Spread of Excitation During Premature Ventricular Systoles

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Pre-vious reports from this laboratory have evaluated the roles of Purkinje fibers, cardiac muscle bundles and syncytial spread in the activation of the ventricular walls, and have described the pathway of depolarization in the interventricular septum. These observations were made chiefly in the dog and extended to the cat, monkey and goat. Successive points on the lower septal endocardium are excited at a rate of about 1 meter per second, apparently by a wave travelling along the endocardial surface. However, most of the mural endocardium is excited almost simultaneously giving the appearance of a very high velocity. This suggests independent, nearly simultaneous activation of many points by a branched conducting system. The electrical wave spreads through the muscle mass syncytially at about 0.3 meter per second. Under papillary muscles, earliest excitation often appears deep within the myocardium and spreads toward both surfaces. In some parts of the wall, folds and trabeculations near the endocardium complicate the pattern of activity, but through most of the septum and wall the velocity is constant. Most of the septum is invaded from both the left and the right endocardium, i.e., double invasion. Near the basal septum, Purkinje fibers are apparently sparse and a slower endocardial velocity results. The septum is excited preponderantly from the left because activity is earlier on this side, and possibly partly because Purkinje fibers are more extensively distributed on the left.

To test certain hypotheses concerning electric activity in the heart, premature systoles were elicited at known sites in the heart. Intramural potentials so produced were examined and the consequent spread of excitation was plotted. These stimulation experiments gave further information on the spread of excitation as outlined above, the possible penetration of Purkinje fibers into the wall, and the cause of isoelectric periods in intramural ventricular leads when other leads demonstrate that the ventricle is active. It was also possible to derive qualitatively the configuration of lead II records from the pattern of excitation produced when premature systoles were elicited in the coronal plane passing through the apex of the heart.

METHODS

As in former studies, the course of ventricular excitation was recorded with the 16-channel oscilloscope and multipolar electrode. Briefly, the electrode is an assembly of 15 fine wires with uninsulated tips staggered along a central shaft at 1.0 mm. or 0.5 mm. intervals. The oscilloscope includes 16 separate cathode ray tubes with a common sweep.
Ventricular excitation generator. A single master generator feeds 5-msec.
time pips into all channels. The pre-amplifiers used are push-pull and direct-coupled, with an input impedance of 1000 megohms and virtually no capacity to ground. As a result, they exhibit no blocking on stimulation and have an excellent frequency response. A switch permits taking of unipolar (each terminal against an indifferent lead) and bipolar (difference between adjacent terminals) leads.

The experiments were performed in 30 open-chest dogs under barbiturate anesthesia. A record of normal excitation was taken with several electrodes. These were left in place and extrasystoles were evoked by stimulating through one of the electrode terminals. The stimulus was a square wave, 1 or 2 milliseconds in duration, with a frequency of 130 to 190 per minute, which was 5 or 10 beats faster than the prevailing heart rate. The negative pole of the stimulator was led to the terminal at which the beat was to be started. The positive pole was connected to another terminal or to an indifferent point on the body surface such as the left forelimb. Stimulation was barely above threshold (0.25 to 1.0 ma.). Repeated stimulation at a site produced a constant electrocardiographic pattern.

**RESULTS**

Potentials recorded on a multipolar electrode inserted through the apical left ventricular wall.

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**Fig. 1.** Potentials recorded by multipolar electrode inserted through apical left ventricular wall. Channels 1 to 14 recorded from 14 electrode terminals (negative potentials down). Channel 15 recorded fixed time-reference potential, and channel 16, Lead II ECG. Unipolar records of series A show cavity potentials on channels 1 to 3. Channel 4 shows potentials which appear identical with these, although this terminal was barely in muscle. Channel 14 recorded from ventricular surface. Time pips at 5-msec. interval. Bipolar records of series B indicate differences between adjacent unipolar electrodes in sequence (1 minus 2, 2 minus 3, etc.). Bipolar convention gives a downward deflection if the more endocardial terminal is excited first. Unipolar potentials average 46 mV. peak-to-peak.
Fig. 2. Potentials along the same multipolar electrode (recorded as in fig. 1) when premature systole was started between terminals 3 and 4. Stimulus artifact appears on all channels. Conventions as in figure 1. Discussion in text.

Wall are shown in figures 1 and 2. Figure 1 is the record during a normal beat; figure 2, the potentials along the same electrode when a systole was elicited at the endocardial surface, between terminals 3 and 4. The stimulus artifact can be seen on most channels in figure 2. The first three terminals were in the cavity and the 15th terminal, recorded on channel 14 of the bipolar record (this channel recorded differences between terminals 14 and 15), was outside the heart. The time of local activity was measured from the negative maxima of the bipolar records. In both the sinus beat and the premature systole, the endocardium was excited earliest and the wave of electrical activity moved to the epicardium. In the normal beat, marked positive activity preceded depolarization on the unipolar records. This is not seen in the records of the premature systole in figure 2. Channel 15 shows a time reference potential and channel 16, a lead II electrocardiogram in all records.
Figure 3. Premature systoles started along electrode 28 at endocardial (ectopic 1) and epicardial (ectopic 3) surfaces recorded on seven multipolar electrodes through left wall. (Normal excitation along these electrodes was recorded before stimulation, but is not shown here.) Position of electrodes and distances between them indicated on left-hand drawing. Figures indicate time of excitation in milliseconds before or after the time reference. Lead II ECG appears in the right of each excitation pattern.

Figure 3 shows the position of seven multipolar electrodes in the anterior wall of the left ventricle and the three-dimensional temporal pattern of excitation they recorded in two premature systoles. Figures opposite each electrode terminal denote time of local depolarization in milliseconds before or after the arbitrary time reference. In the normal beat, which is not shown, electrode 30 pierced the anterior papillary muscle and recorded excitation proceeding from a central point toward both endocardium and epicardium. Electrode 33, which pierced the base of the muscle, displayed slight reversal of the direction of invasion. Otherwise, excitation proceeded from endocardium to epicardium.

The first premature systole (ectopic 1) was started at the endocardial surface of electrode 28, 35 msec. before the time reference electrode was activated, i.e., −35 msec. The earliest activity recorded was 1 mm. from the site of stimulation at −28 msec., i.e. 7 msec. after the stimulus was delivered. The pattern of excitation along each multipolar electrode insertion except electrode 29 was similar to that found during normal beats, and the total time required for excitation of all terminals along any electrode except 29 was within 3 msec. of the time required in the normal beat. The terminals of electrode 29 were excited over a period of 17.5 msec. in the normal beat, while only 7.5 msec. were required for complete excitation along this electrode during the premature systole. This electrode was angled away from the stimulating electrode so that the terminals at the endocardium were farther from electrode 28 than were those at the epicardium. This contributed to the rapid excitation along the electrode in the premature systole. In general, the multipolar electrodes were activated in the order of their distance from the point of stimulation. The endocardial velocities in the premature systole varied from 0.7 to 1.2 M./sec. and transmural velocities from 0.27 to 0.4 M./sec. As in previous studies, velocities were calculated at right angles to successive positions of the advancing wavefront. This procedure prevents erroneous estimates of velocity.

The second premature systole shown (ectopic 3) was initiated at the epicardial end of electrode 28. The nearest electrode, no. 31, like no. 28, recorded excitation proceeding from epicardium to endocardium. Electrode 29 recorded nearly simultaneous activation along its length, as did electrode 34. In this case we believe these electrodes were activated by a wave traversing the muscle and at the same time moving epicardially from the endocardium. Along electrodes 30, 32, and 33, excitation proceeded, as in the normal beat, from the inside out. Transmural velocities in the premature
systole varied from 0.27 to 0.5 M./sec. in those cases where accurate computation was possible.

During both premature systoles, there was a period after the shock was delivered during which no potential appeared in lead II. Lead II records from the two ectopic beats were not identical.

Figure 4 diagrams successive positions of the activating wavefront at 5 msec. intervals in a normal beat and at 10 msec. intervals in a premature systole evoked at the left apical endocardium. The electrodes were placed in a frontal plane through the apex of the ventricle and are shown in the drawing by lines with points along them to indicate terminals. The solid lines indicating the wavefront are accurately fixed only where they intersect electrodes. During the normal beat, the pattern of excitation in the coronal plane showed very rapid endocardial activation followed by movement within the walls from the inside out. The septum was invaded from both endocardial surfaces.

In the apical endocardial premature systole, activity spread toward the epicardium on the apical stimulating electrode, and from apex to base in most of the heart. The spread was from inside out in the walls, and from left to right in the septum. Where accurate measurements could be made, velocities along the endocardium ranged from 0.5 to 0.9 M./sec., and transmural velocities from 0.3 to 0.45 M./sec.

**DISCUSSION**

The spread of excitation in premature systoles is of interest in itself and for the light it throws on the process of normal activation. The potentials recorded by intramural terminals during premature systoles are useful in evaluating certain assumptions and deductions made from intramural records of normal depolarization. If electrocardiographic records are taken on conventional limb leads when a premature systole is evoked and plotted in the coronal plane through the apex of the heart, they can be qualitatively related to the pattern of excitation recorded on intracardiac electrodes.

*Endocardial velocity.* The velocity of endocardial activation in premature systoles varies with location. The slowest velocity, found near the basal septum, may be as low as 0.3 M./sec. (range 0.3 to 0.6 M./sec.). In the basal walls and apical septum the velocity is higher, usually about 0.6 M./sec. (range 0.5 to 0.8 M./sec.). In most of the apical walls the velocity falls between 0.8 and 1.4 M./sec. (average about 1.1 M./sec.). These measurements represent averages of at least 20 values in each instance, and include correction for the low velocity near the
site of stimulation discussed below. We had previously hypothesized that the extreme rapidity of normal mural endocardial activation results from simultaneous excitation at many points by Purkinje fibers conducting at about 1.0 M./sec. The present findings support this view. The variations in velocity encountered at various intraventricular locations and in individual hearts probably reflect the anatomical distribution of Purkinje tissues.

Transmural velocity. After stimulation, the velocity through the thickness of the wall approximately equals that found during the normal beat (ca. 0.3 M./sec.). When the stimulus is delivered at the endocardial terminal, the velocity from endocardium to epicardium along a multipolar electrode is approximately equal to the velocity in the reverse direction when the epicardial terminal is stimulated. A transmural velocity as low as 0.1 M./sec. is often found for 1 or 2 mm. from the origin of a premature systole and will be discussed below.

Penetration of Purkinje fibers into the wall. We have often recorded potentials from the false tendons within the left ventricular cavity and from portions of the A-V conduction system buried in the interventricular and interauricular septa. In premature systoles, these portions of the conduction system are excited and conduct at the same rate as they do during the normal beat. This rate may be variable, but it is more than 1.0 meter/sec. for the false tendons and the interventricular Purkinje tissue of the right and left bundles. Since the transmural velocity found during premature systoles is almost always below 0.4 M./sec., intramural penetration of Purkinje tissue which conducts at about 1.0 M./sec., although suggested in some anatomical studies, seems unlikely. Where transmural excitation along a multipolar electrode is extremely rapid near the endocardium during a normal beat, the high rate is probably due to extension of the Purkinje tissue under papillary muscles and trabeculations, or to folds in the inner myocardial layers. Such anatomical arrangements can cause points along the same multipolar electrode and at different distances from the cavity terminals to lie equidistant from the Purkinje tissue. If a stimulus is delivered along such an electrode, the velocity between any combination of terminals is less than 0.4 M./sec. Where transmural velocity along an electrode in a premature systole is extremely rapid, the velocity along that electrode in the normal record rarely is abnormally high. The recent finding that most of the wall thickness is simultaneously excited is not substantiated in normal records or in records of premature systoles.

Lewis noted that cutting the epicardium between a stimulating and a recording electrode, both epicardial, did not necessarily alter the time required for conduction between them. He rightly deduced that the impulse travelled to the endocardium, along it, and then epicardially. In so concluding he estimated endocardial and transmural velocities. There are several places where Lewis' deduction can be confirmed in the records of ectopic systoles and the velocities we measure are close to his estimates. Thus our findings regarding the mechanism of ventricular activation agree with and extend those of Lewis.

Slow conduction near the site of stimulation. The slow conduction seen for a few millimeters near the site of stimulation may be related to phenomena noted in nerve bundles where the velocity of transmission in one fiber may be altered by activity in adjacent fibers, or it may be related to slowing of conduction noted at nerve branches. Another possibility is that conduction is faster along the long axes of the cardiac muscle fibers. Unfortunately, no evidence can be brought forward to support the first two of these possibilities. According to the third hypothesis, a wave of excitation initiated at a point travels along fibers (parallel to the surface of the heart) away from the ectopic focus, then reverses at a branch of the syncytium and approaches the point of stimulation, etc. This condition could cause a low initial velocity and a higher velocity with syncytial spread when many fibers were active.

The possibility that fiber orientation can determine a preferred pathway is intuitively appealing and has support in investigations by Pruitt and associates. To test this, we have measured premature systolic velocities in sev-
eral directions with a small circle of multipolar electrodes, but the results have thus far been equivocal. Since increased velocity parallel to the long axes of the fibers is not discernible in normal beats or in experimental premature systoles, the question seems academic. During the normal beat, the endocardium is excited at many points almost simultaneously, so that the whole surface is depolarized within a very short period of time. The impulse can then go in one direction, toward the epicardium. This movement may be the resultant of a number of sub-directions, but viewed by recording terminals at 1 mm. intervals, it is quite constant and syncytial. The origin of the slow conduction near the site of stimulation remains in doubt.

Configuration of unipolar potentials. The unipolar intramural records of premature systoles have a great variety of shapes and durations, and cannot be discussed categorically. However, a significant feature is a frequent lack of positive potentials preceding depolarization in records taken near the origin of a premature systole (fig. 2). This is difficult to explain if one follows a prevalent tendency to interpret records in the light of what would occur in muscle strips. As recognized by Lewis, unipolar intramural leads are affected by both local and distant activity. Wilson developed the necessary theory for the interpretation of potentials in a volume conductor, and this theory must be applied in analyzing such potentials.

The potential at any recording point is a function of the charge density across the boundary between active and resting tissue and of the solid angle subtended at the point by that boundary. When the boundary is small or when the geometric arrangement is such that the recording point is affected equally by positive and negative charges (due to approaching and receding activity respectively), little potential will be recorded. In the normal beat and in some extrasystoles, activity may spread so that a recording point "sees" only a small boundary and, therefore, records no potential from an approaching or receding wave. In such a case as in all others, an understanding of the volume conductor theory will permit a rational explanation of the potentials. The lack of positivity preceding depolarization, seen on some normal intramural records, can thus be understood without recourse to the mystical explanations which have been offered.

The electrocardiogram in ectopic beats. The ultimate aim of the multipolar analysis is an understanding of the electrocardiogram. Premature systoles at times offer the chance to relate electrocardiographic potentials qualitatively to the spread of activity under simplified conditions. Figure 4 shows a premature systole started and plotted in the coronal plane, and the simultaneous lead II record. For the first 30 msec. there was a very slight downward deflection in lead II caused by the progress from endo- to epicardium at the apex. Between 30 and 50 msec., the wavefront in the right wall and septum faced the right, and that in the left wall faced the left. The potentials from this potential configuration are still small but in this case upright. We would expect a small potential at each of the viewing electrodes (right forelimb and left hindlimb) since each of these faces the positive side of part of the boundary and the negative side of another part. The difference between them is likewise small. Later, i.e. after 50 msec., the boundaries in the right wall and septum face the right forelimb, and the boundary in the left wall is parallel to the lead and therefore relatively unimportant. A downward deflection results. Detailed, quantitative analysis of electrocardiographic patterns in the open-chested dog is not justified. However, a quantitative study on the closed-chest animal seems feasible.

**SUMMARY AND CONCLUSIONS**

The procedure of inducing premature systoles and tracing the resultant pathway of excitation has confirmed the hypothesis that the extremely rapid velocity of endocardial activation in the normal beat is the resultant of simultaneous excitation at many points by the Purkinje fibers. In premature systoles, the velocity of transmission through the wall is about 0.3 meter per second as in normal excitation. There is little penetration of the fast-conducting endocardial tissue into the wall except under papillary muscles and possibly under deep trabecu-
lations. The spread of premature systoles shows no clear influence of fiber direction on spread of excitation.

In addition, these experiments have demonstrated a slow conduction velocity near the site of stimulation, have validated certain findings of Lewis regarding the effects of cutting the epicardium, and have furnished an opportunity to correlate the lead II electrocardiogram with the premature systolic pathway of excitation.

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