. Biol.*, 1911, iv, 295.

by Henle that the R and T arise from different layers of muscle. The fact that change in the extent of contraction of the musculature at the apex as well as at the base of the ventricle affect the T wave, proves that at the time of occurrence of this wave the apical musculature as well as the basal musculature is in functional activity and that both play a part in its production. This is, of course, opposed to the explanation of the T wave upheld by Gotch and by Kraus and Nicolai.

The production of the T wave, according to the majority of writers, is closely connected with the activity of some special layer or region of ventricular muscle. Only Hoffmann (and perhaps Judin) have suggested that it is representative of contraction of cardiac musculature, irrespective of position. In relation to this conception of great importance is the observation by Straub⁴² of the presence of a T wave from the auricle of the isolated frog's heart. After complete cessation of the contraction of the ventricle with continued contraction of the auricles, Straub obtained a diphasic curve followed by a monophasic curve; the latter resembling the T wave of the ventricle. This observation on the frog's heart has been confirmed by Eiger⁴³ and more recently by Hering.⁴⁴ Hering also finds some indication for the presence of a T wave in a curve obtained from the auricles of a dog beating *in situ* after the ventricles have been cut away. He states, however, that such a conclusion can only be arrived at with great reservation and that further work is required to establish an auricular T wave in the electrocardiogram from mammals and from man.

Before closing a review of the recent literature on the electrocardiogram, reference may be made to the interesting series of observations of Paul Hoffmann⁴⁵ on the electrocardiogram of the invertebrates. Three types of electrocardiograms, according to this work, are to be recognized. The first type is characterized by a series of oscillations, varying in number from two or three to twenty or more and extending throughout the period of contraction. This type is characteristic of the heart of certain arthropods, namely, *Limulus*, *Maia* and *Astacus*. The heart is evidently in tetanic contraction and the curve is simply a number of action currents rapidly following in succession, each corresponding to an excitation received from the cardiac center in the intrinsic cardiac nervous system. No T wave is present, probably due to the rapidly recurring contractions going to make up the tetanus. The second type of electrocardiogram is characteristic of certain hearts which show a peristaltic contraction, a representative of which is found in the gastropod, *Aplysia*. The electrocardiogram is a simple diphasic curve. Finally

42. Straub: Ztschr. f. Biol., 1910, liii, 499.

43. Eiger: Extr. de Bull. de l'Acad. des Sciences de Cracovia, July, 1911.

44. Hering: Arch. f. d. ges. Physiol., 1912, cxliv, 1.

45. Hoffmann, P.: Arch. f. (Anat. u.) Physiol., 1911, p. 135.

the third type is the electrocardiogram characteristic of all the higher animals, found among certain of the higher invertebrates (certain cephalopods) and all the vertebrates. The differences of the electrocardiogram in these different animals are therefore associated with distinct differences in the physiological peculiarities of the heart, and the type of electrocardiogram of the higher animals, including man, is characteristic of the type of activity that is peculiar to the heart of the higher animals.

THE RELATION OF THE ELECTROCARDIOGRAM TO OTHER EVENTS IN THE CARDIAC CYCLE

The work of Kahn^{15, 16, 17} in this connection has already been referred to. Similar observations have been made by Weiss and Joachim⁴⁶ and by Bull.⁴⁷ There is general agreement that the R wave precedes by a few hundredths of a second (.03 to .06) the onset of ventricular systole as shown by the rise of intraventricular pressure and the first heart sound. The relation of the electrocardiogram to the venous pulse has been studied by Rautenberg.⁴⁸ While he agrees that the onset of the R wave precedes the beginning of ventricular systole and finds that the position of the c wave on the venous pulse confirms this view, he concludes that the R wave is nevertheless to be referred to and is representative of the first part of ventricular systole. He assumes that the P wave is to be referred exclusively to contraction of the auricles and its beginning must correspond to the onset of auricular systole. Determining on his curves the distance that the auricular wave of the venous pulse follows the P wave of the electrocardiogram, he applies this correction to the relation between the c wave of the venous pulse (onset of ventricular systole) and the R wave of the electrocardiogram. When this correction is made, he finds that the beginning of the R wave falls in all cases exactly with the beginning of the c wave, and concludes that both represent the same process in the heart, namely, the beginning of ventricular systole. The R wave thus represents the contraction of the ventricular muscles as a whole and not merely of the papillary system, since the contraction of the latter causes no rise in intraventricular pressure. The reason that it occurs in point of time before the cardiac muscle contracts is to be referred to the latent period of the heart muscle. Considering for the time that Rautenberg's assumption that the beginning of the P wave is representative in all cases of the onset of auricular systole, and that the correction as applied to the relation between the R and c waves is correct, the work of Kahn¹⁷ on the relation between mechanical movement and electric response which we have already referred to in some detail, is entirely opposed to Rautenberg's interpretation. As will be discussed

46. Weiss and Joachim: *Ztschr. f. klin. Med.*, 1911, lxxiii, 240.

47. Bull. *Quart. Jour. Exper. Physiol.*, 1911, iv, 288.

48. Rautenberg: *Berl. klin. Wehnschr.*, 1910, lxvii, 2190.

later in this paper, we believe we have strong evidence to indicate that the onset of the P wave in by no means all cases corresponds to the onset of auricular systole. The observation of Einthoven³ and others, that the P-R interval is of different length in different leads to the galvanometer from the same individual, indicates that either the P wave in relation to auricular systole or the R wave in relation to ventricular systole, or both, undergo variation.

We have studied the relation of mechanical systole of the heart to the electrocardiogram, with especial reference to the P-R interval, in man and in the dog. Comparative measurements were made of the a-c interval on the venous pulse and the P-R interval of the electrocardiogram in simultaneous records of the two from fifteen normal men. These show, contrary to the findings of Rautenberg, that the P-R interval on the electrocardiogram does not correspond in the majority of cases with the a-c interval on the venous pulse. Usually the a-c interval is somewhat longer than the P-R interval, so that if P is made coincident with a, c does not fall at the beginning of R, but towards the end of this wave. In a few cases the two intervals are of approximately the same length and in several cycles in these records the a-c interval is definitely shorter than the P-R interval. The probable interpretation of these differences will be discussed later. Our results thus indicate that the P-R interval is not in most cases a measure of the As-Vs interval. The opposite conclusion of Rautenberg seems to have been derived from records which showed a relation other than the usual one. A more interesting point in reference to the interpretation of the electrocardiogram shown by these records is the duration of systole. As is well known, only on certain phlebograms is the end of systole sharply marked by the separation between the t and d waves (Bard⁴⁹). In records from seven of the fifteen individuals, the end of systole was evident and these without exception showed that the length of systole, as measured by the c-d interval on the venous pulse, corresponds to an interval on the electrocardiographic curve beginning near or at the end of R to the end of T. If the end of the T wave is representative of termination of the contraction of the ventricular muscle, as is generally recognized to be true, it is evident that the onset of mechanical systole is represented, not by the beginning of the R wave, but by a point at or near the termination of this wave. Figures 1 and 2 are simultaneous records of the jugular pulse and electrocardiogram in man and show the features discussed above. Figure 3 is a record from a dog and gives a comparison of the a-c interval on the jugular pulse and the P-R interval of the electrocardiogram in the same cycle. The venous pulse was recorded by a sound introduced into the right external jugular vein according to the method used by

49. Bard: Jour. de physiol. et de pathol. gén., 1906, viii, 454.

Fredericq.⁵⁰ The electrocardiogram in all these records is from Lead II of Einthoven (right anterior and left posterior extremities). In several experiments on dogs we have compared the P-R interval with the As-Vs interval as recorded by suspension curves of the right auricle and right ventricle. These have led to the same conclusion. Certain abnormal conditions of the heart which may cause a wide variation between the two will be discussed later. Finally, in simultaneous records of the venous pulse, electrocardiograms and apex beat in four normal men, the venous pulse has been corrected for transmission by comparison with the cardiographic curve and this correction applied to its relation to the electrocardiogram. When this correction is made, the time from the onset of the P wave to the a wave of the venous pulse is less than the time from the onset of the R wave to the c wave of the venous pulse. If the beginning of P is to be referred to the onset of auricular systole, the beginning of R does not correspond to the onset of ventricular systole. From these observations the following conclusions may be drawn:

1. Auricular systole plus auriculo-ventricular conduction time is not accurately represented on the electrocardiogram by the interval from the beginning of the P wave to the beginning of the R wave (P-R interval). In the majority of cases the As-Vs interval corresponds to an interval from the beginning of P to some point on the descending limb of R or the end of this wave.

2. The period of systole of the ventricle, or the time from the rise of intraventricular pressure, as marked by the c wave of the venous pulse, to the closure of the semilunar valves, as marked by the d wave of the venous pulse, is represented in the electrocardiogram by the interval from the end of R to the end of T.

From the work of Keith and Flack,⁵¹ Wybauw,⁵² Lewis and Oppenheimer,⁵³ Brandenburg and Hoffmann,⁵⁴ Ganter and Zahn⁵⁵ and others, we have strong evidence that the cardiac impulse in the mammalian heart arises in a region of tissue representing embryological remains of the primitive sinus and lying in the adult organ along the sulcus terminalis of the right auricle at its junction with the superior vena cava. The excitation spreads from this region to the auricles and thence to the ventricles by the auriculoventricular bundle. The question at once arises whether or not the activity of the so-called sinus region is represented in the electrocardiogram. Is the P wave representative entirely of activity of the auricles, or does the cardiac impulse before reaching the

50. Fredericq: *Arch. internat. de physiol.*, 1907, v, 1.

51. Keith and Flack: *Jour. Anat. and Physiol.*, 1907, xli, 172.

52. Wybauw: *Arch. internat. de Physiol.*, 1910, x, 78.

53. Lewis, Oppenheimer and Oppenheimer: *Heart*, 1911, ii, 147.

54. Brandenburg and Hoffmann: *Med. Klin.*, 1912, viii, 16.

55. Ganter and Zahn: *Zentralbl. f. Physiol.*, 1912, xxv, 782.

auricular tissue proper play a part in the production of the electrocardiographic curve? We have recently studied in a series of experiments on the dog's heart *in situ* the conduction of the excitation from the sinus region, the results from which will form the subject of another paper, but certain facts bearing on the present problem may be discussed here. The Keith-Flack node manifests development of a negative potential in the dog's heart from 0.025 to 0.03 second before the body of the right auricle. This result was obtained by measuring the time from the occurrence of negativity in these two regions in relation to mechanical systole of the auricle. One electrode was placed on the node, another on the auricle and these connected in turn through the galvanometer to an indifferent electrode on the left hind leg of the animal, the systole of the right auricle being recorded at the same time by suspension. There is, therefore, a slight delay in the passage of the impulse from the node to the auricle, a sino-auricular interval which amounts, under normal conditions, to from $1/5$ to $1/3$ the auriculoventricular interval in the same animal. By comparing in the same experiments the relation of the onset of the P wave of the electrocardiogram to mechanical systole of the auricle, it was possible to determine whether the negativity in the sinus region formed the first part of the P wave or whether the wave is to be referred exclusively to excitation in the auricle. An example will make this clear. In one experiment an electrode placed on the sinus region and connected with an indifferent electrode on the left hind leg, showed that the first negativity developed at the sinus preceded the onset of mechanical systole of the auricle by 0.08 second. The lower part of the body of the right auricle developed negativity 0.05 second before auricular systole. The P wave of the electrocardiogram (leads from right anterior and left posterior extremities) finally began 0.07 second before auricular systole. The first two of these determinations were made in the same record by means of a key used to connect the electrodes on the sinus and auricle in turn with the galvanometer and indifferent electrode. The relation of the P wave to auricular systole was determined from a record immediately following the proceeding. It is evident from the data in this experiment that the wave of negativity passed from the sinus node to the body of the auricle within 0.03 second and that the P wave of the electrocardiogram was in part made up of this negativity, while still in the sinus region and in part after it had spread to the auricles. Our experiments have also demonstrated that there is no restricted path of tissue by which the impulse spreads from the sinus to the auricle. Such conduction occurs by diffuse paths, and this is probably the explanation as to why the manifestation of sinus activity and of auricular activity on the electrocardiogram are fused to form a single wave (P), and do not form two separate waves. A splitting of the P wave has been described by Hering⁴⁶ and others. Hering suggested that

the first part represented activity of the sinus, the second part activity of the auricles. We have seen a similar division into two waves in an experiment in which the sinus region was partially isolated from the auricle by cuts through the cardiac tissue, and this suggests that a splitting of the P wave may indicate unusual difficulty in conduction from the sinus node to the auricle. The point we wish to emphasize here, however, is that the P wave of the electrocardiogram, in the majority of cases at least, is a composite of the spread of the excitation in the sinus region and in the auricles. The onset of this wave does not, as a rule, correspond to the development of activity in the auricles, but is coincident with or more frequently begins a short time after the excitation becomes evident in the sinus region. No separate wave occurs normally in the electrocardiogram of mammals indicating activity of the sinus because the region is connected with the auricles by many and diffuse paths and there is a relatively small delay in the passage of the excitation to the auricle. In the cold-blooded heart, the sinus, although present as a separate chamber, the contraction of which is separated by a considerable interval from that of the auricles, does not as a rule produce any effect in the electrocardiogram, probably because its activity is too small. Using a very sensitive thread in the galvanometer we have obtained evidence of a wave preceding the P wave of the electrocardiogram in the tortoise from leads from the body tissues of the animals and perfectly clear and definite results when the leads were from the exposed heart, one from the sinus, the other from the ventricle. An example is given in Figure 4. There is a wave resulting from a sinus activity, followed by the usual P, R and T waves. That leads from the surface of the mammalian heart fail to show under normal conditions any evidence of a sinus wave separate from that of the wave produced by activity in the auricle would seem then to be the essential difference between the electrocardiogram of the cold-blooded heart and the mammalian heart and to be the expression of the difference in the two cases of the physiological relation between the sinus and auricles. In the example given above, the data are such as to lead to the conclusion that the first onset of negativity in the sinus region does not give rise to the P wave. In the majority of cases this is true, and while only in exceptional cases does the P wave begin first when the activity reaches the auricle, usually the very first development of negativity in the sinus does not affect the electrocardiogram. Probably if the galvanometer in all cases were sufficiently delicate, the onset of the P wave would correspond always to initial negativity of the sinus.

Having thus to consider the P wave as made up in practically all cases in part by activity in the sinus region, and the extent to which this enters varying in different cases, we have at once an evident factor to account, in part at least, for differences between the P-R interval and the

interval from auricular systole to ventricular systole (As-Vs interval), as measured by mechanical means. If one explains the electrocardiogram on the hypothesis that it represents two separate processes occurring in the heart muscle during its activity, namely, conduction of the excitation and contraction of the muscle, the P and R wave are to be regarded as representing the former process in the auricles and ventricles, respectively. If the P and R waves are then not manifestations of contraction of the auricular and ventricular muscle, but of the spread of the wave of excitation, another factor may be considered which may act to change the P-R interval independently of the As-Vs interval. It is conceivable that the period from the time of entrance of the excitation into the muscle to the contraction may undergo variations and may be different in the case of the auricle and ventricle. The latent period of mammalian heart muscle to direct stimulation varies markedly at different times in the cardiac cycle (Hirschfelder and Eyster⁵⁶). A third factor which may perhaps alter the P-R interval without changing the As-Vs interval is variation in the conductivity from the sinus region to the auricle. By application of nicotin to the sinus and basal portions of the right auricle we have found that the P-R interval may become actually twice as long as the As-Vs interval, as measured by suspension of the right auricle and right ventricle. The change in the P-R interval in this case was shown to be due entirely to an earlier occurrence of the P wave before mechanical auricular systole. An example of these experiments may be given. Before application of the nicotin the P-R interval averaged 0.10 second, the As-Vs interval 0.13 second. These were measured from the same cycles. The P wave preceded auricular systole by .055 second. Following the application of 50 per cent. nicotin the P-R interval averaged 0.13 second, the As-Vs interval 0.06 second; P preceded auricular systole 0.13 second.

Whether these may or may not be the main factors involved in causing variations in the P-R interval independently of the As-Vs interval, the fact is evident that it can be shown experimentally that the P-R interval is not an accurate measure for this period, and that the two may show independent variation. As we have seen, usually the P-R interval is a few hundredths of a second shorter than the As-Vs period. The occurrence of the P wave before the excitation enters the auricle would tend to make it larger, yet normally the reverse is true. While perhaps a definite answer cannot be given as to the cause of this, it seems to us that it may be well explained on the following grounds: When the excitation reaches the auricle it affects at once muscles the contraction of which cause decrease in the internal capacity of this chamber. This is not true in the case of the ventricle. The excitation

56. Hirschfelder and Eyster: *Am. Jour. Physiol.*, 1907, xviii, 222.

passes down the His bundle into the papillary system and is thence distributed to the remainder of the ventricular musculature. It is not until the circular fibers of the ventricle are in activity that any decrease in the interval capacity of the ventricle occurs and a rise of intra-ventricular pressure results. The work of Hering¹⁰ has demonstrated that the papillary muscles contract at least .02 to .03 second before the main mass of ventricular muscle.

The fact that the length of systole is expressed on the electrocardiogram, not by the distance from the beginning of R, but from the end of R to the end of T, would seem again to point to the conclusion that the R wave can have nothing to do with the contraction of any musculature which tends to decrease the size of the ventricle. In strong support of this is the experimental proof of Kahn,¹⁷ to which we have previously referred, that the muscle which, by its activity, produces the R wave must contract following this wave a much shorter period of time than does the mechanical systole of the ventricle.

THE RELATION OF THE LINE OF ISOPOTENTIAL TO THE FORMATION OF THE ELECTROCARDIOGRAM

As has been pointed out, particularly by Kraus and Nicolai,³ the electrocardiogram is the expression of the algebraic sum of many electric potential differences conducted away from the heart by its interior and exterior surfaces to the peripheral tissues. The whole heart serves as an indifferent conductor for potential differences arising at any point within the organ and the actual potential at any given point at any time is due to the activity in this region modified by activity occurring at this time in all other regions. We may suppose to exist, as was first described by Waller,¹ in reference to any two leads from the extremities, a line or equator of equipotential passing through the heart between base and apex. A preponderance of negative potential above this line (basal portions of heart) causes the movement of the galvanometer connected with the two hands in such a way as to indicate relative negativity of the electrode connected with the right hand. In leads from a hand and foot, the hand assumes this relative negativity. A preponderance of negativity below this line causes movement of the galvanometer in the opposite direction.

We have attempted to afford experimental evidence for this assumption by artificially producing a condition of negativity in various regions of the heart and determining the effect produced on the galvanometer connected in the usual way with two leads from the extremities. Dead dogs were used. The animal was placed in a large sheet-iron tank, the bottom of which was covered with saline solution to a depth of several centimeters. Leads to the galvanometer were made from the right

anterior and left posterior extremities. Six non-polarizable electrodes were placed on various regions of the heart. These were connected with a switch with six contact points by means of which any one of the electrodes could be placed in a circuit with a battery and a large sheet-iron plate on the bottom of the tank containing the animal. By this means a current could be sent through the animal, entering by a large area through the skin of the back and leaving by a much smaller area on the surface of the heart. While this condition probably resembles little the actual condition present in the beating heart in which a potential difference arises between two points from activity of the muscle, we were able to demonstrate the fact that a difference of potential arising under the conditions of our experiment affect the galvanometer connected with the two limbs differently, depending on what region of the heart shows this change in potential. The relation between different points on the heart may thus be compared and a line of isopotential demonstrated under the conditions present. Change in potential along this line causes no movement of the galvanometer. A negative charge above this line causes the galvanometer to move in a direction indicating relative negativity of the electrode connected with the anterior limb. A negative charge below this line causes the galvanometer to move in the opposite direction. The actual position of the line of equipotential in our experiments was an arbitrary one and could be shifted by varying the position and extent of contact of the animal with the salt solution in the tank. The relation of other parts of the heart to the region transversed by this line, however, remained quite constant. The position of the six electrodes was as follows:

1. (a) Region of the sinus (Keith-Flack) node, (b) or body of right auricle.
2. Region of the auriculoventricular (Tawara) node at the base of the interauricular septum.
3. Auriculoventricular bundle near bifurcation.
4. Left ventricular apex.
5. Right ventricular base.
6. Aortic base of left ventricle.

The results from the three experiments of this character may be summarized as follows: When the line of isopotential passed along the region of the ventricles, a movement of the galvanometer indicating negativity of the anterior electrode (right fore limb) occurred when the current was passed through the electrodes on the sinus, the right auricle, the A-V bundle and the region of the Tawara nodes. The extent of movement was in the order named. The two ventricular bases showed movement in the same direction as the above and to about an equal degree. No marked difference was obtained, but in two of the three

experiments the movement was slightly greater for the aortic base than for the base of the right ventricle. Measurements from a record may be given as follows:

Sinus	—13
Intraventricular septum	—12
A-V bundle	—10
Left ventricular apex	+ 4
Right ventricular base	—10
Aortic base of left ventricle.....	—10

The figures refer to the movement of the thread in millimeters. The minus sign indicates movement showing relative negativity of the anterior electrode. The plus sign indicates negativity of the posterior electrode. By shifting the contact of the back of the animal with the salt solution in this experiment, a movement of the thread indicating relative negativity of the anterior electrode occurred in all cases. The relation between the extent of movement in each case remained, however, without change.

While we realize that the application of any results drawn from the above experiments to the normal electrocardiogram must be applied with all due reservation, we believe the fact that the basal regions of the ventricle show similar relations to the leads from the limbs as do the supraventricular regions of the heart, and particularly the absence of any marked difference between the base of the right and left ventricles, is at least suggestive. It would seem to be opposed to the views of Einthoven⁵ and Selenin²¹ that the two ventricles in their activity represent the opposing influences in the production of the normal electrocardiogram and would tend to lay stress on the difference between base and apex in this connection. The fact that a line of isopotential can be obtained experimentally under the conditions described, and that there is general agreement in the curves obtained with those representing potential changes in the normal beating heart, as for example, the fact that activity of the right auricle produces always in the beating heart relative negativity of the anterior electrode while activity of the ventricular apex affects movement in the electrocardiogram in the opposite direction, seem to us to offer support to the view that normally there is such a region of isopotential between base and apex and it is the balance of potential on the two sides of this which determines whether the electrocardiographic curve moves in one direction or the other. The simplest explanation of why the P wave, for example, is monophasic in the electrocardiogram from the extremities while it may be diphasic in direct leads from the auricle, is that all of the activity producing it is above the line of isopotential. Whether or not the T wave is positive or negative in direction may also be well explained by the resultant of activity above and below this line. In a T wave directed in the same

Fig. 1.

Fig. 2.

Fig. 3.

Fig. 1.—Electrocardiogram (Lead II) and venous pulse from man. Time record in 1/5 sec. To show comparative lengths of the P-R and a-c intervals, and the R-T and c-d intervals.

Fig. 2.—Similar to Figure 1.

Fig. 3.—Electrocardiogram (Lead II) and venous pulse from a dog, to compare the length of the P-R and a-c intervals.

Fig. 4.

Fig. 5.

Fig. 4.—Electrocardiogram from superficial leads from the exposed tortoise heart, to show the wave arising from sinus activity. The leads to the galvanometer were from the sinus and ventricular apex. The lowest line signals the mechanical systole of the sinus. The electrocardiographic record shows a sinus wave followed by a P and R wave. The time record is in 1/5 second.

Fig. 5.—Electrocardiographic curve obtained from the exposed tortoise heart (leads from right auricle and ventricular apex) in which the ventricle had ceased beating as a result of the application of a second Stammis ligature. Time in 1/5 sec. intervals. The lowest line signals the auricular systole.

Fig. 6.

Fig. 6.—Electrocardiogram (Lead II) from a dog, showing heart-block as a result of a toxic dose of morphin. The blocked cycles show a small wave following the P which is interpreted as an auricular T wave.

Fig. 7.

Fig. 8.

Fig. 7.—Electrocardiogram (Lead II) from a dog, showing heart-block as a result of pressure applied to the region of the auriculoventricular node. The blocked cycle shows an auricular T. The lowest line records the mechanical systole of the right auricle.

Fig. 8.—Curve from dog's heart *in situ* with leads to the galvanometer from the exposed right auricle and from the left posterior leg. Heart-block from vagus stimulation, showing the auricular T. The lowest line records the mechanical systole of the right auricle.

Fig. 9.—Action current from a longitudinal strip of ventricular muscle from the tortoise ventricle not including any of the region of the aortic base. Shows a diphasic R followed by a T wave accompanying the contraction resulting from mechanical stimulation. The lowest line records the contraction.

Fig. 10.—Action current from a strip of ventricular muscle cut from the apical region of the tortoise ventricle. Monophasic R followed by T. The lowest line signals the contraction of the strip.

Fig. 11.—Similar to Figure 10. T in same direction as first movement of R.

Fig. 12.—Action current from strip cut crosswise from the mid-region of a tortoise ventricle and stimulated mechanically. The contraction of the strip is signaled by the lowest line of the record.

Fig. 13.—Action current from the ventricle of a cat after removal of the basal regions. Mechanical stimulation. The lowest line of the record shows the duration of contraction.

Fig. 14.—Showing the effect on the T wave of the auricle of vagus stimulation. Tortoise heart: ventricle quiescent as a result of a second Stannius ligature. Leads from right auricle and basal part of quiescent ventricle. The period of vagus stimulation is indicated by the small rapid oscillations of the galvanometer thread produced by the escape of the stimulating current. The lowest line records the mechanical systole.

Fig. 15.—Similar to Figure 14.

Fig. 16.—Similar to preceding. Shows the transition stages of the results of vagus stimulation. The record was stopped for a short period in order to obtain recovery stages following the stimulation. The mechanical systole of the auricle is signaled by the lowest line.

Fig. 17.—Action current from auricle of tortoise heart with quiescent ventricle in similar preparation to those of the preceding figures. Shows the effect on the auricular T wave of the application of Ringer's fluid at 4 C. The lowest line records the mechanical systole of the auricle.

Fig. 18.—Similar preparation to preceding, showing the result of the application of Ringer's fluid at 42 C. to the heart.

Fig. 19.—Four electrocardiograms from the same individual taken over a short space of time with thread of different sensitivity, lead II.

direction as the P, the predominant activity producing it would be in the ventricular bases, while a T in the opposite direction (so-called negative T wave) would seem to depend on excess of activity in the more apically lying ventricular musculature.

THE INTERPRETATION OF THE T WAVE

The various views that have been advanced to explain the T wave have been described. Our own observations support the view of Hoffmann,²³ in so far as this investigator separates between conduction and contraction in cardiac muscle and refers the T wave to the latter.

We have succeeded in demonstrating the presence of a wave resembling in all characteristics the T wave of the electrocardiogram in (1) the auricle of the cold-blooded heart; (2) the auricle of the mammalian heart; (3) the ventricle of the tortoise's heart after destruction of the musculature around the aortic ring; (4) in simple strips from the tortoise's ventricle, from the apical as well as the basal regions, and (5) from strips cut from the mammalian ventricle. When isolated, and changes in other regions prevented from modifying the curve obtained, all of these show as the result of stimulation and a sufficiently sensitive galvanometer two sharply marked electrical changes—first, a rapid monophasic or diphasic curve, followed by a much slower and more prolonged variation. Figure 5 shows the curve obtained from a tortoise's heart with a second Stannius ligature and quiescent ventricle. The heart was *in situ* and the leads to the galvanometer from the right auricle and ventricle. Each auricular beat shows a rapid electrical change followed by a much slower variation in the opposite direction. The time of auricular contraction is marked by a signal (lowest curve of record). In this particular case the second wave is opposite in direction to the first and might be considered as the second part of a diphasic variation. Opposed to this interpretation is the great delay between the two movements, the fact that the first wave resembles an R, the second a T wave, and that frequently the two movements are in the same direction, or the first may be clearly diphasic and this be followed after a time by a slower monophasic change. Figure 6 shows a T wave of the auricle of a dog in partial auriculoventricular block resulting from a toxic dose of morphin.⁵⁷ The electrocardiogram was obtained in the usual way from the right anterior and left posterior extremities. Following the P wave of the blocked cycle there is a small but definite prolonged variation in the same direction. Figure 7 shows a small T wave in the auricle in partial auriculoventricular block in the dog's heart arising from pressure on the region of the auriculoventricular node. The position of the auricular T is marked by an X. The lowest line of this record is a

57. Eyster and Meek: Heart, 1912, iv, 59.

suspension curve of the right auricle, the downstroke representing systole. The heart was *in situ*, the chest opened and the leads to the galvanometer from the right anterior and left posterior extremities. This wave occurred regularly in all cycles where the conduction was blocked. It is evident in the unblocked cycles that the development of this wave would be impossible, since it would be entirely obscured by the ventricular R wave. Figure 8 is a curve obtained from a dog with heart *in situ* and leads from exposed right auricle and left posterior leg. As a result of stimulation of the vagus the first two cycles show only auricular contractions. The lowest line of the record records these contractions. Each beat of the auricle causes a rapid diphasic curve followed by a slow monophasic curve. In the third cycle the auricular contraction is followed by a systole of the ventricle and a diphasic ventricular curve obscures the formation of the auricular T wave.⁵⁸ Pronounced T waves have been obtained from the tortoise's ventricle after complete destruction of the aortic regions and from strips of ventricular muscle cut from various regions of the ventricle. Figure 9 is a curve obtained from a longitudinal strip of ventricular muscle not including any of the region of the aortic base. Mechanical stimulation of one end of the strip resulted in a contraction with the production of a diphasic curve followed after a considerable interval by a slow monophasic curve. Figure 10 is a curve from a strip cut from the apex of a tortoise's ventricle and stimulated mechanically. The galvanometer was very sensitive and shows movements that carried the shadow off the record. There is a monophasic curve followed after a pause of over one and a half seconds by another large monophasic change in the opposite direction. Figure 11 is from a similar strip and shows a rapid mono- or partially diphasic curve with a slower change in the same direction as the original movement of the galvanometer thread. Figure 12 is a curve from a strip cut crosswise from the mid-region of a tortoise's ventricle and stimulated mechanically. There is an initial electrical change followed by a slower movement in the same direction.

To explain satisfactorily these curves as a result of contraction alone would seem to be impossible. In Figure 12, for example, it would be necessary on such an assumption to suppose that the contraction began at the end stimulated and spread out from this region, and that after a relatively long period of time there occurred a second contraction following the same course. If one assumes, however, that the two electrical waves actually represent two different processes, conduction of the excitation and contraction of the muscle, the second following the first after a certain interval, the interpretation is not difficult.

58. Fig. 13, Plate 17 of Samojloff's paper⁵⁹ shows a well developed auricular T wave in auriculoventricular block from vagus stimulation. The author makes no reference to this in the text.

Figure 13 is a curve obtained from mechanical stimulation of the ventricle of a cat, removed from the body and suspended. The auricles and whole basal region of the ventricle, including the region of the origin of the aorta and pulmonary artery, were cut away. The lowest line of the record records the contraction. It will be seen that this begins after the first electrical wave is completed and ends coincidently with the termination of the second electrical wave. The relation of the contraction to the two waves is strikingly like the relation of the R and T waves of the normal electrocardiogram to mechanical systole of the ventricles as discussed in a preceding section of this paper.

That we are actually dealing, in all cases considered above, with a wave similar in all essential details to the T wave of the electrocardiogram is indicated on several grounds. In the first place it is difficult or impossible to interpret the curves in any other way. In the second place, the wave which we believe to be the T wave in the ventricular strips shows a peculiarity in reference to its form which was first noted by Einthoven as characteristic of the T wave of the electrocardiogram. The T wave is characterized by a slow rise and a relatively rapid fall and in this is unique among physiological curves. Finally, we have performed a series of experiments on the supposed auricular T wave of the tortoise's heart which show it to undergo variations in size and direction under certain experimental conditions which have been shown to be characteristic of the T wave of the electrocardiogram of the ventricle. These include the effect of vagus stimulation and of heat and cold applied directly to the heart. Samojloff¹⁹ has analyzed the influence of vagus stimulation on the electrocardiogram of the frog's heart as follows: During vagus stimulation the T wave of the ventricle shows a decrease in the upward direction (when the leads are such that R is positive in direction), or changes from a positive to a negative T. The R wave is not affected, but the R-T interval is shortened. Following the stimulation the T gradually returns to its normal direction and size and the R-T interval becomes normal. During the vagus stimulation the T does not change in direction abruptly as a rule, but the first effect is usually that along with the decrease of the T, a movement in the opposite direction begins preceding the original purely positive wave. At this time the T is really diphasic with the first movement in the opposite direction to the original wave. Finally, the last part of the diphasic curve disappears and the T is represented by a monophasic curve in the opposite direction to the original wave. This also explains why the R-T interval is shortened. The reverse process occurs during the return to normal after the stimulation.

Figure 14 shows that similar changes occur in the T wave of the auricle as a result of vagus stimulation as described by Samojloff for the T wave of the ventricle. The record is from a tortoise's heart in

which the ventricle is quiescent as a result of a second Stannius ligature. The leads to the galvanometer were from the right auricle and basal part of the quiescent ventricle and are connected in such a way that the P wave (which for convenience of description may be designated here as the "R" wave of the auricle) is directed downward. The lowest line is the contraction curve of the auricle recorded by suspension. It is evident here, as in previous records, that the contraction begins after the "R" is completed and ends near the end of T. Stimulation of the right vagus was begun toward the end of the second cycle shown on the record, and its duration is indicated by the small oscillations it produces in the thread of the galvanometer. The first two cycles are before vagus stimulation and show an auricular T wave in the same direction as the P (auricular "R"). In the third cycle the T has already begun to manifest change in direction as a result of vagus stimulation, while the "R" wave is unchanged. In the fourth cycle the change is complete. Following the stimulation, the first few beats show a still further development of this change with a marked shortening of the R-T interval. The condition tends to pass off toward the end of the record. Figure 15 shows a similar result to a less marked degree. The conditions here were the same as in the preceding experiment. The "R" wave is diphasic. The T wave before stimulation is a long slow change opposite in direction to the initial change of the "R." Vagus stimulation, the onset and duration of which is shown by the effect on the thread, decreases the T wave slightly in height and apparently splits it into two parts. The "R" is unchanged. Figure 16 shows the transition stages in the change of the auricular T wave as described by Samojloff for the ventricular T. The conditions were the same as in preceding experiments. Before stimulation, the T wave is directed downward and is a long, slow wave, resembling the T of Figure 15. The recording apparatus was stopped for a short time following the vagus stimulation and during the recovery a diphasic T wave with the initial change in the opposite direction to the original T is apparent. The onset of auricular systole in this record is marked by a signal.

Straub²⁰ has shown that in the frog warming the heart increased the size of the T wave of the ventricle, while cooling the ventricle causes the T wave to become small or negative. We have found that the T wave of the auricle of the tortoise behaves similarly. Figure 17 shows the effect of application of cold Ringer's fluid (4 C.) to the exposed heart of the tortoise. The ventricle was quiescent as a result of a second Stannius ligature. The leads to the galvanometer were from the right auricle near the tip and the base of the quiescent ventricle. The cold saline solution was applied after the third cycle. The effect is a practically complete abolition of the T wave of the auricle. The P wave is also reduced and shows division. Figure 18 is from a similar preparation

and shows the effect of application of Ringer's solution at 42 C. The T wave increases in size from 10 to 20 millimeters. The effect in each case passed off shortly after the records shown and the condition returned to normal.

In a recent paper,⁵⁹ in which we have attempted to trace experimentally the course of the excitation over the tortoise heart, we have given a number of facts which we believe incompatible with Gotch's interpretation of the T wave. The excitation in its spread over the heart was traced by means of the action current recorded by leads from various points on the surface of the heart. The experiments are fully described in this paper and only certain points will be referred to here. In leads to the galvanometer from the aortic base and apex of the ventricle, the negativity in the former preceded in all of eighteen experiments. In eleven of these the T wave was in the same direction as the initial movement of the R wave, in seven it was in the opposite direction. It is difficult to understand on Gotch's view how the T wave can ever be opposite to the R in this lead, since such a feature would imply, on his interpretation, terminal activity of the apex. In the experiments of this series eighteen different leads from various regions of the heart were compared. In twelve of these leads the results were uniform in a great majority of the experiments as to the direction of the initial movement in the R wave. In some of these cases the R was monophasic, in others diphasic, and this was true not only in different leads in the same heart, but the same lead in different hearts. Marked variability was present, however, in the direction of the T wave. The variations in one lead, the aortic base and apex, are given above. While in most leads there was a distinct majority of cases in which the T wave had a certain direction in relation to the direction of the R, and thus a more or less typical curve for any given lead, exceptions were always present and in some cases the T was in the opposite or in the same direction as the R in about an equal number of cases. Certain other examples of this besides the aortic base-apex lead may be given. In eighteen left anterior base and apex leads the R wave in all cases was in a direction indicating primary negativity of the base. The T wave was in the same direction in twelve cases, in the opposite direction in six. In the lead from the left and right posterior ventricular bases, the former showed initial negativity in eighteen of twenty-three cases. In these eighteen cases the T was in the same direction in ten cases; in the opposite direction in eight. Many other examples could be given, but these are sufficient to illustrate the fact that the T wave in the same leads from the heart may vary in direction in reference to the R to a marked degree. Two hearts which show in the various leads exactly the same sequence of activity in the

59. Meek and Eyster: *Am. Jour. Physiol.*, 1912, xxxi, 31.

different regions, as indicated by the direction of the R waves, may thus have T waves in the opposite direction. If the T wave as well as the R is to be referred to conduction of the excitation we should have to assume, therefore, marked differences in the spread of the excitation in these two cases. In each case the initial course of the impulse as shown by the same direction of the R waves is the same, but if the T wave is involved in the interpretation the final course of the impulse would be exactly opposite. That the initial course should be so constant, while the terminal course shows such marked variations, would seem very improbable. A much more satisfactory explanation, and one more in accord with other known facts, is to assume that the R and T waves represent different phenomena. The former we believe to be representatives of the spread of the excitation, the latter of the active contraction of the muscle. Since the spread of the excitation in the normal heart is probably a constant factor, the R wave in the same leads from different hearts is practically constant in direction. The direction that the T wave assumes in relation to the R is probably determined by the region of the ventricle that manifests the greatest activity in the contraction or that remains contracted for the longest time. Many known experimental influences may modify the extent of contraction in different regions of the ventricle and such modifications probably occur as a result of the action of various uncontrolled factors in many experiments, particularly when the heart is exposed. Whether this be the true explanation or not, the facts stated offer other examples of variations in the direction and character of the T wave with unchanged R wave and offer additional support to the view that these two waves represent essentially different activities in the heart.

The R wave with leads from two points on the exposed heart, or from two ends of a strip of cardiac muscle, may be either monophasic or diphasic. The same lead in two hearts may give a monophasic R in one case and a diphasic R in the other. The curve obtained in the passage of an excitation over a muscle between two electrodes is usually diphasic, but as is well known, monophasic curves are not infrequent. The apparent explanation in the latter case is that the activity associated with the excitation, while spreading to the second electrode, remains preponderant at the region of the first electrode.

A further point may be noted in reference to our experiments on the exposed heart of the tortoise, namely, that the size of the T wave is usually greatest when one or both of the electrodes were on a part of the heart which enters into strong contraction. The smallest T waves were obtained from leads from the auriculoventricular ring where contraction is very small.

We shall not attempt to give in this paper a review of the rather large literature concerned with the question as to whether conduction and contraction are to be regarded as different phenomena in skeletal muscle. The studies of v. Brücke⁶⁰ and Noyons,⁶¹ concerning the action of asphyxia on the relation between the action current and extent of contraction would seem to show that the two may vary independently. The mere fact that a nerve manifests conduction and no contraction would suggest the possibility of the independence of the two processes in muscle. The experiments of Hoffmann on the heart in which contraction was abolished by drugs and the R wave unaffected, have been referred to in detail. Trendelenburg,⁶² in a recent study of the relation between the refractory phase of the heart and the action current, finds that one may be made to vary independently of the other. He finds also in standstill from muscarin, that the action current of the heart may be very little affected.

The normal electrocardiogram is usually described as showing a level phase between the end of the R and the onset of the T wave, explained, as we have seen, by most writers as due to simultaneous contraction of the whole musculature of the ventricle and the numerous action currents arising neutralizing one another so as to give no demonstrable difference in potential. This explanation has been objected to by certain writers (Rautenberg, Rehfish) on the theoretical ground that such a perfect antagonism could not be expected in all cases. We have become convinced by a study of our electrocardiographic curves, as well as those published by others, that the normal electrocardiogram is not characterized by a period of equal potential between base and apex at this time. In the great majority of records, especially when the galvanometer is somewhat more sensitive than that ordinarily used in recording electrocardiograms from man, the curve shows a gradual rise following the end of R (or S). When the T is well developed the curve may proceed upward at once on the completion of the R without any evidence whatever of a horizontal period. Records obtained from the same individual with successive increase in the sensitiveness of the galvanometer, show that the apparently horizontal portion of the electrocardiogram disappears with increase in delicacy (Fig. 19). The condition, therefore, which gives rise to the T wave is actually present very soon after the termination of the R wave. It may reach its full development rapidly and the crest of T be reached without interruption, or at first it may be present in relatively small degree and develop more rapidly toward the end of systole.

60. v. Brücke: *Arch. f. d. ges. Physiol.*, 1908, cxxiv, 215.

61. Noyons: *Onderzoek physiol. Lab. Utrecht v. Ruks.*, 1909, x, 215.

62. Trendelenburg: *Arch. f. die ges. Physiol.*, 1912, cxliv, 39.

THE INTERPRETATION OF THE NORMAL ELECTROCARDIOGRAM

Our own experiments and a review of the literature has led us to agree essentially with the interpretation of Hoffmann, that the normal electrocardiogram is the expression of two different processes occurring in the heart muscle during its activity, namely, the spread of the excitation and the mechanical shortening of the muscle. The facts which speak for such a view may be stated briefly. In the nerve where conduction alone is present, a single monophasic or diphasic electric response is obtained. In skeletal muscle this rapid electrical change is followed by a slower and more prolonged monophasic variation. These two electrical manifestations, present also in cardiac muscle from all parts of the ventricle as well as from the auricle, may vary independently, one may be abolished and the other persist, or either may change in size independently of the other.

The electrocardiogram as obtained in the usual way with leads from the extremities is an expression of those two processes. In the usual electrocardiogram there is no electrical expression of the contraction of the auricle, while the electrical expression of the ventricular contraction is evident (T wave). This is due to the fact that the ventricle contracts much more strongly, but especially that the electric wave resulting from this contraction is not obscured by any process of conduction occurring at this time. The auricles during their contraction as well as the ventricle develop electrical energy, but the movement of the galvanometer that is produced is ordinarily obscured by the wave (R) associated with conduction of the excitation in the ventricle. When such conduction is prevented (auriculoventricular heart block, isolated auricles), the contraction of the auricles causes a definite electrical change (T wave of the auricle) to be evident on the electrocardiogram.

The P wave of the electrocardiogram is to be referred to passage of the excitation from the point of origin in the sinus region over the auricle. In the cold-blooded heart, where the activity of the sinus and of the auricle are separated by a relatively long interval, the P wave is preceded, when the galvanometer is sufficiently sensitive, by a wave representing the passage of the excitation over the sinus. In the mammalian heart, on the other hand, where the sinus is closely incorporated with the right auricle, while its activity precedes that of the auricle by only a very short period (.03 second), even with the most sensitive galvanometer no evidence is obtained of a separate activity preceding the P wave. There may be, however, a division of the P wave when the conduction is delayed between the sinus and auricle and the conditions approach that present in the cold-blooded heart. Under normal conditions in the mammalian heart, however, the P wave is due in part to sinus activity, as is shown by comparative measurement between the onset of sinus activity and auricular contraction, on the one hand, and

of the P wave and auricular contraction on the other hand. Whether or not the passage of the impulse through the auriculoventricular conductive system, the His bundle and its main branches to the right and left ventricle enters into the formation of the R wave, is not clear from our present knowledge. Against this is the presence of an R wave in the cold-blooded heart, where the auriculoventricular conduction system is less specialized and in conduction between any parts of the ventricle or over a strip of heart muscle. It is also extremely difficult to explain the Q wave on this assumption. While this wave may perhaps not be a feature of the strictly normal electrocardiogram, it is present in many cases, and must be explained when present. Hoffmann does not commit himself to the exact portion of the conducting system which is responsible for the R wave. Nicolai has attempted to explain, however, in detail, as we have seen, how the various normal modifications in the R group (Q, R, S) may occur by variations in the distribution of the impulse to the ventricle. It would seem that more experimental knowledge is necessary before we will be in a position to state exactly what anatomical structures are involved in this interpretation. We believe the evidence is sufficient at present to refer the R group mainly or exclusively to the process of conduction of the excitation. The question as to the exact structures involved we believe to be capable of experimental test and we hope to return to this in a later paper.

The T wave of the ventricle in the normal electrocardiogram we believe to be the expression of preponderance of contraction on one side of the line of equipotential. Whether this wave is directed in the same or the opposite direction to the R wave depends on a balance between the action current produced by the contracting muscle on each side of this line. The direction of the T wave and its size in either direction would seem to depend on (1) the position of the line of equipotential in relation to any given lead, (2) the extent of contraction of the ventricular muscle as a whole and (3) the relative degree of contraction in the basal and apical regions of the ventricle. The T wave is essentially a manifestation of contraction and occurs as a result of contraction of cardiac muscle from all parts of the heart. Its size and direction in the electrocardiogram is, however, modified by the factors named.