Analysis of Ventricular Activation and Repolarization from Intramural and Epicardial Potential Distributions for Ectopic Beats in the Intact Dog

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ABSTRACT

Ventricular activation and repolarization were examined by measuring intramural and epicardial potential distributions during ectopic sequences in intact dogs. Potential distributions were used because they provided a direct measure of all of repolarization. Ectopic sequences produced almost unidirectional excitation across the heart along with repolarization events that were different from normal. During ectopic repolarization, positive potentials occurred over a broad area surrounding the ectopic focus, and negative potentials occurred over a large area on the opposite side of the heart where excitation terminated. The potentials in the walls of both ventricles were more positive in the outer layers and more negative in the inner layers, a gradient similar to normal. A maximum initially was at the ectopic site with a magnitude greater than that of the minimum, but the maximum subsequently decreased in magnitude and shifted toward the minimum while the minimum increased in magnitude. The steepest gradients were initially around the maximum, and they then shifted toward the minimum. The results show that ventricular repolarization potential distributions during ectopic beats are predominantly influenced by gradients from one side of the heart to the other (transventricular gradients) in contrast to normal repolarization distributions which are predominantly influenced by gradients across the wall (transmural gradients).

In this investigation, we studied ventricular repolarization by using potential distributions to directly measure ventricular repolarization throughout the heart both intramurally and epicardially (1). Schaefer (2) noted in 1957 that there was little hope of gaining a perfect and lasting theory of the order of repolarization processes with the knowledge available then. Subsequently, in 1964 van Dam and Durrer (3) pointed out that most current knowledge about the T wave was based on theoretical considerations and indirect evidence, and Christian and Scher (4) stated in 1967 that no adequate data indicated how the T wave originated. A primary objective of experiments related to the T wave has been to determine the distribution of currents throughout the heart, as considered initially for a single cardiac fiber by MacLeod (5). In contrast, however, most of the studies related to the genesis of the T wave have been oriented toward body surface electrocardiograms as measured with a small number of leads and have been designed, in one way or another, around the idea of the ventricular gradient as originally put forth by Wilson et al. (6). The ventricular gradient concept considers only the average T-wave effects (2, 7), not moment-by-moment events, and is limited in other ways as noted by Schmitt (8) and Simonson et al. (9). The concept has been expanded from the original frontal plane analysis (6) to the vectorcardiographic three-dimensional analysis by Harumi et al. (10) and further extended by Abildskov et al. (11). However, all of these studies have been directed toward QRS-complex and T-wave deflections on the body surface for either standard electrocardiographic or vectorcardiographic wave forms, and, consequently, have not provided direct information about the heart.

Indirect measurements of repolarization made from the heart have consisted of the determination of refractory periods at different sites in the ventricles (12–15). In such experiments, Burgess et al. (15) have shown that transmurally the order of recovery of ventricular excitability is from epicardium to endocardium and from base to apex. Such findings pertain only to a limited time interval near the peak of the T wave and provide no basis for explaining the major portion of the entire ST-T wave, a phenomenon occurring over a much longer period of time. van Dam and Durrer (14) have concluded that such indirect measurements do not provide information to explain the epicardial T wave.
waves recorded in their experiments. Direct measurements of repolarization in the heart have focused on its time course as measured intracellularly (16, 17), limited to only a few sites in vitro with emphasis on the papillary muscle (18) and on epicardial monophasic action potentials (19, 20).

In the present report, the results show that repolarization in normal hearts is controlled by two predominant influences: (1) the time difference between the earliest and the latest area of ventricular activation and (2) the characteristic tendency of the epicardium to repolarize before the endocardium, with unidirectional change in repolarization progress across the wall. Although the left and right ventricular ectopic excitation sequences presented are principally used to produce varied repolarization events, they are noteworthy in themselves, since no total ventricular excitation sequences for ectopic beats have previously been reported. These excitation sequences are presented as potential distributions as well as isochrones, since the overlapping of depolarization and repolarization events, which occurs over a long interval, is only apparent from the potential distributions.

Methods

The experimental design was to establish a dog preparation in which normal repolarization events could be measured intramurally and epicardially. Our plan was to first study normal distributions throughout the heart and, once these patterns were established, to go on to the study of ectopic foci. In the present study, we used the same intact dogs that we used previously (1) to investigate normal excitation and repolarization potential distributions throughout the heart; in each dog, detailed checks ensured the absence of local injury effects in the wave forms recorded at each site (1).

The final ventricular intramural and epicardial potential maps for the ectopic beats were based on measurements from over 300 sites in each heart and for one or two epicardial pacing sites for each ventricle.

THE PREPARATION

The details of the pre- and postoperative screening of the dogs with isopotential body surface maps and the operative procedures have been reported in detail previously (1). Twenty to 25 intramural ventricular electrodes (each with recording points 1–2 mm apart to provide equal spacing across the ventricular wall) and 25–45 epicardial electrodes covered the entire heart. Additionally, bipolar pacing wires were sutured to the sinus node area to control atrial rate, and similar pacing electrodes were sutured subepicardially to the ventricles near the atrioventricular ring so that ectopic sequences could be generated from sites at multiple points encircling the ventricles. The insulated recording and pacing wires were looped within the chest, and the distal ends were implanted superficially beneath the skin of the abdomen. Postoperatively, all of the dogs did well; when repolarization had returned to normal 9–21 days after surgery, as judged from body surface maps, each dog underwent study.

PROTOCOL FOR MEASURING HEART POTENTIALS

Each dog was studied under sodium pentobarbital anesthesia (30 mg/kg, iv). The wires from the heart were exteriorized and connected to individual cards, which in turn, were inserted into a switching box that allowed rapid sequential recording of the wave forms at each of the 15 points per intramural electrode and each of 15 epicardial points simultaneously. All potentials were recorded in reference to the left leg. In several sequences, bipolar recordings were made from adjacent points 1 mm apart.

Since changes in heart rate produce well-known changes in the T wave (17, 21), for each dog heart rate was held constant throughout each sequence, and the same rate was used for the different sequences to allow comparisons of the different sequences at the same rate. The fixed pacing rate for different dogs fell within a range of 100 to 140 beats/min. The pacing stimuli were 1-msec impulses at 1.5 times the threshold value.

We encountered several problems related to the control of heart rate. First, any alteration of rate on a beat-by-beat basis frequently changed the amplitude or the shape of the QRS complex and the T wave locally and required 15–60 seconds to return to the previous steady state. Consequently, any change in rate during a recording sequence meant that the previously recorded data had to be discarded and the entire sequence reinstituted. Second, if the stimulus artifact occurred before repolarization was complete in the previous beat, we could not establish a base line to use in each unipolar wave form to construct isopotential maps. Careful control of the pacing rate was necessary, since the pacing rate had to exceed the spontaneous one and, thereby, shortened the time interval between the end of the T wave and the onset of the next beat.

Finally, in most of the dogs, complete control of the atria via retrograde propagation did not occur when the ventricle alone was paced. This situation resulted in intermittent fusion beats in which the sequence of ventricular excitation was affected by both the ectopic focus and septal activation via the His bundle. When fusion beats occurred, there were frequent intermittent rate changes due to interpolated beats being conducted from the atrium. Since mild degrees of fusion frequently were detectable only on selected leads, eight reference epicardial leads and lead II were recorded simultaneously with the 15 data points from each electrode to ensure that there were no beat-to-beat changes in the excitation sequence. Furthermore, since rate interruption had to be avoided, the heart was controlled by simultaneously pacing the right atrium and the ventricle with the ventricular stimulus delivered 40 msec after that to the sinus node area. By frequent checks of the duration of the P-R interval with right atrial pacing alone, we could ensure that there was no influence from atrioventricular transmission, since ventricular activation was completed before the P-R interval ended. This pacing procedure produced a stable rate without interruption for many hours.

The pacing sequence was controlled by a PDP-11/20

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computer which synchronized the pacing stimuli with the data recording. The recording ensemble consisted of 24 a-c amplifiers; the output of each amplifier was sampled at a rate of 1,000 samples/sec. The computer stored the data and displayed the wave forms immediately on a Tektronix 4002 display unit. After it was established that each beat was free of artifact, the wave forms were recorded on digital tape. At the end of each experiment, the heart was removed, the electrode sites were documented, and direct imprint drawings were made of three sections of the ventricles.

The digitally recorded wave forms were redisplayed and photographed for detailed inspection of each wave form to ensure that no base-line shifts occurred. A second computer program was used to convert the data from time sequences to potential distributions, and potential maps were printed for each millisecond throughout ventricular activation and every 5 msec throughout the ST-T waves. Additionally, the unipolar or bipolar wave forms were used to construct isochrone activation sequences.

Results

The duration of the ectopic ventricular activation sequences, measured from the onset of the stimulus to the J point (the instant at which ventricular excitation has just ended), varied from 132 to 140 msec compared with the control normal duration of 45–52 msec. For similar ventricular pacing sites, all 12 of the dogs demonstrated very consistent potential distributions during ventricular excitation and repolarization. To compare these results with the normal events in the same dog, the sequences to be presented are from the same dog for which the distributions and the positions of the recording electrodes have been presented in a previous report on normal ventricular excitation and repolarization during right atrial pacing (1).

LEFT VENTRICULAR ECTOPIC FOCUS

Potential Distributions during Ventricular Activation.—After the stimulus artifact disappeared, negative potentials developed in the immediate area of the ectopic pacing site. This small area remained markedly negative with peak values between -20 and -30 mv for a considerable interval as it required up to 18 msec for initial excitation to form a circular-shaped excitation wave with a diameter of 1 cm.

By 32 msec (Fig. 1), negative potentials were still localized to a rather small area in the left ventricular wall near the base and positive potentials were present throughout the rest of the heart. An intense minimum occurred in the inner wall in the small zone of negative potentials; this early minimum had the most negative potential value encountered throughout ventricular excitation. The two maximums in the left ventricular wall were of much lower magnitude than the minimum. At the base, negative potentials occurred in the inner and outer walls with an intervening region of positive potentials. This distribution was associated with the double envelopment of the basal wall laterally with both endocardial and epicardial excitation waves propagating toward one another, presumably as a result of the inner wall excitation wave spreading via the Purkinje system.

By 46 msec (Fig. 1), the epicardial area of negativity had expanded both anteriorly and posteriorly with persistence of the anterior and posterior left ventricular maximums. Intramurally, the minimum remained in the lateral left ventricular wall with the expansion of negative potentials endocardially into the apical region; the intramural maximums were located anteriorly and posteriorly near the left ventricular epicardial maximums. The demarcation line separating positive and negative potentials showed good agreement with the location of the isochrone excitation wave in the lateral wall with negative potentials extending beyond the excitation wave into the left ventricular side of the septum. The potential distributions and the position of the isochrones at this time (46 msec) indicated that, although the sequence had been initiated subepicardially, spread occurred endocardially throughout much of the left ventricular free wall, especially in the areas known to contain the Purkinje system. This situation resulted in endocardial-to-epicardial spread, and in some areas there was double envelopment of the free wall as the epicardial excitation wave continued to enlarge.

The major feature of ventricular activation thereafter was the relatively simple pattern of the potential distributions compared with the normal pattern (1), with the boundary between positive and negative potentials coinciding in position with the isochrones (Fig. 2). The excitation waves, although located in different ventricular regions, were oriented in a very similar direction intramurally (59 msec); epicardially, there was a large posterior and an anterior excitation wave, and both of these waves had a similar orientation like the intramural excitation waves. The epicardial potential distribution (59 msec) reflected the intramural status in that the anterior and posterior maximums and the distribution of positive potentials over the right ventricle and right atrium were associated with intramural positive potentials in the septum and right ventricular cavity, and the epicardial negative potentials over the left ventricle and left atrium corresponded to similar negativity in the left ventricular wall and cavity.

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The continued progression of the expanding negative potential area into the septum was associated with continued simplicity of the distributions such that at 80 msec (Fig. 2) the demarcation line between positive and negative potentials, i.e., the excitation wave, was confined almost totally to the septum. It formed a single flat plane which bisected the heart, with positive potentials throughout the right ventricle and its cavity and negative potentials throughout the left ventricle and its cavity. Epicardially, the intramural events were mirrored with similar separation of positive and negative potentials with the anterior and posterior maximums shifting onto the right ventricular free wall paraseptally.

At 97 msec (Fig. 3), the excitation wave had moved into the posterior wall of the right ventricle with an associated minimum and negative potentials medially and with positive potentials near the lateral margin; little change had occurred in the position of the anterior epicardial excitation wave over the septum. Intramurally, negative potentials occurred in the inner wall throughout the apical region and adjacent cavity of the right ventricle, and positive potentials continued in the basal septum and adjacent cavity. The potential distributions and isochrones indicated endocardial-to-epicardial excitation wave spread in the right ventricular wall, and the excitation maximum was located in the basal septum near the aortic valve (97 msec). Although the excitation waves continued with a similar orientation and still produced a rather simple potential distribution throughout the right ventricle, the total heart distribution had become more complex due to the appearance of repolarization positive potentials in the lateral left ventricular wall with a repolarization maximum located in the area of the ectopic pacing site (Fig. 3, 97 msec). That these positive potentials in the area of the pacing site were repolarization potentials and not due to depolarization is apparent from the fact that excitation had already occurred (see Fig.
FIGURE 2
Potential distributions during the middle of the left ventricular ectopic activation sequence. Note that the epicardial distributions correspond well with the intramural distributions and that the excitation waves have a similar orientation at 59 msec. At 80 msec, note that the shape of the septal excitation wave is that of a flat plane and its position bisects the heart at the time coinciding with the peak QRS deflection in lead II.

FIGURE 3
Potential distributions showing simultaneous depolarization and repolarization potentials (left ventricular ectopic beat). Repolarization positive potentials with an associated maximum developed in the area of the ectopic focus while most of the right ventricle was yet to be depolarized (97 msec). Note the subsequent decreasing area of excitation positive potentials in the right ventricle and the increasing repolarization positive potentials in the left ventricle (106 msec).

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1, 32 msec) as indicated by both unipolar and bipolar wave forms and, additionally, is apparent because subsequently this region of positive potentials increased in magnitude and area as the cardiac cycle continued into the ST segment and the T wave.

The remainder of ventricular excitation consisted of a decreasing area of depolarization positive potentials in the anterior right ventricle and an increasing area of repolarization positive potentials in the left ventricle. The epicardial maximum on the anterior wall of the right ventricle moved toward the pulmonary valve with an associated minimum nearby (Fig. 3, 106 msec). Intramurally, negative potentials enveloped r−t of the right ventricle and the cavity except in the basal region where excitation was being completed in the free wall and in the septum near the aortic valve. The repolarization maximum at the ectopic focus site became more prominent, and the area of repolarization positive potentials expanded through an increasing region of the left ventricle (106 msec).

This situation resulted in a complex distribution with a prominent depolarization maximum with associated positive potentials in a discrete area of the upper right ventricle and a prominent repolarization maximum and an area of positive potentials in the left ventricular wall. There were intervening negative potentials in between the two positive areas.

During the last 10 msec of ventricular excitation, which occurred in the right ventricle beneath the pulmonary valve (Fig. 4, 123 msec), the potential distributions were dominated by repolarization positive potentials that expanded throughout most of the left ventricle with a continuing increase in the magnitude of the repolarization maximum which remained stationary in the left ventricular wall adjacent to the ectopic site.

ST-T-Wave Potential Distributions.—Immediately after the J point there was a minimum at the site where excitation had terminated and a repolarization maximum where excitation had started at the ectopic focus (not shown). During the next 15
msec, while the maximum remained stationary and gradually increased in value, the minimum changed rapidly. It reached a peak negative value of \(-2.0\) mv within 6 msec and then returned rapidly to near base-line values. The minimum then shifted slightly away from the site of terminal excitation to result in the distribution shown at 169 msec (Fig. 4). Early repolarization (ST segment) was characterized by negative potentials throughout the right ventricular wall, right ventricular cavity, and right atrium and by positive potentials throughout the left ventricle, most of the septum, the left ventricular cavity, and the left atrium. The magnitude of the maximum and the positive potentials was much greater than that of the minimum and the associated negative potentials. It was difficult to localize a specific maximum and minimum intramurally due to the potentials of similar magnitude encompassing large areas. However, the highest potentials occurred at the pacing site and the lowest potentials in the anterior right ventricular free wall (169 msec).

The major feature of the distributions during the inscription of the T wave was that epicardially positive potentials were present over the left ventricle and negative potentials were over the right ventricle, while intramurally there was an unidirectional gradient across the walls of both ventricles with more positive potentials in the outer layers and more negative potentials in the inner layers. This transmural gradient was similar to normal (1). During the upstroke of the T wave, the maximum increased in amplitude as it remained stationary at the ectopic focus and the minimum remained in the anterior right ventricular wall (Fig. 5, 219 msec). The steepest gradients occurred around the maximum. As repolarization continued, the maximum and minimum remained stationary with a marked distance separating the two, as shown at the peak of the T wave at 237 msec. The gradient became less steep around the maximum which diminished in amplitude, and the gradient became more steep in the region of the minimum as it became greater in magnitude.

**FIGURE 4**

Potential distributions during the T wave of the left ventricular ectopic beat. The major feature throughout the T wave was the presence of positive potentials over the epicardium of the left ventricle and negative potentials over the right ventricle; transmurally, there were more positive potentials in the outer wall and more negative potentials in the inner wall of both ventricles. Initially the maximum increased (219 msec) with the steepest gradients in this area. At the peak of the T wave (237 msec), the magnitude of the maximum and the associated gradient diminished while the magnitude of the minimum in the right ventricle increased and the gradients nearby also increased. During late repolarization (299 msec), the maximum shifted toward the minimum, and the positive potentials in the area of the ectopic focus decreased markedly, while the minimum remained quite prominent with associated steep gradients.

**FIGURE 5**

The major feature of the distributions during the inscription of the T wave was that epicardially positive potentials were present over the left ventricle and negative potentials were over the right ventricle, while intramurally there was an unidirectional gradient across the walls of both ventricles with more positive potentials in the outer layers and more negative potentials in the inner layers. This transmural gradient was similar to normal (1). During the upstroke of the T wave, the maximum increased in amplitude as it remained stationary at the ectopic focus and the minimum remained in the anterior right ventricular wall (Fig. 5, 219 msec). The steepest gradients occurred around the maximum. As repolarization continued, the maximum and minimum remained stationary with a marked distance separating the two, as shown at the peak of the T wave at 237 msec. The gradient became less steep around the maximum which diminished in amplitude, and the gradient became more steep in the region of the minimum as it became greater in magnitude.

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Although the steepest gradient shifted in location between the maximum and the minimum, transmurally the unidirectional gradient persisted with more positive potentials in the outer wall and more negative potentials in the inner walls of both ventricles (Fig. 5, 237 msec).

During late repolarization (Fig. 5, 299 msec), the maximum moved away from the ectopic focus and shifted toward the minimum; also, the maximum decreased further in magnitude and the gradients near the ectopic focus diminished markedly. Simultaneously, steep gradients continued in the anterior right ventricular wall in the area of the minimum as it shifted into the region just beneath the pulmonary valve where terminal excitation had occurred. Finally, repolarization ended with diminution of all values as positive potentials continued over the left ventricle and negative potentials over the right ventricle with a minimum in the inner wall of the right ventricular outflow tract and a maximum in the left ventricle next to the septum.

**RIGHT VENTRICULAR ECTOPIC FOCUS**

Potential Distributions during Ventricular Activation.—The ectopic stimulus site was near the atrioventricular ring laterally on the anterior wall of the right ventricle (Fig. 6). Initially, negative potentials developed in the immediate vicinity of the pacing site and remained confined to this small area which gradually expanded to a size of 1 cm² by 15 msec. During this time, the magnitude of the minimum reached the most negative value (−17 mv) found throughout the right ventricle during the entire sequence. By 23 msec (Fig. 6), two maximums with an intervening narrow area of positive potentials were located over the right ventricle in the area of the leading edge of the excitation wave as it propagated across the anterior right ventricular wall away from the nearby atrioventricular ring. There were low-level negative potentials throughout most of the heart and on the epicardium of both ventricles (23 msec); however, in the area undergoing depolarization the position of the isochrone excitation wave correlated with the demarcation line between positive and negative potentials except that the excitation wave propagating in the lateral wall posteriorly was in an area of negative potentials (basal section, 23 msec).

The negative potential area surrounding the pacing site then increased rapidly. Positive poten-
tials developed throughout the left ventricle, and at 38 msec (Fig. 6) one excitation wave had reached the ventricular septum anteriorly and another right ventricular excitation wave propagated toward the septum posteriorly. Excitation occurred in much of the right ventricle in an endocardial-to-epicardial direction. By this time, the correlation of the position of the isochrone excitation wave with the line demarcating positive and negative potentials was excellent and remained so as ventricular activation continued (Fig. 7, 47 msec).

The major characteristic of the ventricular activation that followed was the presence of rather simple potential distributions with the line demarcating positive and negative areas indicating the presence of both anterior and posterior ventricular excitation waves which remained unidirectionally oriented perpendicular to the lateral left ventricle. When excitation had invaded the septum at 53 msec (Fig. 7), it formed an excitation wave similar to, but of opposite polarity from, that encountered when the ectopic focus had been on the lateral left ventricle (see Fig. 2, 80 msec). Its shape was that of a single flat plane which bisected the heart with negative potentials enveloping the right ventricle and positive potentials enveloping the left ventricle (53 msec).

As the excitation wave propagated into the left ventricular wall, it maintained the unidirectional orientation as the area of positive potentials decreased in size and the maximum moved to the lateral left ventricular wall (Fig. 8, 89 msec). Then, while the excitation wave changed little other than to decrease in size, the potential distribution became more complex at 93 msec (not shown) with the appearance of repolarization positive potentials in the right ventricle at the ectopic stimulation site. This appearance was followed rapidly by the scattered spread of positive potentials in the adjacent right ventricular wall and in the septum so that by 105 msec (Fig. 8) the area of positive repolarization potentials in the right ventricle exceeded the area of decreasing positive excitation potentials in the lateral left ventricle at the base.

**ST-T-Wave Potential Distributions.**—The potential distribution during the ST segment consisted of a repolarization maximum at the pacing site in the anterior right ventricle and a minimum at the site of terminal excitation at the base of the left ventricle posteriorly.

Throughout the course of the T wave, the intramural potential distributions demonstrated a transmural gradient of more positive to more negative potentials from the outer to the inner.
Ectopic right ventricular focus: late ventricular excitation potential distributions. Note the decreasing area of positive potentials as the excitation wave maintained a unidirectional orientation in the left ventricular wall at 89 msec. As this phenomenon continued, scattered repolarization potentials appeared in the right ventricle and septum with the repolarization maximum at the ectopic stimulation site (105 msec).

portions of the walls of both ventricles; the highest potentials occurred in the anterior right ventricle and the lowest potentials were in the lateral ventricular wall (Fig. 9). Although the magnitude of the negative potentials had been quite small during the ST segment (early repolarization), these potentials became more prominent during inscription of the T wave. While the T wave in lead II approached its peak (188 msec), the magnitude of the maximum at the ectopic site continued to increase and the steepest gradients occurred in the vicinity of the maximum. As repolarization continued, the positive potentials and the gradient decreased markedly at the right ventricular pacing site, and the maximum shifted toward the minimum to become located anteriorly at the septum (235 msec). Associated with these changes, the steepest gradients shifted toward the minimum which increased in magnitude. At this time the epicardium demonstrated a minimum at the base of the left ventricle at the site of terminal excitation and another minimum near the apex; intramurally, the minimum was located in the inner wall of the apical portion of the left ventricle. During terminal repolarization (266 msec), the epicardial distribution showed a decrease in the magnitude of the anterior maximum, and the highest potentials on the diaphragmatic surface (235 msec) shifted to a position closer to the minimum to form another maximum at the septum posteriorly (286 msec). Both the epicardial and the intramural distributions showed diminishing gradients in the vicinity of the maximum while steep gradients continued in the region of the minimum. On the epicardium, the minimum remained at the site where ventricular activation had ended; intramurally, the minimum and the lowest potentials were in the inner wall of the lateral left ventricle near the apex (266 msec), a location similar to that found for the minimum during normal repolarization (1).

**COMPARISON OF WAVE FORMS WITH POTENTIAL DISTRIBUTIONS**

On the epicardium there was a consistent and reciprocal relationship of the QRS complex and the T wave at the earliest and latest areas of excitation, as shown for the left ventricular ectopic focus in Figure 10A. At the site where excitation began, the QRS complex was negative with a prominent ST segment and a T wave of opposite polarity. In the area of terminal epicardial excitation on the anterior wall of the right ventricle, the QRS complex...
was upright with a prominent negative T wave. When the excitation sequence was reversed by placing the ectopic focus on the lateral right ventricle, the shape of the epicardial QRS complex and the T wave reversed (Fig. 10B). These findings are similar to those previously reported for the atrium for the earliest and latest areas of excitation as the atrial pacemaker position was shifted (22).

The prominent ST-segment elevation and the positive T wave at the site of earliest excitation were shown by the potential distributions to be related to the location of the maximum in this region during the ST segment and up to the time of the peak of the T wave in lead II. The markedly negative T wave at the terminal excitation site was related to the repolarization minimum being located in this area throughout repolarization. Also, the sequential potential distributions demonstrated spatially why the peak of the negative T wave occurred after the peak of the positive T wave by 70 msec (Figs. 10A and B) for both ectopic sequences (see Figs. 5 and 9). Following the peak of the positive T wave, the maximum at the ectopic site decreased in magnitude and moved toward the minimum, while the minimum increased in magnitude as it remained in the area of terminal excitation.

Although the configuration of the unipolar wave forms showed good agreement between the earliest and latest excitation sites on the epicardium, intramurally the reciprocal polarity of the QRS complex and the T wave did not hold, as shown in Figure 10C, for the lateral left ventricular wall (apical section) during the ectopic left ventricular sequence. Excitation in the area of the electrode occurred 43-56 msec from onset, and there was endocardial-to-epicardial spread. This situation was associated with a negative QRS complex in the inner wall with an increasing R wave in the wave forms in the middle and outer layers. The T waves, however, were negative in the inner layers and positive in the outer layers. The potential distributions indicated that, although the transmural electrode was located in a relatively early area of excitation, the inner wall became negative during repolarization in association with the unidirectional transmural gradient which persisted throughout the T wave with more positive potentials in the outer layers and more negative potentials in the inner layers (see Fig. 5).

Lead II tracings are shown in Figure 10D to compare the peripheral wave forms with the excitation and repolarization potential distributions of the heart. At time instant a the excitation wave was located in the ventricular septum at a time when its position bisected the heart for both ectopic sequences originating in the left ventricle (see Fig. 2, 80 msec) and in the right ventricle (see Fig. 7, 53 msec). For both, the position of the excitation wave occupied the largest cross-sectional area possible with respect to the axis of lead II. The solid angle method of predicting body surface...
FIGURE 10

Wave forms related to potential distributions. A and B illustrate epicardial wave forms recorded at the earliest and latest sites of ectopic excitation. A: Wave form 1 was recorded near the ectopic left ventricular focus and wave form 2 was recorded in the area of terminal excitation just beneath the pulmonary valve on the right ventricular outflow tract. B: Epicardial wave form 1 was recorded on the lateral left ventricle at the base during the right ventricular ectopic sequence and wave form 2 was recorded near the ectopic right ventricular focus. Note for both sequences that in the area of the ectopic focus there was a positive ST segment and the peak of the positive T wave occurred approximately 70 msec before the peak of the negative T wave on the opposite ventricle. C: The wave forms were recorded during the left ventricular ectopic sequence from a plunge electrode in the lateral left ventricle near the apex in the inner wall (1), middle wall (2), and outer wall (3). D: Lead II wave forms for both left (1) and right (2) ventricular ectopic sequences are shown. At time (a) the deflections in both wave forms were of approximately equal amplitude (1.7 mv). Although the amplitude in trace 1 diminished thereafter, it increased in trace 2. The rapid positive deflection during the terminal QRS complex in trace 1 was produced by repolarization rather than by depolarization potentials.

potentials (23, 24) would give the greatest deflection in lead II at this instant for both sequences, since the excitation waves were largest at that time with respect to lead II. For the left ventricular ectopic sequence (trace 1), this instant was associated with the greatest negative deflection (Fig. 10D) in lead II. However, for the right ventricular ectopic sequence (trace 2), the peak positive deflection at b occurred later when the excitation wave had become smaller in cross-sectional area after it had propagated into the lateral left ventricular wall (see Fig. 8, 89 msec). The potential distributions showed that, although the excitation wave maintained a similar orientation as it became smaller in cross-sectional area, the epicardial maximum shifted from the diaphragmatic surface (see Fig. 7, 53 msec) to the lateral left ventricular wall (see Fig. 8, 89 msec), and it had become much greater in magnitude at time b. This comparison indicates that knowledge of the potential distribution can be useful when trying to analyze cardiac excitation waves with respect to body surface potentials by use of the solid angle approach where the only known variable is the size of the boundary between resting and active muscle (23).

Finally, the potential distributions illustrated that the rapid positive deflection during the terminal QRS complex (Fig. 10D), indicated by the arrow for lead II of the left ventricular ectopic sequence (trace 1), was due to repolarization potentials in the left ventricle at a time when the excitation wave in the right ventricle was diminishing in size (see Fig. 4, 123 msec). That this was the case can be seen by the fact that the right ventricular excitation wave was positioned so that it would produce negative potentials in lead II and the left ventricular repolarization maximum and positive potentials were oriented to produce the positive deflection before ventricular excitation was complete, resulting at the end of the QRS complex in the considerable ST-segment elevation in lead II.

Discussion

There were two major features of the potential distributions during ventricular activation of ectopic beats. First, both the intramural and the epicardial distributions were quite simple due to the unidirectional propagation of the excitation waves throughout most of the QRS complex with clear separation of a positive and a negative region by the position of the excitation waves. This situation contrasts to normal ventricular excitation potential distributions (1) which demonstrate complex patterns, especially after epicardial breakthrough, due to the presence of multiple excitation waves which merge, collide, and terminate. Second, although the distributions in the region of the

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excitation wave remained simple, the total heart distribution became complicated for a considerable time during the latter portion of the QRS complex as repolarization potentials developed in the area of the ectopic focus and there was increasing dominance of repolarization positive potentials near the ectopic site while excitation terminated in the opposite side of the heart. These two major features were reflected well in both the intramural and the epicardial distributions, whereas in the normal sequences the intramural distributions are more complex than those on the epicardium.

The ectopic repolarization potential distributions during the ST-T waves were characterized by four features. (1) Epicardial positive potentials occurred over a broad area surrounding the ectopic focus, and negative potentials occurred over a large area on the opposite side of the heart where excitation terminated. (2) During early repolarization (ST segment), the maximum was located in the area of the ectopic focus and the minimum was located near the site of terminal ventricular excitation in the opposite ventricle. (3) Throughout the T wave, the transmural potential difference in the wall of both ventricles was more positive in the outer layers and more negative in the inner layers, the direction of the transmural gradient being the same as that during the normal T wave (1). (4) There were sequential changes during the T wave with the maximum initially being located at the ectopic stimulus site with the magnitude of the maximum and the positive potentials being greater than the magnitude of the minimum and the associated negative potentials. This distribution then changed with the maximum decreasing in value and shifting toward the minimum while the minimum increased in magnitude. These changes in the maximum and minimum were accompanied by a shift in the location of the steepest gradient which initially surrounded the maximum and then moved toward the minimum.

The results showed that the time course of ventricular repolarization at one site as related to that at another during ectopic sequences is determined by the relative times of activation. The consequence of this fact is that during repolarization there is a maximum and a minimum on the opposite ventricles. These extracellular potentials require that the intracellular potentials be distributed in an opposite direction with the lowest intracellular potential in the region of the extracellular maximum and vice versa. That is to say, for ectopic sequences both the intracellular and the extracellular gradients are primarily from one ventricle to the other (transventricular gradients). The measured distributions also showed that the epicardium repolarizes ahead of the underlying endocardium unidirectionally across the wall of the ventricles as evidenced by the unidirectional extracellular gradient with higher potentials in the epicardial layers and lower potentials in the endocardial layers of both ventricles. Thus, the transmural intracellular and extracellular gradients are of secondary importance in determining the ventricular potential distribution during repolarization of ectopic beats.

We believe that the events of normal repolarization (1) are controlled predominantly by the same factors noted in the present paper. However, because excitation occurs more nearly simultaneously in the left and right ventricles, the prominent transventricular potential difference (e.g., from the lateral left ventricular wall to the lateral right ventricular wall) that is present in ectopic beats is minimum or not present in normal beats. Thereby, the transmural potential difference (i.e., from the endocardium to the epicardium) is the predominant effect during the normal T wave. As a result, during the normal T wave, the cardiac potential distributions show positive potentials over the entire ventricular epicardium with a minimum and associated negative potentials over the atria (1), thus reflecting the intramural status of positive potentials in the outer layers of the ventricular walls and the more negative potentials in the inner layers. This distribution is produced by the unidirectional intracellular potential difference across the wall with the highest intracellular potential at the endocardium and the lowest intracellular potential at the epicardium throughout the T wave. This situation would explain the results of van Dam and Durrer (3) as well as those of Christian and Scher (4), who found that little or no change occurred in the T wave despite marked changes in ventricular excitation as long as the duration of ventricular activation was no longer than normal, even to the extreme of the total heart being simultaneously depolarized.

Measurements with the Brody chamber (25-27), a spherical cylinder in which a turtle or a rabbit heart is immersed, have shown that for ectopic beats the ST-T complexes can be represented by a dipole that remains predominantly in the left ventricle for both right and left ventricular ectopic beats. The main thrust of such studies as well as those derived from the ventricular gradient (6, 10,11) has been to characterize cardiac repolarization as viewed from various distances from the
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Heart. In contrast, the present paper used the potential distributions throughout the heart and over the epicardium to directly measure ventricular repolarization. The results of this paper would likely reduce to the same findings at points away from the heart that were first reported in these other studies. In addition, these results provide a direct picture of considerable change throughout the ventricles that occurs in a reproducible and sequential manner as repolarization continues from beginning to end, and these intracardiac distributions can be explained on an intracellular basis.

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