The Pathway of Ventricular Depolarization in the Dog

By Allen M. Scher, Ph.D., and Allan C. Young, Ph.D.

With collaboration of Robert V. Erickson, Rolfe A. Becker, Juhan Läkane and Otis F. Brown

Studies of ventricular depolarization with multichannel recording techniques permit detailed threedimensional analysis of the process. Activity commences on the mid left septal surface, followed by activity on the right septum. Rapid endocardial excitation follows and leads to endoepicardial activation of the walls. The latest areas activated are in the basal septum. These findings are related to the genesis of the normal QRS. Theories of simultaneous activation and electrocardiographic silent areas are discussed.

Recent studies from several laboratories have dealt with the mode of ventricular excitation.1-4 These studies have employed electrodes of varying design which were inserted into the myocardium of the ventricular walls and septum to examine the shapes of potentials in various parts of the heart and to time the onset of local activity during ventricular depolarization. Such procedures as ventricular stimulation and cutting the right or left bundle of His have also been employed. The results of these studies are in general agreement regarding the rapid excitation of the endocardium and the slower movement of the activating wave through the myocardium. This agreement is most marked between studies1-4 in which multipolar electrodes were used to trace the three-dimensional course of the wave of excitation in a block of myocardium. However, none of the published studies have depicted completely the passage of the wave of depolarization through the ventricle. This paper is a description of the movement of the activating wave through the total ventricular mass, based on measurements at many points in each of several hearts with a multipolar electrode and multichannel recording apparatus.

METHODS

The multipolar electrode and multichannel oscilloscope used in this study have been described in detail.4 Briefly, the electrode consists of 15 fine insulated wires with their bare tips staggered along a central shaft at 1 or .5 mm. intervals. For the investigation of activity in the entire ventricle, electrodes 29 mm. long with recording tips 1 mm. apart were often used. The potentials at the electrode tips are amplified by direct-coupled amplifiers of special design with an input impedance of $10^{12}$. The indicating unit is a bank of 16 oscilloscopes, controlled by a single sweep generator and photographed with a Grass camera. Time pips are fed into all channels from a master oscillator. A switch permits taking unipolar (potential between each terminal and an indifferent body surface point) or bipolar (difference between adjacent terminals) records. The fifteenth oscilloscope continually records a fixed time reference potential and the sixteenth a lead II electrocardiogram.

Dogs weighing between 8 and 15 Kg. were anesthetized with Dial. The heart was widely exposed by removing the anterior chest wall. Electrodes were then inserted into the heart in a regular pattern designed to include the major portion of the myocardium. Most commonly, the electrodes were inserted across the heart in planes parallel to the base. In each heart a number of such planes were studied and these extended from apex to base. Electrodes in each plane were often placed completely through the heart and gradually withdrawn, each recording position overlapping the previous one. Various devices were used to mark the electrode positions so they could be accurately plotted in scale drawings of the heart. After an experiment, the cross sections of the heart with the electrodes

Received for publication March 5, 1956.
in place were drawn to scale. The time of local activity, measured from the bipolar records, was noted opposite the position of each terminal. Finally, additional information from unipolar records and from electrodes which lay outside the planes was also utilized, and successive positions of the wavefront were drawn on the sections.

Results

The first figure shows a section of a heart containing three long electrode paths. A number opposite the position of each terminal shows the time of activity at this spot in milliseconds before or after the fixed time reference potential. Unipolar and bipolar potentials are shown at several positions along one insertion. In this section, activity moved from endocardium along all of the mural insertions. Septal activity proceeded roughly from both sides toward the center of the septum. The latest septal activity was central. Figure 2 shows a heart cut by four planes parallel to the ventricular base. These planes contain 19 electrode tracks. (In this experiment a total of over 60 insertions were studied, including over 900 points.) Much data to extend and corroborate that shown and to facilitate the drawing of wavefront positions were found by insertions which did not lie in the planes shown. The earliest myocardial activity recorded in this heart preceded the beginning of the QRS complex in lead II, and is represented on the drawing by the crosshatched areas in the two center sections on the left septal border. Supplementary data indicated that the active tissue probably extended between these sections as a sheet of muscle bordering the left cavity and septum. The activity may have extended beyond these sections, but did not reach either the apical or the basal section, and no activity was recorded on the right septal surface during this interval.

Five msec, after the beginning of the QRS complex, as indicated by the areas of large dots, the active area increased in size to become an irregular, truncated cone of activated muscle on the left. This tissue partially surrounded the cavity in the left apical section, and almost completely surrounded the cavity in the second section. In the third section, an incomplete ring of depolarized muscle lay near the septum on

![Fig. 1. Cross section of dog heart with three long electrode tracks. Opposite each terminal is listed time of local depolarization in milliseconds before or after fixed time reference potential. Unipolar and bipolar potentials recorded at several places along one of the tracks are shown. Time reference potential A and lead II QRS B were recorded simultaneously with unipolar records below the center of the figure, C and D, simultaneously with bipolar records on the upper half of the figure.](http://circres.ahajournals.org/lookup/fig/1)
cause of the connective tissue between the left cavity and the aorta. The depolarized muscle formed a complex shape resembling two cups, which were separate in all sections except the third where they join anteriorly. On the right, active tissue extended closer to the base anteriorly and laterally than posteriorly. On the left, it appeared to extend about as far basally on all sides.

Fifteen msec. after the onset of QRS, as indicated by the regions marked with contour lines plus the regions already described, a cup of depolarized muscle extended through the three sections nearest the apex. A supplementary insertion indicated that the surface of the heart at the apex was active during this period. Activity had broken through to the epicardium on the right in all sections, and anteriorly in the second and third sections. The septum was completely depolarized in all three of these sections.

In the fourth section there was some epicardial breakthrough on the right, and anteriorly on the left. There was also a union of the previously separated rings of invaded tissue posteriorly in this section. However, a large septal area in this section remained in the resting state, and was continuous with other resting muscle bordering the anterior surface to right and left of center. During this period the endocardial terminations of the papillary muscles in the three apical sections became completely depolarized. In all sections the depolarized cup of muscle was surrounded by inactive muscle lying anteriorly, posteriorly, and to the left. During the next 5 msec., as indicated by the diagonally lined areas, activation proceeded to the left in the apical section and posteriorly in the second section to complete depolarization in the apical half of the heart. In the third section, there was further spread toward the epicardium in the walls on the left and centrally. Activation in the basal section extended further into the posterior wall and into the center of the septum.

The period between 25 and 30 msec. after the onset of QRS saw completion of mural and septal invasion in, and undoubtedly between, all of the sections examined. According to supplementary data, the remaining 5 msec. of QRS were devoted to completion of excitation in the basal septum.

The shape of the depolarized portion of muscle at 15 msec. after the beginning of QRS indicated by the contour lines in figure 2, is also shown in figure 3. It can be seen to have conformed generally to the shape of the heart, and to have been largely bounded by the epicardial surface anteriorly and to the right. Near the base anteriorly, the resting tissue cut an irregular trench into the activated cup.

Figure 4 shows a heart cut by three planes parallel to the base. In most respects activation in this heart was similar to that shown in figure 2, although of the 11 hearts studied, this one represented the greatest departure from the average pattern shown in the earlier figure. The differences from the more usual pattern were that some tissue on the basal right mural
endocardium was excited unusually early, that during the first 5 msec. there was no activity in the central section on the left, that the breakthrough to the right endocardium was less extensive during the early portions of the QRS complex, and that no septal points were depolarized late in the QRS interval. This last difference may reflect only the location of the electrodes in this heart. Despite the noted differences, the shape of the depolarized muscle at various instants during the QRS wave was generally the same in this heart as it was in the previous plot of activity.

DISCUSSION

Earliest and Latest Ventricular Activity. Since this survey was designed to show the general pattern of ventricular excitation, no attempt was made to include in the sections the sites of either the earliest or the latest ventricular excitation. In a previous publication we reported that parts of the septal surface, particularly on the left, are excited before any part of the lead II QRS complex is written (at normal amplification). This "silent" tissue, the earliest site of ventricular activity, is not at all extensive, but was penetrated by electrodes in most experiments.

The last tissue to be excited is not easily located. Usually the latest activity recorded was in the upper septum. In the second of the experiments presented, the latest recorded activity was in the posterior walls, but even in this experiment it is doubtful if this mass of tissue could have given the final "S" deflection in lead II. During a study of potentials from Purkinje tissue buried in the interventricular septum, electrodes were inserted into the most basal parts of the septum. Unipolar recordings in this region show (fig. 5) an initial slow negativity due to receding activity in the apical portions of the ventricles. As the lower walls become fully excited, the potential returns gradually to zero and then becomes positive as approaching activity predominates. Finally, with local depolarization, the potential returns rapidly to zero. A small negative potential follows local depolarization, indicating that some muscle, probably in this basal region of the septum, is activated after the end of QRS. The bipolar records demonstrate that local activity is close to or coincident with the end of the QRS complex. These results are contrary to our previous conjecture that septal activation does not extend to the end of the QRS complex and confirms early work by Sodi-Pallares and co-workers.

Conduction Velocity, Simultaneous Excitation
of Inner Layers. Detailed analysis of excitation in small blocks of myocardium \textsuperscript{1} - \textsuperscript{4} has led to the finding that most of the endocardium is excited at a high velocity by the branched Purkinje network, elements of which conduct at a rate of 1 M./sec. Through most of the myocardium, in the inner and outer layers, the velocity of conduction is about 0.3 M./sec.\textsuperscript{4} This velocity is also approached in those portions of the endocardium lacking Purkinje fibers.

As first noted by Durrer,\textsuperscript{1} parts of the left ventricular endocardial wall display very rapid excitation, at velocities well above 1 M./sec., and also some reversals of the direction of excitation. During the present experiments, such apparently rapid excitation occurred in various parts of the left ventricle and septum. It has been our belief that this phenomenon is more apparent than real, and results from penetration of Purkinje fibers under papillary muscles and trabeculations, and from the unevenness of the endocardial surface, rather than from intramural penetration of Purkinje fibers. A study of many insertions indicates that the inner layers are generally activated at a slightly higher velocity than the outer layers, although very rapid excitation often occurs in outer layers, particularly when a region is excited through double envelopment by two wavefronts. It must be remembered that only in three dimensional studies can accurate velocities be calculated since a single electrode or an electrode pair may lie parallel to the wavefront and thereby give a falsely high velocity.

Electrocardiographic Silence. Several years ago the theory was advanced by Kisch and his co-workers\textsuperscript{5} that the electrocardiogram reflects largely the activity in the epicardial layers of the heart. This conjecture was based on the fact that injecting necrotizing solutions of KCl into the deeper ventricular layers caused little or no change in the S-T segment. The basic assumption of this group is that areas cannot contribute to QRS if injury to them does not affect the S-T segment. The general case of the last statement is also supported, i.e., a body surface potential of a particular shape arises from an intramural region displaying a similar shape during QRS.) Although these assump-

![Fig. 5. A: lead II QRS. B: Simultaneous unipolar record high in posterior interventricular septum. B shows an initial negative (downward) deflection caused by receding activity in apical ventricle. As activity approaches, voltage goes through zero to a positive value. Depolarization in this septal region (final fast negative-going deflection) begins at about time of "S" wave in the electrocardiogram. A small potential from Purkinje tissue precedes QRS deflection by about 22 msec. on B.](image-url)
tions are not always clearly stated, they are used in going from the data described to the conclusion stated.

The findings of both groups are otherwise explained by the volume conductor theory. A completely enclosed infarct (one which nowhere intersects either endocardial or epicardial surface) will give no S-T segment change in any body surface lead, although potentials from muscle which does not depolarize will be absent from QRS. Such an infarct was probably produced by Kisch and co-workers. The lack of positive potentials preceding depolarization in some intramural leads, which is so important to the arguments of Prinzmetal and associates, has been noted by other workers who, however, did not consider it universal. This finding is undoubtedly largely explained by the fact that activity spreads so that some intramural points are equally affected by approaching and receding waves of depolarization. The result is that no positive activity precedes local depolarization. In any case, this finding can eventually be understood by knowledge of the conduction pathways and of the resistivity of the ventricular tissues and of the blood.

The assumptions made by Prinzmetal and co-workers in interpreting these potentials, noted above, are not valid. Areas with similar wave shapes need not be simultaneously depolarized, a continuous ring of myocardium in a homogeneous medium excited by a continually circulating activation wave at any velocity, would show the same potential shape at all points. Time of local activity cannot be infallibly determined by measurements made on intramural records, particularly not by measurements on unipolar records which show both local and distant activity. Simultaneous excitation of a large part of the heart will give an electrocardiographic deflection in some external lead unless the depolarized tissue is, or is equivalent to, a completely closed mass of tissue. The fact that potentials recorded on a given intramural lead have the same or similar shape as those recorded at some body surface point does not indicate that the body surface potentials arise only in the region near the lead.

Multipolar recording technics indicate that there is cancellation of some potentials by others during most of the ventricular depolarization. The volume of tissue excited before QRS (at normal electrocardiographic amplification) and therefore electrocardiographically silent, is extremely small.

Consistency of Results. All experiments in this series showed the same general picture of cardiac excitation. The results presented in figure 2 were the most divergent from the norm, and here the differences were of degree rather than kind. In each experiment we have found a high degree of internal consistency. When wavefront positions are drawn, the points line up well with one another; there are no significant discrepancies between electrodes which lie in the planes and those nearby which lie between planes. When sections are drawn connecting planes, the curves again join smoothly.

Although no substitute for statistical study, this internal consistency and the high degree of agreement among all experiments, and between these and other experiments of less extensive nature, indicate indisputably that the ventricles are excited in the fashion described.

In examining the data from a particular heart we have found it profitable to make large scale, clear plastic models of the ventricular cross sections and to use transparent colors to represent the successive areas activated. These sections are then spaced at proper distances to form a three dimensional outline model of the heart. Viewed in this fashion, each experiment shows a high degree of internal consistency.

Summary of Ventricular Excitation. The earliest activity is found at the region of the terminations of the left bundle on the midleft septal endocardium. From this region, a small portion of septal myocardium is excited for a few milliseconds before the QRS deflection. Activity on the right begins slightly later, again at the Purkinje terminations. Through rapid Purkinje conduction, much of the endocardium bordering the apical and central cavities bilaterally is excited within the first few milliseconds of QRS. At about a quarter of the way through QRS, irregular cones of active tissue surround both cavities. Owing to double envelopment of the septum these may have
joined, and even at this early time, activity has usually reached the epicardial surface on the midanterior right. With the passage of time, activity moves outward and the cones of depolarized muscle around each cavity (rings in each section) continue to join in the septum to form a single cone surrounding both cavities. Finally, only portions of the basal and lateral left ventricle and of the basal septum remain to be excited. The mural regions are depolarized by activity proceeding centrifugally from the endocardium. Activity during the last few milliseconds of ventricular activity is predominantly in the upper septum which is excited by a wave proceeding from apex to base.

Genesis of QRS. If we consider the canine heart to be centrally placed and vertical in the chest cavity with the anterior cardiac surface, as indicated in the figures, facing the anterior chest wall, we can qualitatively derive the QRS deflection. Often, the complex shapes of depolarized tissue at various instants, once determined, can be reduced to simpler equivalent shapes by utilizing the principle that all shapes with the same boundary are electrically equivalent. In the first few milliseconds the thin sheet of depolarized muscle bordering the septum presents a boundary with positive charges to the right and negative to the left. About one-fourth through the QRS deflection, the boundary between resting and active tissue is equivalent to a plane parallel to and close to the base, about half as large as the ventricular cross section at this level, showing positive charges toward the base and negative charges toward the apex. Halfway through QRS, the extensive epicardial breakthrough of activity on the anterior and right removes boundaries in this region, and leads to greater influence of boundaries in the posterior and left walls. With further breakthrough on the anterior surface apically, the effects of posterior and basal boundaries become predominant. In the last few milliseconds of activity, the small septal area still to be depolarized shows negative charges toward the base and positive charges toward the apex. These phases of activity follow one another in a smooth transition. This pattern of activity will give a QRS deflection of the diphasic or triphasic type commonly recorded in lead II or in chest leads in the dog. Preliminary experiments on several species of monkey, whose hearts closely resemble that of man, make it probable that the depolarization of the human heart is quite similar to that described for the dog. It should, however, be noted that depolarization of the human heart requires over twice as much time as does depolarization of the dog heart. In attempts to analyze human ventricular activity, the figures obtained in the dog should be multiplied by about 2.5.

We may summarize ventricular depolarization in terms of three successive "vectors." A first vector points from left to right in the septum, a second from inside out in the walls, and a third moves basally in the upper walls and septum. The transition between these is smooth and gradual. This picture agrees well with analyses of human ventricular activity from body surface leads, particularly the recent studies of Penaloza and Tranchesi. The classical deductions of Garborg and Ashman were made at a time when little information was available regarding depolarization pathways. When this limitation is considered, the vectors which were indicated in their work are remarkably similar to those described.

A physical analysis of the electrocardiogram cannot stop at this descriptive stage. Accurate prediction of the potential, \( E_p \), at any body surface point, \( P \), at any instant of ventricular excitation requires knowledge of the solid angle \( \Omega \) between that point and the boundary between resting and active tissue. This data can be derived from the present study, which permits accurate measurement of the boundary area. The solid angle is determined by drawing any sphere with radius \( R \) and origin at \( P \) which cuts all lines from \( P \) to the boundary between resting and active tissue. The solid angle \( \Omega \) is equal to \( A \), the area of the sphere enclosed by lines to the boundary, divided by the square of the radius, \( R \). Thus, \( \Omega = A/R^2 \). In an infinite, homogeneous conducting medium the solid angle is multiplied by \( \phi \), the dipole movement per unit area across the boundary.\(^{10}\)

\( \phi \) has the dimension of \( V/4\pi \) where \( V \) is the...
voltage across the membrane as depolarization occurs. \( \phi \) gives the voltage \( E_p \) at the point P in a homogeneous conducting medium, but this picture is modified in the body. First a resistive heterogeneity exists at the boundary between resting and active tissue which reduces the value of V from the 120 mv., or so, found across the cell membrane to about 50 mv. This correction, \( K_1 \), is a constant one.

A second and more complex correction must be made for the fact that the tissues are heterogeneous and that there are interfaces between tissues of various resistivities and a further interface at the body surface. At each such interface, complex reflections cause the image of each dipole to become several dipoles, as if the boundary were an irregular mirror. The correction for this situation cannot be theoretically derived. It is, however, possible to determine empirically what constant, \( K_2 \), must be applied to determine the potentials at a given body surface point when the boundary between active and resting tissue is at a given intracardiac location. Our simple equation is thus modified by two constants. \( E_p = \phi K_1 K_2 \).

**Summary**

The earliest ventricular activity is found on the septal border of the central left cavity. Activity on the right begins on the septal border closer to the base of the heart and slightly later. From these two sites activity spreads out to form a cone, or a segment of a cone, around each cavity, with the apex of the cone in the apical region of the heart. This movement is accomplished through endocardial spread at about 1 M/sec. (with faster apparent velocity due to the branching of the endocardial Purkinje fibers) and spread through the muscle at 0.3 M/sec. The cones around each cavity eventually unite through double envelopment of the septum, and gradually break through to the epicardial surface, first on the right, then anteriorly in the central and apical regions, and finally basally and posteriorly on the left. Activity travels up the septum with a slower speed on the basal septal endocardium. The last areas to be depolarized are in the basal septum.

**Summary in Interlingua**

Le prime activitate ventricular se trova al margine septal del central cavitate sinistre. Activitate al dextera comencia al margine septal plus proxe al base del corde e leve-mente plus tarde. Ab iste duo locos le activitate se estende e forme un cono o segmento de cono circa cada cavitate, con le apice del cono in le region apical del corde. Iste movimento es effectuate per diffusion endocardial a un velocitate de circa 1 m per secunda (con un plus alte velocitate apparente a causa del brançage del endocardial fibres de Purkinje) e per diffusion muscular a un velocitate de 0.3 m per secunda. Le conos circa le cavitates se reuni alora per un duplo inveloppamento del septo, e gradual-mente illos prorumpe verso le superficie epicardial, primo al dextera, postea anteriormente in le regiones central e apical, e finalmente al sinistra baso-posterior. Le activitate ascende le septo con minus velocitate super le endocardio baso-septal. Le areas que es dispolaristate al fin es le areas del septo basal.

**References**


---

**Discovery and Rediscovery**

*(1806)*

All the accessory sciences seem to be intelligently united to enrich medicine with their new discoveries; yet the light which they have imparted has reflected merely a glimmering ray on a path where many of those who are hastening have already been bewildered.

Slow experience and correct observation must establish or destroy those brilliant theories and ingenious systems, the seducing fruit of a vivid and fertile imagination; and they must appear before these two rigid judges, observation and experience, in order to know whether, like so many others, after having shone a moment, they will, in their turn, be buried in oblivion, in order to be rediscovered in whole or in part, after an indefinite passage of time.

The Pathway of Ventricular Depolarization in the Dog
ALLEN M. SCHER, ALLAN C. YOUNG, Robert V. Erickson, Rolfe A. Becker, Juhan Liikane and Otis F. Brorun

Circ Res. 1956;4:461-469
doi: 10.1161/01.RES.4.4.461
Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1956 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/4/4/461