Ventricular Intramural and Epicardial Potential Distributions during Ventricular Activation and Repolarization in the Intact Dog

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ABSTRACT
Ventricular intramural and epicardial potential distributions were measured during normal excitation and repolarization in intact dogs. Potential distributions were chosen because they can be unambiguously measured, are useful in understanding the shapes of wave forms at many specific sites, and provide a direct measure of repolarization. Unipolar wave forms were recorded from intramural and epicardial electrodes and converted into potential distributions. Well-known shapes of wave forms recorded at the inner and outer layers of the ventricles as well as peak-to-peak voltages were shown by the potential distributions to be determined primarily by superposition effects of distant excitation waves. These effects were most prominent before epicardial breakthrough and then receded during the last half of the QRS complex. However, the potential distributions became more complex as excitation waves merged, collided, and terminated. During terminal depolarization, there were scattered positive repolarization potentials intramurally. Normal repolarization was characterized by positive potentials over the ventricular epicardium while there were changes intramurally and on the atrium. Throughout the T wave, there was a predominant transmural unidirectional gradient with the inner wall being more negative than the outer wall. This finding confirms that the sequence of repolarization is from the epicardium to the endocardium with the middle layers having an intermediate time.

This paper considers the use of potential distributions throughout the ventricular myocardium and surrounding the heart as a way of characterizing cardiac electrical activity during ventricular depolarization and repolarization. To date such characterization has been done primarily by the use of isochrones (1-3) and restricted to ventricular depolarization. We chose to use potential distributions because of certain severe limitations imposed by the isochrone method. One experimental limitation is that the construction of isochrones requires intuitive judgment as to the exact instant to be used to represent depolarization. This problem occurs primarily for complex wave forms, e.g., when there are two prominent deflections within 5-10 msec of one another on either unipolar or bipolar leads.

A more fundamental limitation of isochrones is that such a representation provides no information concerning the intensity of activity along the isochrone. Consequently, it is not possible from the isochrones alone to determine how much effect a given excitation wave will have on a distant point. This fact has two significant repercussions. First, isochrones alone cannot provide adequate information to account for the shapes of the unipolar wave forms recorded throughout the heart, since the wave forms can show effects from local or distant activation. Second, body surface activity cannot be deduced from heart isochrones without some assumption about the intensity of current along the isochrone. The assumption is usually made that all parts of the isochrone generate equal current per unit area (4-8). Some question exists about this assumption, however, since experimental data have shown that potential maximums and minimums are not distributed evenly along the isochrons in the atrium (9). The present paper will show similar results for the ventricle.

Finally, isochrones provide no way at all to study the T wave. Van Dam and Durrer (10) have eloquently pointed out this problem: "For a great part, present knowledge of the genesis of the normal T wave and its alterations in pathologic conditions is derived from interpretations based on certain theoretical considerations and on indirect evidence, obtained as well in animal experiments as from clinical observation. This is because it is as yet impossible to obtain sufficient information by direct recording of local repolarization throughout the ventricles." Furthermore, they have noted that
for the spatial and temporal sequence of repolarization neither bipolar or unipolar leads are suitable to study repolarization. This limitation also affects the QRS complex, since initial repolarization potentials overlap those of terminal excitation.

We believe that the use of potential distributions to characterize heart electrical activity overcomes these limitations for both excitation and repolarization. Experimentally, the potential distribution is precisely defined and can be produced by enumeration of the voltages measured on unipolar leads. Potential distributions are especially useful in understanding the shape of unipolar wave forms, since they provide a way to determine the origin of each phase of the positive and negative deflections.

Finally, we know of no other way to directly measure ventricular repolarization beginning during the QRS complex and continuing throughout the T wave.

Whatever the limitations of the isochrone method, it has proved of inestimable value in understanding excitation of the heart. The intent of this paper is not to minimize the value of the isochrone but to show that potential distributions offer a more comprehensive and detailed representation of heart events.

Methods

We first developed an intact dog preparation with chronically implanted ventricular transmural electrodes along with epicardial electrodes over both the atria and the ventricles. Our idea was that it would be more useful to look at major segments throughout the heart than to make a large number of measurements within a few localized areas and that this procedure would provide useful information about underlying intramural potential distributions and the distributions they produce on the epicardium. The final ventricular intramural and epicardial potential maps were based on measurements from over 300 sites in each heart.

In all of the dogs, control preoperative QRS and T wave isopotential body surface maps were recorded under sodium pentobarbital anesthesia. Only the ten dogs that had T wave maps characterized throughout most of the ST-T wave by a left precordial maximum and lower body positive potentials with negative potentials over the upper and posterior torso were used. Thus, all of the experimental dogs had an upright T wave in lead II. Dogs with negative T waves in lead II demonstrated different body surface T wave potential distributions characterized by positive potentials on the upper and negative potentials on the lower thorax similar to the T wave distributions shown by Taccardi (11), who suggested that such distributions are abnormal. Since in our experience many of these dogs were found to have heart worms on postmortem examination, for this study we elected to include only those control dogs that had upright T waves in lead II.

The Preparation

Intramural plunge electrodes and epicardial electrodes were implanted via a median sternotomy. The plunge electrodes, each with 15 insulated tungsten wires 50 μm in diameter, were 0.5 mm in diameter and had a right angle bend just distal to the last point on the shaft; the bend allowed the electrode to be anchored to the epicardium. The recording points were 1 mm apart for free wall electrodes and 2 mm apart for extra-long electrodes inserted into the ventricular septum. Twenty to 25 electrodes were inserted transmurally and in the ventricular septum in each heart. Epicardial electrodes were anchored with superficial stitches at the exit point on the epicardium of each transmural electrode. Additional epicardial electrodes were sutured to intervening areas of the ventricle and over the surface of the atrium so that 25-45 epicardial electrodes covered the entire heart. The epicardial electrodes were of the type previously used to determine atrial epicardial potential distributions (9) and consisted of silver-coated copper wire with an exposed 1-mm tip on the epicardium. Bipolar pacing electrodes were sutured to the upper right atrium in the sinus node area and to ventricular locations near the atrioventricular (AV) ring. The insulated wires were looped within the chest, and the distal ends were brought out superficially, implanted beneath the skin of the lower abdomen, and exteriorized at the time of the study.

Postoperatively, all of the dogs survived, did well, and appeared to be active and healthy. During the first 5 days after surgery, all of the dogs exhibited a negative T wave in lead II, a finding similar to that noted postoperatively by Barnes and Mann (12) following temporary control exposure of the dog heart. Thereafter, the T wave was of positive polarity in lead II, and the associated QRS-T wave body surface maps had returned to the preoperative state.

Protocol for Measuring Intramural and Epicardial Potentials

Each dog was studied 9-21 days postoperatively under sodium pentobarbital anesthesia (30 mg/kg, iv). The resulting preparation was quite stable for 12-18 hours (small amounts of fluid along with supplemental doses of sodium pentobarbital were administered intravenously periodically throughout the recording procedure). All potentials were recorded in reference to the left leg. For some sequences, additional bipolar recordings between adjacent points on the plunge electrodes were done.

The heart rate was constant for each recording sequence during which recordings were made from all of the electrodes. The recording ensemble consisted of 24 a-c amplifiers (13), the outputs of which were sampled by an analog-digital converter at a rate of 1,000 samples/sec. A PDP-11/20 computer stored the data and displayed the wave forms immediately on a Tektronix 4002 display unit. The wave forms were inspected and, if they were free of artifact, recorded on digital tape. Thirty to 40 minutes were required to record from all of the electrodes for a single sequence. At least two sequences were recorded in each dog; one during normal sinus rhythm and the other during right atrial pacing.

The spontaneous rates varied from dog to dog between 80 and 120 beats/min. During the recording sequences that involved pacing the heart, the rate was held...
constant; the fixed rates for the different dogs fell within a range of 100 to 140 beats/min.

At the end of each experiment, the heart was removed, and a detailed dissection was performed to isolate each electrode on the epicardium. Following this procedure, the ventricles were cut into three sections, the division being made parallel to the AV ring. Direct imprints of the sections were made for replica drawings of the heart. The lungs appeared to be normal except that a mild atelectasis of the upper lobes occurred bilaterally in two of the dogs and a small amount of pleural fluid accumulated posteriorly next to the spine in all of the dogs.

The digitally recorded wave forms were redisplayed and photographed from the Tektronix display units. Detailed inspection of each wave form was done to ensure that there were no base-line shifts (maximum shift was ± 50 μV). The common time reference wave forms for each sequence were used for time-alignment purposes, and potential maps were printed for each 1-msec interval throughout ventricular activation and for each 5-msec interval throughout repolarization. The printed results had four parts. One was for the epicardial potentials, and the other three were for the three intramural sections. For each instant of time, values were transcribed to drawings of the heart. The final equipotential lines were drawn by hand. Finally, the unipolar wave forms were utilized to construct isochrone intramural and epicardial activation sequences. Use of either bipolar or unipolar wave forms gave identical results (9).

EVALUATION OF METHODS
To determine the extent of local anatomical damage produced by transmural electrodes, histological studies were made of 30 insertions. An example of the typical findings is shown in Figure 1. Surrounding the hole produced by the electrode (approximately 0.5 mm in diameter) was an area of connective tissue within which there were minimal or no muscle cells. The connective tissue sheath surrounding the cavity left by the electrode varied from 0.1 to 1.0 mm in thickness, and other changes of an inflammatory nature may have occupied an even larger zone. Other than these discrete connective tissue encasements, all remaining ventricular muscle appeared to be normal. Since the electrodes were surrounded by thin layers of connective tissue, it was obvious that the recording points were not in direct contact with ventricular muscle cells and, therefore, that the electrophysiological processes of the cells in the immediate vicinity of the electrode were probably changed from normal. However, the heart appeared to be normal except for the small areas represented by the electrode penetrations, and we considered the measured potentials to be only minimally distorted, since the great mass of muscle surrounding these electrodes was left undisturbed. Finally, in over 20 dogs, we implanted only epicardial electrodes, without transmural insertions, and measured normal excitation and repolarization distributions in similar chronic preparations. Since the results of the epicardial distributions in those dogs without intramural plunge electrode insertions were similar to those presented in this report, we consider the damage produced by the plunge electrodes to be insufficient to alter the overall excitation sequence and repolarization distributions of the ventricles as depicted.

Histology of the intramural electrode site. This figure shows the typical changes produced by the chronically implanted intramural plunge electrodes. Note the healthy muscle outside the localized area of connective tissue that formed a sheath of variable thickness (0.1–1.0 mm) around the cavity left by the removed electrode.

To test each recording site for the presence of local injury, the effects of which produce positive potentials locally during early repolarization (1), the wave forms at all sites were altered by shifting the ventricular pacing site at the beginning of each experiment to reproduce the sequence shown in Figure 2. When the intramural or the epicardial recording site was near the earliest activation point, repolarization produced positive potentials during terminal ventricular excitation with an ST-segment elevation that could be confused with local injury effects (Fig. 2A). If these shifts were produced by normal repolarization potentials, they disappeared or even became negative when the pacing site was moved to result in the area coming to lie in a region of terminal ventricular activation (Fig. 2D). By altering the sequences of excitation by shifting the ectopic ventricular pacing site so that the recording points were located during various portions of the QRS complex, the ST-T wave shape varied between those of earliest to latest excitation as illustrated in Figure 2B and C. The phenomenon shown in Figure 2 was used to indicate the absence of local injury. However, if local injury was
Wave forms indicating the absence of local injury. Wave forms were recorded from each electrode while the position of the ventricular pacing site was rotated in location around the basal area. This procedure resulted in each recording site being located in an area of early excitation (A), in an area of terminal excitation (D), and in areas of intermediate excitation (B and C). The wave forms shown in this figure were recorded in the left ventricular free wall (points 1-3 were located in an epicardial-to-endocardial direction) and on the nearby epicardium. When the recording points were located in the region of early activation (A), there was considerable elevation of the ST segment which could have been due to local injury. However, when the same points were located in an area of terminal excitation (D), the ST segment was at the base line or negative. As the recording sites were located at positions which were intermediate in time between the onset and the end of ventricular excitation, the shape and the amplitude of the QRS wave form changed, and there was a decrease in the magnitude of the ST-segment elevation as local excitation occurred progressively later.

Results

All of the dogs demonstrated similar distributions for the major features of normal activation and repolarization to be presented. Dog-to-dog variations primarily were differences in the position of the terminal excitation site at the left ventricular base. These variations are consistent with differences found by Durrer et al. (2) in postmortem perfused human hearts. The duration of normal ventricular activation varied from 45 to 52 msec. Because of the similarity of results, the potential distributions will be presented for a single dog.

Figure 3 shows the locations of the epicardial electrodes on the anterior and diaphragmatic heart surfaces and the positions of the plunge electrodes within the basal, middle, and apical sections of the ventricle. To indicate step changes in the drawings of the potential distributions, solid lines enclose areas with different values of positive potentials and broken lines are used correspondingly for the negative regions. Although not labeled as such, the extensions of these lines indicate the presence of maximums and minimums.

NORMAL VENTRICULAR ACTIVATION POTENTIAL DISTRIBUTIONS

The onset of ventricular activation occurred with the development of an intramural maximum and minimum in the lower ventricular septum with extension of positive potentials into the middle septum toward the base and throughout the right ventricle and the medial left ventricle (Fig. 4, 3 msec). Negative potentials extended into the lower left ventricular cavity and the lateral wall. On the epicardium, there was a maximum on the anterior right ventricle and a minimum at the lateral left ventricular base inferiorly. Also, these initial ventricular activation potentials (3 msec) were associated with an atrial repolarization maximum on the superior portion of the atrium at the base of the left atrial appendage (9).

By 11 msec (Fig. 4) the intramural distribution became more complex. In the middle section of the ventricles, there was one maximum in the anterior interventricular septum and another maximum nearby in the adjoining anterior right ventricular wall; the two maximums were separated by an area of negative potentials. Note that the intervening negative area relates to the position of two excitation waves, each propagating away from the nega-
VENTRICULAR INTRAMURAL POTENTIAL DISTRIBUTIONS

FIGURE 3
Location of ventricular intramural and epicardial electrodes. The electrode positions are shown for the dog whose potential distributions are presented in the subsequent figures. The epicardial electrodes were located adjacent to the exit point of the plunge electrodes. The epicardial outlines represent a view of the heart as seen from the anterior chest (top) and a view of the diaphragmatic surface (bottom) as seen through the heart from a superior position. The three intramural outlines were drawn from direct imprints of the basal, middle, and apical sections of the heart. Although the three intramural sections as shown suggest that all of the electrodes within each section were oriented in one plane, the plunge electrode tracts were oriented at variable angles with respect to the cut surfaces shown. For example, electrode 18 (apical section) extended in the plane of the cut surface from the epicardium on the septum anteriorly through the septum and the left ventricular cavity into the posterior papillary muscle. However, plunge electrode 21 (apical section) was oriented at approximately a 40° angle to the plane of the cut section. Thereby, the tip of electrode 21 was located in the posterior papillary muscle more basally than shown; in fact, it was in the middle section above. This type of three-dimensional problem, versus the one-plane illustration of the figure, accounts for the fact that in some of the potential distributions shown in subsequent figures there are isopotential lines drawn to show gradients in locations where, as viewed in the one-dimensional presentation, there appear to be no recording points (for example, Fig. 5 shows negative gradients in the posterior papillary muscle in both the apical and middle sections of the ventricles).

Positive potentials extended posteriorly from the septal maximum produced by the posteriorly directed septal excitation wave located in the anterior septum. This situation produced a diaphragmatic epicardial change with positive potentials extending across the interventricular septum from the right ventricle. This projection, equivalent to a diaphragmatic epicardial maximum, accompanied the persistent and increasing anterior right ventricular maximum, but the minimum persisted on the left ventricle at the base posteriorly.

The epicardial distribution suddenly changed at 13 msec (Fig. 5) with a minimum developing anteriorly just beneath the pulmonary valve with surrounding negative potentials projecting downward over the medial right ventricle. At the same time there was little change intramurally except that the area of anterior septal negativity had increased in size and moved closer to but had not reached the anterior epicardial surface. Then, epicardial breakthrough occurred (Fig. 5, 15 msec) with a rapid shift of the epicardial minimum at the pulmonary valve down to the mid-right ventricular paraseptal breakthrough site; the epicardial anterior right ventricular maximum remained stationary. Intramurally, in the middle section, negative potentials occupied both sides of the septum with positive potentials in between. This distribution was related to double envelopment of the septum with separate excitation waves propagating toward one another with the positive potentials in between (leading edge of both excitation waves).

Following right ventricular breakthrough, both intramural and epicardial distributions became more complex due to the simultaneous presence of an increasing number of separate excitation waves throughout the ventricles (Fig. 6). There was an isolated positive region in the middle septum due to colliding excitation waves which formed a single elliptical excitation wave propagating toward its center (17 msec). In the anterior right ventricular free wall, the excitation wave propagating inferiorly was associated with the persistent anterior wall maximum and adjacent negative potentials demarcating the excitation wave; however, the excitation wave propagating superiorly through the upper anterior right ventricular wall was in the negative potential area. The presence of the excitation wave in the negative potential area relates to superposition of the currents from other heart areas, as can be surmised from the intramural distribution at 17 msec (Fig. 6). Similarly, at this time the excitation wave in the left ventricular wall (middle section) was in the negative potential area, and its position was related to steep negative gradients in the trailing edge of the excitation wave. Isochrone excitation waves in the negative potential regions usually coincided in time with
rapid notches in a predominantly negative unipolar wave form, the typical wave form recorded from these sites.

Excitation waves propagated bidirectionally across the right ventricular free wall in some areas, e.g., as shown at 17 msec by the isochrones in the lateral right ventricular free wall in the negative potential region beneath the pulmonary valve. Similar double wall envelopment at sites in the lateral left ventricle occurred at 24 msec (Fig. 6) following epicardial left ventricular breakthrough near the apex.

Left ventricular epicardial breakthrough (Fig. 6, 24 msec) occurred with the development of negative potentials surrounded by positive potentials anteriorly on the lateral left ventricular epicardium. The inner heart was predominantly negative with a shell of positive potentials located over the lateral left ventricle and the posterior right ventricle. After apical left ventricular breakthrough, there was a clearer association between the position of the excitation wave and the line separating positive (leading edge) and negative (trailing edge) potentials for the large excitation wave in the lateral left ventricular wall. However, excitation waves in the upper right ventricle and the upper septum still occurred in a negative potential region (24 msec). The diaphragmatic portion of the right ventricular free wall continued to excite with the excitation wave oriented perpendicular to the base as it propagated toward the septum, as can be seen from the epicardial potential distribution and the isochrone position at this instant. Epicardially, the different right ventricular and left ventricular excitation waves resulted in both an anterior left ventricular maximum and a posterior right ventricular maximum with intervening negative regions.

The potential distributions during the remaining portion of ventricular excitation were characterized by multiple regions of positive activity superimposed on predominantly negative intramural and epicardial potential distributions. The multiple positive potential areas reflected the continued development of numerous separate excitation waves which were a consequence of the preceding excitation waves merging, colliding, fragmenting,
or ending. For this remaining period of ventricular activation, the leading and trailing edges of the excitation waves correlated well in position with the separation of positive and negative potentials. Note at 32 msec (Fig. 7) that the excitation wave propagating in the upper right ventricle anteriorly now has positive and negative potentials demarcating the excitation wave which had become part of an excitation wave extending over the left ventricle. On the anterior left ventricle, the epicardial distribution was more complex with an isolated positive area related to two merging wave fronts, one from the basal and the other from the apical direction. The diaphragmatic surface revealed an additional maximum as excitation was being completed in the right ventricular free wall, producing a pattern and an excitation wave position similar to the diaphragmatic position of the excitation wave depicted by Durrer et al. (2) in some human hearts. (Their data have been the only information we have found which depicts activation epicardially of the ventricular diaphragmatic surface.) The left ventricular epicardial excitation wave in this region became crescent shaped due to the excitation wave propagating from apex to base with slower movement of the excitation wave into the area adjoining the septum; the right ventricular free wall did not activate in an apex-to-base sequence, rather the orientation remained perpendicular to the AV ring as the excitation wave propagated from the lateral right ventricular margin toward the septum. The resultant potential distribution on the diaphragmatic surface was that of positive potentials confined to the area where both excitation waves were directed toward one another as they propagated to merge (32 msec).

The distributions then developed into multiple unconnected positive potential areas, as shown at 34 msec (Fig. 7). On the anterior left ventricle, an island of excitation was present with an elliptical excitation wave colliding on itself producing an isolated region of positive potentials with an adjacent right ventricular epicardial minimum. Another maximum was adjacent to the pulmonary valve as the upper right ventricular free wall completed excitation with excitation waves nearby.

FIGURE 5
Potential distributions surrounding the time of right ventricular epicardial breakthrough. Note at 13 msec that the outflow region of the right ventricle beneath the pulmonary valve was enveloped with negative potentials with a minimum at the valve. The intramural potential distributions showed that the anterior septal region of negativity had enlarged due to the excitation waves progressing posteriorly and medially in the septum and to those in the anterior wall. At the time of right ventricular breakthrough (15 msec), there was a sudden shift of the epicardial minimum from the pulmonary valve to the mid-right ventricular region parasagitally, but little change occurred in the intramural distributions.
Potential distributions following right ventricular epicardial breakthrough (17 msec) and left ventricular breakthrough (24 msec). Note at 17 msec that the isochrone excitation wave coincided rather closely in position with the demarcation of positive and negative potentials in the lower right ventricular free wall. Anteriorly and superiorly in the right ventricular free wall, the excitation wave propagated toward the pulmonary valve in the negative potential region. The potential gradients are not shown with sufficient resolution to see minor changes in the level of the negative potentials in the region of the excitation wave in the upper right ventricular free wall. The wave forms recorded from this region can be seen in Figure 10B.

During the terminal portion of the QRS complex (Fig. 8, 45 msec), excitation was limited to the basal region and produced positive potentials posteriorly in a small left ventricular region and in the septum at the aortic valve with negative potentials throughout most of the ventricles and over the epicardium. Repolarization became apparent during the last 5–8 msec of ventricular excitation with the development of scattered positive potentials in the apical septum in the region where earliest excitation had occurred and in the right ventricular free wall (45 msec). Epicardially, this development was associated with a decrease in the magnitude of the negative potentials on the anterior right ventricle. Therefore, positive repolarization potentials developed quickly throughout a large region of the ventricles anteriorly and in the septum. The combined presence of an excitation maximum at the base of the left ventricle and a repolarization maximum in the septum continued to the end of ventricular excitation. By the end of excitation (50 msec), repolarization positive potentials had extended over both ventricles to produce an epicardial repolarization maximum on the left ventricle in addition to one on the right ventricle.

VENTRICULAR REPOLARIZATION FOLLOWING THE NORMAL SEQUENCE OF ACTIVATION

As soon as ventricular excitation had ended (Fig. 8, 50 msec), the intramural distribution was characterized by a maximum in the area of earliest ventricular excitation in the septum and a minimum at the ventricular basal area of terminal excitation. There were immediate and transient changes of the minimum following the instant at which ventricular excitation ended (these rapid changes are not illustrated in the figures). The minimum reached a peak negative value (−1.0 to −1.6 mv) within 6 msec and then changed rapidly to near base-line values by 10–15 msec after excitation ended; during this time the maximum remained stationary in position and gradually in-
creased in magnitude with further spread of the positive potential area.

The major feature of normal repolarization was that positive potentials were present over the ventricular epicardium throughout the ST segment and most of the T wave while there were changes intramurally and on the atrial epicardium. During early repolarization (Fig. 8, 132 msec) most of the ventricle had positive potentials intramurally with higher values in the inner walls and lower potentials in the epicardial layers. The regions of negativity at this time had small values and were at the endocardium, especially in the inner right ventricular free wall and the basal right ventricular region. This intramural distribution was associated with two maximums on the ventricular epicardium, one on the anterior right ventricle and the other on the posterior left ventricle; simultaneously, the atrial epicardium was more positive on the left atrium than it was on the right atrium.

During the upstroke of the T wave, positive potentials continued over the entire ventricular epicardium and negative potentials enveloped the atrium (Fig. 9, 161 msec). The predominant transmural gradient of both ventricles changed such that the outer ventricular wall and the epicardium were more positive than the inner wall. The direction of these transmural gradients persisted throughout the T wave. During the upstroke of the T wave, the values of the intramural and epicardial maximums were much greater than the values of the negative potentials (161 msec). Also, in contrast to the frequently encountered close positions of the maximums and minimums with steep gradients within a few millimeters during excitation, during repolarization the steepest gradients extended over distances of 1–2 cm and the maximum and minimum were usually much further apart than this. At times, a distinct localized maximum or minimum was difficult to identify within a large intramural region of similar positive or negative values, respectively.

FIGURE 7

Distributions indicating the simultaneous presence of multiple excitation waves. Note at 32 msec that, although the primary direction of excitation wave movement on the diaphragmatic surface of the left ventricle was from apex to base, the diaphragmatic surface of the right ventricle was excited from the lateral margin toward the septum with the excitation wave oriented approximately perpendicular to the AV ring. Additionally, note on the anterior left ventricle that the distributions and isochrones indicate a complex pattern with multiple excitation waves such that near the base the excitation wave was moving toward the AV ring; however, an additional major excitation wave was moving toward the apex to form an isolated region where the elliptical excitation wave completed excitation by collision (34 msec). The two instants shown in this figure indicate that, although the general pattern of ventricular excitation was from apex to base, for considerable portions of the QRS complex there were major excitation waves that propagated in the opposite direction.
Although the transmural distributions remained with a gradient of more negative potentials in the inner wall to more positive potentials in the outer wall, the values of the potentials and the magnitude of the gradients changed at a time near the peak of the T wave (Fig. 9, 180 msec). The inner wall became more negative with a minimum developing in the inner wall of the apical portion of the left ventricle. Associated with the greater negativity of the inner ventricular walls, the potentials in the ventricular septum and the ventricular cavities and those on the atrium became more negative. This change produced an epicardial distribution with a minimum and negative potentials over the atria and two ventricular maximums with positive potentials enveloping the ventricular epicardium (180 msec).

After the peak of the T wave, the magnitudes of the maximums and associated positive potentials decreased, and the maximum located near the AV ring on the anterior right ventricular free wall shifted toward the septum (Fig. 9, 218 msec). Simultaneously, the magnitude of the minimum and the negative potentials increased in value with steeper gradients developing in the region of the left ventricular inner wall minimum. During this final portion of the T wave, the epicardial distribution changed with negative potentials developing over the lateral or apical left ventricular area near the inner wall minimum (218 msec). Also, negative potentials extended from the atrium across the AV ring into the base of the ventricles in many areas. Thereafter, there was a continued decrease in the magnitude of all potentials with the left ventricular inner wall minimum persisting in its position with the epicardial apical negative area nearby. Terminal repolarization epicardial patterns were variable but consisted primarily of changing patterns with disappearance of the left ventricular maximum; the anterior right ventricular paraseptal maximum persisted to the end, and the minimum on the atrium shifted to the basal left ventricle. The gradient across the free walls of both ventricles maintained a direction of more positive potentials in the outer wall to more negative potentials in the inner wall with the steeper gradients in the negative regions.

**COMPARISON OF WAVE FORMS TO POTENTIAL DISTRIBUTIONS**

By knowing the potential distribution throughout the heart, it is possible to interpret the shapes of the unipolar wave forms recorded from various
VENTRICULAR INTRAMURAL POTENTIAL DISTRIBUTIONS

Selected illustrations are presented in Figure 10 for the QRS complex (A–C) and for the T wave (D).

The QRS wave forms recorded from endocardium to epicardium in the free wall of the right ventricle in the areas that were activated early (A: 19–25 msec) were different from those in the areas that were activated late in the sequence of activation (B: 31–39 msec), although both areas had endocardial-to-epicardial spread. The tracings in A (electrode 5) were recorded from the posterior right ventricle with point 1 being located in the wall near the endocardium and point 4 being located near the epicardium. Note that the initial small positive deflection recorded at all points was related to positive potentials in this area (see Fig. 4, 3 msec) generated by early septal excitation. The wave forms then became negative (11–17 msec) with notching to biphasic deflections occurring on the “downstroke.” The notch, or intrinsic deflection (15), in the tracing at point 1 corresponded to the time of local activation, a time when that area was negative (see Fig. 6, 17 msec, basal section). Excitation at points 2 and 3 in the middle of the wall and at point 4 near the epicardium occurred at progressively later times when the potentials became progressively more positive in the area of the electrode as the right ventricular maximum moved around the lateral margin of the right ventricular free wall and shifted into the diaphragmatic area near the electrode site. Local excitation of points 2–4 was associated with a greater peak-to-peak voltage, due primarily to the increasing value of the positive component of the biphasic deflection.

There was endocardial-to-epicardial spread also in the anterior right ventricular wall adjacent to the pulmonary valve (Fig. 10, B: electrode 2); however, excitation occurred later in this area. Points 1 and 2 were near the endocardium, and points 3 and 4 were near the epicardium. Note the notching during the “upstroke” of the wave forms recorded at point 1 at a time coincident with local excitation (31 msec) when the inner wall region at the electrode site was still negative (see Fig. 7, 32 msec). By the time the excitation wave reached points 3 and 4 in the outer wall (36 and 39 msec, respectively), the wave forms there were positive as the excitation wave propagated toward the nearby annulus of the pulmonary valve to terminate. Not only were the shapes of the wave forms at this late

FIGURE 9

Potential distributions during the T wave. During most of the T wave the entire ventricular epicardium was enveloped by positive potentials, and the minimum was located on the atrium. The shifting potential distribution on the atrium reflected changes of greater negativity in the endocardial regions. The distributions remained rather stable on the epicardium, although there were changes in the values and the gradients, but the negative potentials became more prominent over the atrium and in the inner ventricular walls.
Unipolar wave forms recorded at different ventricular sites. The wave forms shown were recorded from the intramural plunge and epicardial electrodes used to record the potential distributions shown in the previous figures. The locations of the electrodes are shown in Figure 3. A: Wave forms recorded from electrode 5, located in the diaphragmatic wall of the right ventricle near the base. The wave forms were recorded at points located progressively from the inner to the outer wall (points 1–4). B: Wave forms recorded from electrode 2 in the outflow area of the right ventricular free wall just beneath the pulmonary valve. Points 1–4 also were located progressively from the endocardial layers to the epicardial layers. C: Wave forms for epicardial electrodes 17, 22, and 23 on the anterior left ventricle. The wave forms were recorded in the region of the colliding excitation wave shown on the anterior left ventricle in Figure 7, 34 msec. D: Progressive changes in the repolarization wave forms from the inner to the outer wall (points 1–3) for electrode 2 in the outflow tract of the right ventricle.

excitation area different from those recorded by electrode 5 in the basal diaphragmatic wall of the right ventricle, but the peak-to-peak amplitudes of the wave forms were different. The negative peaks at electrode 5 were much greater than those at electrode 2.

Figure 10C (epicardial electrodes 17, 22 and 23) shows a complicated double-peaked wave form at left ventricular epicardial lead 23 with simpler wave forms recorded nearby from electrodes 17 and 22. The peak of the wave form at electrode 17 occurred coincident with the first peak of the wave form at electrode 23; the peak at electrode 22 occurred later and was coincident with the second peak of the wave form at electrode 23. The potential distributions at 32 and 34 msec (Fig. 7) show that the wave form at electrode 17 comes from activation proceeding in a base-to-apex direction on the upper anterior left ventricle. However, the distributions show that the wave form at electrode 22 comes from activation in an apex-to-base direction from the lower left ventricular epicardium. The result at 34 msec was the isolated area of positive potentials where the excitation waves were colliding; the double-peaked wave form at electrode 23 was at the site of the collision. This phenomenon in ventricular muscle is analogous to similar collisions in the Purkinje system (16). The presence and the location of the collisions were easily seen from the potential distributions (Fig. 7, 34 msec).

Figure 10D illustrates the transition of the wave forms recorded during repolarization at points 1–3 from endocardium to epicardium. The ST segment in the inner wall is slightly more positive than that in the outer wall with an intermediate potential in between. Thereafter, a negative T wave was recorded from the inner layers (point 1) and a positive T wave from the outer layers (point 3) with an intermediate wave form in between (point 2). The magnitudes of the intramural T waves were small and of uncertain significance when only the measurements of a single electrode were compared. However, when measurements from all of the electrodes were pooled to construct potential distributions, these distributions showed a coherent pattern. During the T wave there were unidirectional gradients across the wall which, extracellul- arly, were more positive on the epicardium than they were at the endocardium.

Discussion

The results indicate that a comprehensive picture of the distribution of potentials throughout the ventricles and over the epicardium can be obtained experimentally in the intact dog. Taccardi et al. (17) performed in vitro measurements of the potential distributions in the volume conductor with the isolated dog heart in a tank by making measurements 5 and 10 mm from the epicardium. For similar times, our in vivo epicardial potential distributions were like those measured near the epicardium in their tank studies. They noted that the understanding of body surface maps would be enhanced by knowing more about how the potentials and currents are distributed between the heart.
surface and the body wall. We agree but would extend their comments to the use of intramural potential distributions to better understand the epicardial potential distributions, since they provide a means for understanding how the epicardial potentials come about.

INTERPRETATION OF WAVE FORMS

Craig (18) and Scher et al. (1) have presented the general principles of interpretation of unipolar epicardial and intramural wave forms. As is well known, excitation waves approaching the recording site produce more positive potentials, and the excitation waves receding from the recording site produce more negative potentials. Wilson et al. (19) have pointed out that as seen on unipolar records these effects can be measured at considerable distances from their source. One can use the general principles they outlined and the potential distributions we have shown to explain in detail the three-dimensional location of cardiac electrical activity that is giving rise to each of the successive phases of the wave form however complex it is in shape. The reason for focusing attention on waveform analysis is not just to show that potential distributions can be used for this purpose but also to show that it is possible to use a relatively small number of wave forms to learn much more about the electrical events of the heart than would be possible using only a single time value from each one.

The shapes of the wave forms shown in Figure 10 A and B have been well known since their original description by Durrer et al. (15) in regard to the "embryonic r wave" making its appearance in the outer left ventricular wall and the "QS" deflection with the intrinsic deflection (rapid notch) in the downstroke of the wave forms found in the inner wall during the normal excitation sequence. The potential distributions indicate that these changes in wave forms are a consequence primarily of changes in distant excitation waves and are not due to the inherent properties of the inner versus the outer wall. Rapid deflections on the downstroke of the QS deflections were found only when there were prominent excitation waves located apically in the ventricles, primarily before epicardial breakthrough occurred in either ventricle. As the apical excitation waves disappeared, this influence rapidly diminished and, as the wave forms in the free wall were affected less and less by the apical region, the remaining polarities were determined by local excitation. The phenomenon of QS versus "QR" deflections as related to epicardial breakthrough was similarly found for the right ventricular free wall.

In particular, the intramural distributions provide an explanation for the differences in the wave forms recorded at electrodes 5 and 2 (Fig. 10A and B), both of which were in the right ventricular free wall and both of which demonstrated endocardial-to-epicardial spread. The greater peak-to-peak amplitudes at electrode 5 were from superposition effects of excitation waves in the distant left ventricular free wall producing marked negativity at the time of local excitation at electrode 5. However, when excitation occurred later in the right ventricular outflow tract at electrode 2, there was much less superposition from the left ventricle because by this time left ventricular breakthrough had occurred in the anterior left ventricular wall and at the apex and the left ventricular wall excitation was more nearly complete (see Fig. 7, 32 and 34 msec).

The wave form at point 4 of electrode 2 (Fig. 10B) has an additional complexity, as can be surmised from the potential distribution at 34 msec (Fig. 7). Point 4 was near a site of terminating excitation where the wave form changes from a biphasic one to a totally upright one as excitation ends (16). Thus, at the time of local excitation of point 4 (39 msec), there was minimal superposition of negative potentials from the left ventricle, and the characteristic positive potentials of terminating excitation waves could be seen in the wave form.

The amplitude of the intrinsic deflection is influenced greatly by superposition (19). For normal sequences the greatest values are found in the septum and in the left ventricular free wall (30-40 mv). A note of caution is indicated in evaluating peak-to-peak amplitudes. Any residual injury effect decreases the magnitude of biphasic wave forms, primarily by decreasing the peak negative value (20, 21). In our experience, 9-12 hours was required after electrode insertion to convincingly demonstrate the absence of local injury. Such local injury potentials, although small compared with the QRS complex, can often be detected in wave forms obtained in acute experiments (1, 3, 15, 22).

VENTRICULAR REPOLARIZATION

Most attempts to account for the T wave have involved experiments designed to determine the sequence of ventricular repolarization by indirect methods, especially the measurement of functional refractory periods at different layers of the left ventricular wall (23, 24) and recently at a variety of sites in both ventricles and the septum (25).
Particularly, the results of Van Dam and Durrer (23) have served as the basis for the development of initial theoretical models of the T wave posed by Harumi et al. (24). The potential distributions in this study indicate that repolarization occurs primarily from an epicardial to an endocardial direction. That is to say, the extracellular potentials are more negative on the endocardium than they are on the epicardium and there is a unidirectional gradient between the two. This situation requires that the intracellular gradient across the wall also be a unidirectional one but in the opposite direction so that the intracellular potentials near the epicardium are at a lower level than are those near the endocardium throughout the T wave. This situation is not consistent with the original results of Van Dam and Durrer (23) which indicate that the middle wall repolarizes earlier than the epicardial or endocardial layers; however, our results are consistent with the more recent results of refractory period measurements of Burgess et al. (25).

Since the refractory period measurements produce only a single time value at each point, they give no indication of the changing spatial characteristics of repolarization that are indicated by the changing potential gradients. These gradients become steeper in the negative potential areas during the last half of the T wave. These deficiencies with the refractory period measurements support the conclusions of Van Dam and Durrer (23) that even though refractory periods are measured in several areas of the heart the results still provide insufficient information to account for the repolarization wave forms encountered in their experiments.

The persistence of relatively negative potentials extracellularly in the inner layers as compared with the outer layers of the ventricular walls accounts for the epicardial potential distributions with positive potentials over both ventricles and negative potentials with a minimum over the atrium, the atrium reflecting the state of the endocardium during normal sequences. Additionally, the development of a minimum intramurally near the endocardium in the apical free wall of the left ventricle (Fig. 9, 180 msec and 218 msec) indicates that the potential distributions confirm the suggestion of Burgess et al. (25) from their refractory measurements that repolarization occurs later in the apical endocardial region than it does in the basal region of the left ventricle.

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