Mapping of ventricular tachycardia induced by programmed stimulation in canine preparations of myocardial infarction

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ABSTRACT To investigate the mechanism of uniform ventricular tachycardia induced by programmed stimulation, we recorded His bundle electrograms and unipolar electrograms from 64 subepicardial, subendocardial, and intramural sites in dogs. Isochronal maps were generated off-line by computer. Two groups of dogs were studied 3 days after occlusion of their left anterior descending coronary arteries; one group underwent reperfusion after 2 to 2.5 hr of occlusion and the other methylprednisolone treatment before permanent occlusion. In the former, subepicardial sequences presented either a pattern suggesting circus movement or a radial pattern in which excitation at intramural sites could precede earliest subepicardial excitation. In the latter preparations, subepicardial excitation patterns consistently suggested circus movement in the subepicardial muscle layer surviving over necrotic tissue. Assuming complete circus movement, the "missed" time interval, measured as the interval left unaccounted for by actual recording of local excitation between ventricular tachycardia cycles, ranged from 3% to 64% of the cycle length of ventricular tachycardia. While surviving subepicardial and intramural layers appeared to be involved in the mechanism of ventricular tachycardia, a late second breakthrough on the right ventricle, in conjunction with fixed-coupled H deflections on the His bundle electrograms, suggested the involvement of the conducting system in propagation of the impulse.


RECENTLY much attention has been directed to ventricular tachycardia, which can be induced by programmed electrical stimulation of the heart (PES) several days or months after coronary occlusion in dogs, and particularly to sustained ventricular tachycardia with uniform surface lead complexes. The mechanism of these arrhythmias has been investigated with the use of epicardial mapping in several laboratories. Klein et al.¹ found that some episodes of uniform ventricular tachycardia induced by PES had an early right ventricular activation pattern identical to sinus rhythm. They suggested that, in these instances, the impulse might be conducted via the right bundle branch, and that the probable mechanism for this occurrence was reentry in the main bundle branches. They considered as an alternate mechanism the presence of a focus of excitation (either reentrant or triggered) associated with infarcted left ventricular myocardium, which could activate the left bundle branch by retrograde penetration of the distal Purkinje system and then enter and finally emerge from the right bundle branch. This study raised the possibility that the ventricular conducting system and/or subendocardial layers might be involved in the mechanism, or at least in the conduction of, ectopic impulses.

On the other hand, El-Sherif et al.² ³ emphasized the role of subepicardial muscle in the mechanism of uniform ventricular tachycardia induced by PES in the late phase after coronary occlusion in dogs. They showed by epicardial and transmural mapping that uniform ventricular tachycardia was associated with reentry in a subepicardial layer surviving over infarcted myocardium.

However, ventricular tachycardia induced by PES rarely displays a uniform pattern and its duration rarely exceeds 10 beats after permanent coronary occlusion
without additional intervention. Several investigators have sought interventions to increase the incidence and prolong the duration of uniform ventricular tachycardia induced by PES in infarcted canine hearts. The incidence of inducible sustained ventricular tachycardia with uniform complexes has been reported to be higher in reperfused infarct preparations or after permanent occlusion with methylprednisolone pretreatment than after permanent occlusion.

In the reperfused infarct preparation there is extensive survival of intramural muscle strands; compared with those of permanent occlusion, the morphologic characteristics of infarction are more inhomogeneous and complex. Reperfusion within 6 hr of coronary occlusion has been shown in dogs to salvage myocardium. The proponents of this preparation suggest that this salvaged myocardium might be arrhythmogenic, perhaps providing reentrant pathways, and thereby lending greater stability to the ventricular tachycardia, which would then be of a uniform pattern and last for several minutes. Accordingly, Wit et al. found that the protracted ventricular tachycardia with uniform complexes that they induced in reperfused infarct preparations could not be accounted for by reentry at the subepicardial level and appeared to involve intramural and perhaps subendocardial layers.

Administration of corticosteroids has also been reported to salvage myocardium after coronary occlusion in dogs. On the other hand, Guse et al. found that, compared with a preparation of permanent occlusion without intervention, methylprednisolone treatment produced transmural extension of necrosis toward the epicardium and that this effect might be important to sustain ventricular tachycardia.

Thus, the participation of subepicardial, subendocardial, and intramural layers, as well as the possible involvement of the ventricular conducting system in uniform ventricular tachycardia induced by PES, are unclear. We therefore investigated these issues with the use of His bundle recording and mapping of excitation in two modified preparations of infarcted myocardium in which the incidence of uniform ventricular tachycardia has been reported to be increased, namely: (1) a reperfused infarct preparation, and (2) a preparation of permanent occlusion pretreated with methylprednisolone.

Methods

Seventy-one dogs were anesthetized with sodium pentothal (25 mg/kg iv, followed by infusion of 8 mg/kg/hr). By a sterile technique the heart of each was exposed through a left thoracotomy at the fourth intercostal space; the pericardium was incised. The left anterior descending coronary artery (LAD) was occluded about 1 cm from its origin by a two-stage Harris procedure. Occlusion at this level was usually proximal to any large diagonal branch; whenever a large branch originated within 1 cm of the origin of the LAD or ran down from the circumflex artery to the anterior portion of the heart, it was occluded to ensure extensive anterior ischemia. Lead II of the electrocardiogram (ECG) was monitored throughout surgery and for several hours thereafter. Seven dogs had ventricular fibrillation within 15 min of total occlusion and died. In 43 dogs the ligature was released 2 to 2.5 hr after complete occlusion and arterial blood flow was restored distal to the site of occlusion (reperfused infarct preparation). In 21 dogs 30 mg/kg iv methylprednisolone was administered before permanent occlusion (preparation of permanent occlusion with methylprednisolone treatment). The pericardium and chest were then closed and postoperative care was given, including the administration of analgesic (Innovar, 1 ml im) and antibiotic (penicillin G, 2 million IU, infused intravenously in 1000 ml of saline over 10 hr). Five dogs in the reperfused infarct group and three with permanent occlusion and methylprednisolone treatment died suddenly from 12 to 72 hr after occlusion.

Three to four days later, the 56 surviving dogs were anesthetized with sodium pentothal (15 mg/kg iv). ECG leads I and III or aVF were recorded. A bipolar electrode catheter with an interelectrode distance of 1 cm was positioned through a femoral vein at the atroventricular junction to record a His bundle electrogram (lower and upper filter settings of 30 or 100 and 500 Hz, respectively). Observations and measurements of intervals on the His bundle electrogram are only reported for experiments in which a stable His bundle deflection was continuously recorded in sinus beats before induction and after termination of ventricular tachycardia. A bipolar electrogram was recorded in the right or left atrium. Wire electrodes were plunged across the left paraseptal free wall to record electrograms from the endocardial surface neighboring infarcted myocardium. Signals were monitored on an Electronics for Medicine VR-6 and a Beckman R411 dynograph paper recorder and stored on magnetic tape by means of a Hewlett-Packard instrumentation recorder; selected portions were reproduced with the use of an Electronics for Medicine VR-12 optical recorder at a paper speed of 100 mm/sec to measure intervals.

The animals were subjected to programmed electrical stimulation of the heart through epicardial bipolar electrodes that had been sutured during surgery at five sites: at the base of the right and left ventricles, anteriorly over the septum, on the left ventricular free wall, and at the apex. The latter three sites were usually located at the periphery of the infarcted region, where stimulation has been reported by Michelson et al. to be most effective for induction of ventricular tachycardia. Driving stimuli (S₃) and from one to three extrastimuli (S₁, S₂, and S₃) were applied to these sites. The stimuli were constant-current pulses of 1 msec duration and three times threshold intensity (BM-SCP programmable stimulator; Institut de Génie Biomédical, Ecole Polytechnique de Montréal). A run of 10 driving stimuli was applied after 12 sinus beats at a cycle length 50 msec shorter than the sinus cycle length and S₂ was applied at a progressively shorter coupling interval in 5 msec decrements until 220 msec, and in 2 msec decrements thereafter. The stimulus was shut off when sustained tachycardia was initiated. If S₁ failed to initiate ventricular tachycardia, it was set at a coupling interval 20 msec above the refractory period and S₂ was applied at a decreasing coupling interval; the protocol was similar with regard to S₃. Ventricular tachycardia was defined as a run of at least 3 unstimulated beats.

A sock electrode containing 64 evenly spaced unipolar recording contacts was used to map the global epicardial activation sequence (see Results and figure 3) during sinus rhythm and...
uniform ventricular tachycardia, when it could be induced, in 20 preparations. Thirteen of these had been subjected to permanent occlusion with methylprednisolone pretreatment and the seven others to coronary occlusion for 2.5 hr. A data acquisition system capable of simultaneously recording 64 channels on magnetic tape was used (Institut de Génie Biomédical, École Polytechnique de Montréal). The signals were amplified by programmable-gain amplifiers, multiplexed, sampled at 500 Hz, and converted to a 10-bit digital format. Data processing was done off-line on a PDP11/34 computer. Each electrogram from a selected time window was displayed on an oscilloscope. Excitation times that were automatically detected by the program were indicated by vertical cursors, and the operator normally edited the detections by moving the cursors on the basis of the interpretation by Durrer et al.16 of unipolar electrograms recorded in canine hearts infarcted over a long term. Local excitation time was detected as the point of most rapid change in potential. Most excitations corresponded to a slope in excess of $-1.0$ mV/msec. However, the minimum threshold for detection was set at $-0.5$ mV/msec after it was established in several experiments that organized propagation of wavefronts was still observable for electrograms showing this low rate of change. Isochornal maps were then printed for selected cycles of ventricular activation beginning with the earliest excitation detected by our electrode array.

In four preparations subjected to permanent occlusion with methylprednisolone treatment, 32 wire electrodes of the type described by Scherlag et al.17 were plunged into the left paraseptal and ventricular free walls under each of the 32 epicardial recording sites on the anterior surface of the heart (see Results and figure 5). In three permanent occlusion preparations and four reperfused infarct preparations, 16 wire electrodes with recording ends at the 0 (epicardial), 4, 8, and 12 mm levels were plunged into the wall in a $4 \times 4$ electrode array (see figures 7 and 9). These were basically Scherlag-type electrodes, with three straight recording ends in addition to the endocardial hook (12 mm). Any desired distance could be maintained between the recording ends by twisting the wires a few centimeters away from the needle. This method enabled us to do transmural recordings at four levels. At the subendocardial level, excitation of muscle fibers, but not Purkinje fibers, could be detected on unipolar electrograms, which were recorded at a sampling rate of 500 Hz.18

In 22 experiments, the heart was excited after electrophysiologic study and cut into 5 mm thick slices that were incubated at 37°C for 45 min in a buffered triphenyltetrazolium chloride (TTC) solution. This oxidation-reduction indicator produces a bright red coloration of tissue with normal dehydrogenase activity.19 Stimulating and recording electrodes were localized with regard to infarcted myocardium, which was identified as the negative TTC stain area. Each slice was drawn on a clear plastic sheet with indications for infarcted and noninfarcted areas. These areas were measured by planimetry; the area of necrosis was expressed as a percent fraction of the total left ventricular myocardium.

Statistics for areas of necrosis and timing intervals were expressed as mean $\pm$ SD and were compared by Student’s t test for unpaired data. The number of beats in each episode of ventricular tachycardia were counted; statistics for the duration of ventricular tachycardia were expressed as the median value, defined as the duration of that episode of ventricular tachycardia for which there were equal numbers of episodes of ventricular tachycardia with lower and higher numbers of beats.

All procedures for animal care and experimentation were done in accordance with the guidelines of the Canadian Council for Animal Care and monitored by an institutional animal care committee.

Results

Inducibility of ventricular tachycardia in the reperfused infarct preparation and the preparation of permanent occlusion with methylprednisolone treatment. Ventricular tachycardia with multiform beat-to-beat morphologic characteristics, ventricular tachycardia with uniform beat-to-beat morphologic characteristics, and ventricular fibrillation were induced by PES in our preparations. Multiform ventricular tachycardia lasted for up to 40 beats (median 8). Uniform ventricular tachycardia lasted for from 5 to 300 beats (median 170) before terminating spontaneously or by application of two closely coupled stimuli. In a total of 38 reperfused infarct preparations that were subjected to PES, ventricular tachycardia and/or ventricular fibrillation could be induced in 28. Of these 28 preparations, multiform ventricular tachycardia could be induced in 27 (96%), uniform ventricular tachycardia in eight (29%), and ventricular fibrillation in 19 (68%). In a total of 18 preparations of permanent occlusion and methylprednisolone treatment that were subjected to PES, ventricular tachycardia and/or ventricular fibrillation could be induced in 17: multiform ventricular tachycardia could be induced in all 17 (100%), uniform ventricular tachycardia in 10 (59%), and ventricular fibrillation in 12 (71%).

In a group of 12 reperfused infarct preparations in which necrotic areas were measured necrosis encompassed $13.2 \pm 5.5\%$ (mean $\pm$ SD) of the left ventricular mass, compared with $20.1 \pm 7.5\%$ in a group of 10 preparations of permanent occlusion and methylprednisolone treatment; this difference was statistically significant ($p < .05$). Transmural extension of necrosis toward the epicardium was less in the former than in the latter (see below). Within this permanent occlusion group, areas of necrosis were not significantly different in the six preparations in which uniform ventricular tachycardia could be induced ($21.4 \pm 8.9\%$) than in the four preparations in which it could not be ($18.2 \pm 5.3\%$). The two preparations of this reperfused infarct group in which uniform ventricular tachycardia could be induced had $22.4\%$ and $12.0\%$ necrosis, respectively.

Role of the ventricular conducting system and surviving subepicardial and subendocardial muscle layers in uniform ventricular tachycardia. In most episodes of multiform and uniform ventricular tachycardia, the atrial electrogram indicated atrioventricular dissociation; there was retrograde atrioventricular conduction during uniform ventricular tachycardia in three dogs. His bundle deflections were difficult to detect and occurred inconsistently during multiform ventricular tachycardia. How-
ever, they had a fixed coupling to ventricular complexes in many episodes of uniform ventricular tachycardia, as shown in figure 1.

Figure 1, A, illustrates the failure to induce ventricular complexes and resumption of sinus rhythm after three closely coupled premature impulses; B and C illustrate the uniform ventricular tachycardia that was induced after a slight reduction in coupling interval of the last extrastimulus. During ventricular tachycardia His bundle (H) deflections were clearly detectable: they were inscribed 15 msec later than the onset of surface lead complexes (QH interval) and preceded V deflections of the His bundle electrogram by 25 msec; HV intervals on the His bundle electrogram were similar during ventricular tachycardia and sinus rhythm. In fusion beats (figure 1, C), H deflections were coincident with or slightly preceded the onset of surface lead complexes.

In figure 1, A, there is no late H deflection after the third premature impulse, which was initiated at a coupling interval only slightly greater than that required for induction of ventricular tachycardia in B. In this series of experiments we did not observe delayed retrograde activation of the His bundle or bundle branches, which has been shown in patients to result in bundle branch reentry.20

Table 1 lists the mean frontal plane axes, cycle lengths, durations of surface lead complexes, and timing of deflections on the His bundle electrogram during sinus rhythm and uniform ventricular tachycardia in nine dogs. During ventricular tachycardia timing of deflections on the His bundle electrogram was ex-

![Figure 1](https://circ.ahajournals.org/)

**FIGURE 1.** Fixed-coupled His bundle activation during uniform ventricular tachycardia. In each panel, traces are from top to bottom, surface leads I and III, His bundle (HBeg), and right atrial (Aeg) electrograms. H deflections of HBeg are indicated by arrows. A. Resumption of sinus rhythm after application of three extrastimuli at coupling intervals of 160 msec. AH and HV intervals were 60 and 25 msec, respectively, during sinus rhythm. Note the absence of delayed H deflection in response to premature stimuli. B. Induction of uniform ventricular tachycardia at a slightly shorter coupling interval. H deflections preceded V deflections by 25 msec. C. Vertical broken lines indicate the onset of surface lead complexes for a fusion (F) and a ventricular beat. H was inscribed 15 msec after the onset of ventricular complexes (QH, 15 msec) and at the onset of F complexes. Duration of surface lead complexes was 80 msec during ventricular tachycardia compared with 50 msec during sinus rhythm. Calibrations are shown in the upper right-hand corner.

**TABLE 1**

<table>
<thead>
<tr>
<th>Characteristics of surface lead complexes and His bundle electrograms during sinus rhythm (SR) and ventricular tachycardia (VT) with uniform complexes</th>
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<tbody>
<tr>
<td>Preparation No. and type</td>
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<tr>
<td>Sinus rhythm</td>
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<td>9 PO</td>
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OR = preparations of temporary occlusion and reperfusion; PO = preparation of permanent occlusion and methylprednisolone pretreatment; AQRS = frontal plane electrical axis of surface lead complexes; duration = duration of QRS complexes; A and B = two distinct patterns of uniform VT.
pressed relative to the onset of surface lead complexes (Q). Several episodes of uniform ventricular tachycardia with a constant pattern could be induced in dogs 1 to 6, and tachycardias of two patterns were seen in dogs 7 to 9. During sinus rhythm frontal plane axes and all intervals were within the normal range for dogs. During uniform ventricular tachycardia there was atrioventricular dissociation and no timing of A deflections could be determined. As shown in figure 1, B and C, H deflections were clearly detectable in nine of a total of 12 ventricular tachycardia patterns; the deflections were inscribed from 0 to 30 msec after the onset of surface lead complexes and preceded V deflections by HV intervals similar to those during sinus rhythm. In the three other patterns V deflections were inscribed at the onset of surface lead complexes and H deflections could not be detected.

Figure 2, A, shows that subendocardial excitation in the left anterior paraseptal area occurred at the very onset or slightly preceding surface lead complexes during uniform ventricular tachycardia; this area was in the vicinity of infarcted myocardium. During ventricular tachycardia, subendocardial activation preceded H deflections by 20 msec, while in sinus beats this sequence was reversed (figure 2, C). In fusion beats inscription of H and subendocardial excitation were coincident (figure 2, B).

The upper tracing in figure 3 shows a spontaneous change in the morphologic characteristics of electrically induced ventricular tachycardias from one in which H deflections of the His bundle electrogram were detectable (VT1) to one in which they no longer were (VT2). In VT1 H deflections were inscribed 20 msec after the onset of surface lead complexes and preceded V deflections by 15 msec. In VT2 V deflections were inscribed earlier. Figure 3, A, shows the distribution of epicardial recording sites from which maps of activation isochrones were made for a sinus complex (figure 3, B) and complexes of each pattern of ventricular tachycardia (panel C, VT1; panel D, VT2). Histochemo-chemical staining in the region of infarction (shaded area) showed a subepicardial layer of myocardium surviving over necrotic tissue in this preparation of permanent occlusion and methylprednisolone treatment (see below). During sinus rhythm left epicardial breakthrough occurred in several areas at the periphery of the surviving subepicardial layer and the impulse was slowly conducted to its center. Epicardial breakthrough on the right ventricle occurred over a broad area on its anterior surface. The posterior surface was rapidly activated.

During VT1 earliest epicardial breakthrough occurred in a small area within the surviving subepicardial layer; the impulse then spread toward the left ventricular apex, broke up into two wavefronts that circulated back around the area of initial activation (curved arrows), and propagated into normal regions. Epicardial breakthrough on the right ventricle took place 88 msec later, at the same location as during sinus rhythm, although over a smaller area; activation isochrones spread concentrically from this area, and the corresponding impulse collided over the septum with the earlier impulse spreading from the left ventricle. Thus, the septum appeared to be activated by double envelopment from the right and left sides.

During VT2 earliest epicardial breakthrough took place in the same area, with a later breakthrough at the left ventricular apex. However, the pattern of excitation in the surviving subepicardial layer was similar to that in VT1. In contrast, there was no second break-

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**FIGURE 2.** Early subendocardial activation during uniform ventricular tachycardia. In each panel, traces are from top to bottom, surface leads I and III, the His bundle electrog-ram (HBeg), and a subendocardial electrogram that was recorded in the left anterior paraseptal area (ENDO). Arrows in HBeg indicate His bundle (H) deflections. Arrows point to fast downstrokes in the END0 electrogram, indicating local excitation; this unipolar electrogram displayed noise during its QS complex. The vertical broken lines indicate the onset of selected surface lead complexes. A, Induction of uniform ventricular tachycardia in the same preparation as in figure 1. Subendocardial excitation occurred at the onset of VT complexes and preceded H by 20 msec. B, In fusion (F) beats, subendo-}

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**CIRCULATION**
FIGURE 3. Patterns of subepicardial excitation during electrically induced uniform ventricular tachycardia (VT) with a spontaneous change in pattern. Top, Surface leads I and aVF and atrial (Aeg) and His bundle (HBeg) electrograms during VT and sinus rhythm (NSR). Atrial (A), His bundle (H, arrow), and ventricular (V) deflections of HBeg are indicated. A, The entire epicardial surface, which is depicted as if the ventricles were folded out into their anterior and posterior halves (left and right, respectively) after an imaginary cut was made through the free wall of the right ventricle (lateral edges), and through the apex partially up the interapillary free wall of the left ventricle (middle cut). The left anterior descending coronary artery (LAD) was occluded below the most proximal of three large diagonal branches. Each point indicates the position of a recording electrode. The infarcted region (shaded area) extended over the anterior portion of the septum and left ventricle and a small portion of its posterior surface. B, C, and D, Activation maps during NSR (10 msec spacing between isochrones), and tachycardiac complexes with the first (VT1) and second (VT2) pattern (20 msec spacing between isochrones). In both patterns of VT earliest epicardial breakthrough occurred within the surviving subepicardial layer, with impulses circulating on its anterior and lateral sides (curved arrows) and back to the area of initial excitation (large arrowhead) if circus movement is postulated. In VT1, activity broke through over the right ventricle in the same area as in NSR, 88 msec later than earliest epicardial breakthrough. In VT2, activity broke through in two areas on the left ventricle, but not on the right ventricle. H deflections of the HBeg could be detected in VT1, but not in VT2. Vertical calibrations in the upper right-hand corner of the surface lead ECG are 0.5 and 1mV for leads I and aVF, respectively.

through over the right ventricle. This change in the overall epicardial activation pattern, together with the fact that H deflections were no longer detectable and no longer preceded V deflections of the His bundle electrogram in VT2, suggested to us that the change in pattern of ventricular tachycardia from VT1 to VT2 might be associated with an interruption of the possible participation of the conducting system in propagation of the impulse from the left to the right ventricle. The broadening of surface lead complexes in VT2 compared with VT1 could not be accounted for by a prolongation of overall epicardial activation time, but it could have been associated with cancellation of electrical forces when the impulse broke through on both ventricles (VT1), compared with one only (VT2).

Figure 4 illustrates selected epicardial electrograms during the type of ventricular tachycardia depicted in figure 3. During normal sinus rhythm sites of earliest breakthrough were located anteriorly in normal regions of the left ventricle (site 1) and in the right ventricle (site 7); unipolar electrograms at these sites displayed rS patterns. Unipolar electrograms recorded from sites 2 to 5 were typical for subepicardial layers surviving over necrotic tissue in chronic infarction: a QS form with "embryonic r wave" (site 2), a QR form (sites 3 and 5), an RS complex delayed beyond the
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**FIGURE 4.** Selected epicardial electrograms during normal sinus rhythm (NSR) and each of the two patterns of ventricular tachycardia (VT) shown in figure 3. The uppermost diagram indicates the sites at which the displayed unipolar electrograms were recorded (see figure 3 for description of diagram; the infarcted region is surrounded by a broken line). The vertical dotted line indicates the onset of the single beat shown for NSR and the onset of the second of two tachycardiac cycles, which are shown for VT1 and VT2. Local excitation is indicated by an arrowhead. Sites displaying latest excitation during NSR (4 and 5) were activated earliest during VT1 and VT2. In each tachycardiac cycle, electrogram 5 displayed an early (full arrowhead) and a late deflection (open arrowhead) with suprathreshold slopes for excitation. The sequence of excitation appeared to progress from sites 4 and 5 (early deflection), to 3, 2, 5 (late deflection), and back to 5 (early deflection) and 4. The missed time interval left unaccounted for by actual recording of local excitation was 70 msec.

initial QS complex (site 4). These different patterns were associated with increasingly delayed subepicardial excitation. Recording of a simple QS waveform was taken as an indication that local excitation failed to occur at the recording site.

During VT1 and VT2 earliest subepicardial excitation occurred at sites at which it had been late during normal sinus rhythm (sites 4 and 5). Conversely, sites 1 and 7 were activated later, with excitation at site 7 taking place earlier in VT1 than in VT2. During ventricular tachycardia activity appeared to progress from sites 4 and 5 (early deflection), to sites 3 and 2, and back to site 5 (late deflection); 70 msec later there was inscription of the early deflection at site 5, reactivation at site 4, and repetition of this cycle. If circus movement excitation were postulated as the mechanism of ventricular tachycardia from this sequence of excitation, a “missed” time interval of 70 msec between the end of a cycle of ventricular tachycardia and the beginning of the next would be left unaccounted for by actual recording of local excitation. The clumping of isochrones that is seen above the area of initial excitation in figure 3, C and D, would then represent slow conduction in the direction indicated by the large arrowhead.

Table 2 shows that patterns of subepicardial excitation suggesting circus movement excitation could be mapped during uniform ventricular tachycardia of all patterns induced by programmed stimulation in preparations of permanent occlusion with methylprednisolone treatment. Uniform ventricular tachycardia with each pattern could usually be induced several times by repetition of the same stimulation protocol or application of a different one in a given preparation. The pattern of excitation was constant from one episode of VT to the other with the same morphologic characteristics. The circus movement pattern consisted of double circulating wavefronts, as in figure 3, or of a single

**TABLE 2**

<table>
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<tr>
<th>Characteristic of excitation patterns during uniform ventricular tachycardia (VT) in preparations of permanent occlusion with methylprednisolone treatment and reperfused infarct</th>
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<tr>
<td>Pattern*</td>
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<tr>
<td>Permanent occlusion with methylprednisolone treatment</td>
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*Pattern refers to the sequence of activation isochrones displaying double circus movement (Dbl. circ.), a single circus movement (Sgl. circ.), or a radial pattern spreading away from an area of excitation.

Missed interval is expressed as percentage of VT cycle.

Diameter of block refers to that around which impulses are circulating, expressed in terms of number of interelectrode distances (about 5 mm).
circulating wavefront (see below, figure 8). In four distinct patterns of uniform ventricular tachycardia that we induced and mapped in reperfused infarct preparations, two displayed circus movement patterns, and the two others displayed patterns with radial spreading away from an area of earliest breakthrough (see below, figure 9). Assuming complete circus movement, the missed time interval that could not be accounted for by actual recording of local activity ranged from 3% to 64% of the ventricular tachycardia cycle. The diameter of areas of block around which the wavefronts circulated measured one or two interelectrode distances, i.e., 5 to 10 mm.

To investigate whether the excitation wave originated closer to subepicardial or subendocardial layers, we simultaneously mapped activation at 32 epicardial sites and corresponding subendocardial sites on the anterior surface of the ventricles. Figure 5 shows the activation pattern during another episode of ventricular tachycardia induced by programmed stimulation in the same experiment as in figures 3 and 4. During sinus rhythm earliest activation occurred subendocardially in the septal area; the entire subendocardial surface was activated within 20 msec, along with normal subepicardial areas; excitation progressed slowly toward the center of the surviving subepicardial layer. During ventricular tachycardia earliest excitation occurred subepicardially within this layer and spread slowly in a circular pattern toward normal areas. Activity broke through at the subendocardial level 74 msec later. In the last beat of ventricular tachycardia (figure 5, D) the excitation pattern within the surviving subepicardial layer was different and was more radial.

Figure 6 shows the surface-lead ECG and selected unipolar electrograms of the ventricular tachycardia shown in figure 5. As in figure 2, subendocardial excitation in the left paraseptal area took place at the very onset of surface-lead complexes during ventricular tachycardia. However, figure 5 shows that this activity represented breakthrough at the subendocardial level.

**FIGURE 5.** Epicardial and endocardial activation maps during electrically induced ventricular tachycardia. Top. Surface leads I and aVF and atrial (Aeg) and His bundle (HBeg) electrograms during the last 4 beats of ventricular tachycardia induced by three premature extrastimuli, and resumption of normal sinus rhythm (NSR). The first 3 beats of ventricular tachycardia in the tracing have a uniform pattern; in the fourth, an H deflection precedes the V deflection in HBeg. A. Anterior epicardial surface of the ventricles and the corresponding endocardial surface. Each dot indicates the position of a recording electrode; wire electrodes were plunged into the wall under each of the 32 epicardial recording sites. B. C. and D. Activation maps during sinus rhythm (B, over lead I; 10 msec spacing between isochrones), and two ventricular tachycardia complexes (C and D, over lead I; 21 msec spacing between isochrones). During sinus rhythm earliest excitation took place subendocardially in the septal area; during ventricular tachycardia, it occurred subepicardially within the surviving subepicardial layer. In the 3 beats of ventricular tachycardia with a uniform pattern, the pattern of subepicardial excitation (panel C) displayed an arcing movement of excitation (indicated by arrows) around an area of block. Vertical calibrations in the upper right-hand corner of the surface lead ECG are 1 mV.
of a sequence of subepicardial activity. In three other preparations of permanent occlusion and methylprednisolone treatment in which subepicardial and subendocardial excitation was mapped in this fashion, endocardial breakthrough followed earliest subepicardial excitation by 40, 42, and 20 msec, respectively. Earliest subepicardial excitation was always located anteriorly in layers overlying necrotic myocardium.

Role of intramural muscle layers in the methylprednisolone-treated permanent occlusion and reperfused infarct preparations. Figure 7 shows the general morphologic features and multiple intramural recording of electrical activity in a preparation of permanent occlusion and methylprednisolone treatment. Histochemical staining showed that necrosis encompassed 24% of the left ventricular mass and extended over two-thirds to the entire ventricular wall thickness. Accordingly, intramural recordings at the 4 and 8 mm levels into the wall (as well as at 12 mm, which is not shown) displayed QS patterns reflecting the endocavitary potential, without indication of local activity. At the subepicardial level, site A displayed an rs complex that followed the QS potential in sinus rhythm and preceded it during ventricular tachycardia. Site B displayed narrow rS complexes during normal sinus rhythm and ventricular tachycardia, and site C a low amplitude rs complex during ventricular tachycardia only. Thus, both morphologic examination and electrical recording indicated the presence, over necrotic tissue, of surviving myocardium that generated electrical activity.

Figure 8 illustrates the maps of activation isochrones and subepicardial electrograms recorded at sites A, B, and C during the same episode of ventricular tachycardia (VT1) and during ventricular tachycardia of a different pattern (VT2) in the same preparation. Missed time intervals made up 50% and 64% of the cycles of ventricular tachycardia, respectively. The changes in morphologic characteristics of the surface lead were associated with a change in the sequence of excitation in the subepicardial layer (dark and clear arrows) from counterclockwise in VT1 to clockwise in VT2.

![Diagram](http://circ.ahajournals.org/Downloaded_from http://circ.ahajournals.org/ by guest on April 22, 2017)
FIGURE 8. Excitation patterns within the surviving subepicardial muscle layer in two patterns of ventricular tachycardia (VT1 and VT2) induced in the same MP-treated permanent occlusion preparation. Top. Diagrams show the patterns of subepicardial excitation in the anterior surface of the heart, with 15 msec interval between isochrones. Dark arrows indicate the direction of the circular movement of excitation in areas in which a full sequence of local activity could be recorded. Clear arrows indicate the spread of activity, which is estimated in areas in which local activity could not actually be recorded, assuming complete circular movement. The conduction time corresponding to the clear arrow is expressed as the missed time interval, which measured 135 and 180 msec in VT1 and VT2, respectively. Traces from top to bottom are surface lead aVF, and subepicardial electrograms recorded at sites A, B, and C. Distinct morphologic characteristics of the surface leads are related to a counterclockwise (VT1) or clockwise (VT2) sequence of excitation within the surviving subepicardial layer.

Whereas a surviving subepicardial layer was the prevalent morphologic characteristic in the permanent occlusion preparations, the pattern was more complex in reperfused infarcts. Figure 9 illustrates results of a correlative examination of electrophysiologic-morphologic data from a reperfused infarct preparation. Necrosis made up 12% of the left ventricular mass and the maximum extension of the necrosis was three-fourths of the way into the ventricular wall thickness in an apical slice (upper slice). In the other slices necrosis was of a more subendocardial location and spotty; islands of necrosis surrounded by viable myocardium were seen (lower slice). In contrast to in the permanent occlusion preparations, in reperfused infarct preparations several intramural recording sites displayed low-amplitude rs complexes. This local activity followed QS complexes in sinus rhythm and preceded them during ventricular tachycardia. The subepicardial pattern of excitation during ventricular tachycardia was radial, with earliest activity taking place concomitantly at epicardial and intramural recording sites. In another reperfused infarct preparation that displayed a radial pattern of excitation during uniform ventricular tachycardia, earliest excitation took place at intramural recording sites and preceded excitation of overlying subepicardial sites by 20 msec.

Discussion

Role of the ventricular conducting system in uniform ventricular tachycardia. Experimental studies dating back to those of Lewis and Durrer and van der Tweel have indicated that subendocardial Purkinje fibers might be involved in conducting excitation waves that were electrically initiated at ventricular epicardial sites. The possibility that the His-Purkinje system might be involved in conducting ectopic ventricular impulses induced in canine hearts infarcted over a long term was raised by Klein et al. in the case of uniform ventricular tachycardia with an early right ventricular activation pattern identical to sinus rhythm. They suggested that the impulse was conducted via the right bundle branch and that its mechanism might be bundle branch reentry, rather than a focus (either reentrant or triggered) associated with infarcted left ventricular

FIGURE 9. Results of transmural histochemical staining and recording in the reperfused infarct preparation. Same layout as in figure 7, with intramural recording at an additional level (12 mm into the wall). A map of epicardial excitation during ventricular tachycardia (lower right) is also included. The pattern of subepicardial excitation was radial, and earliest subepicardial excitation occurred concomitantly with excitation at some intramural sites.
myocardium. They favored the former mechanism because they did not observe an early breakthrough in the infarcted region, an occurrence that would be expected with the latter. We observed early subepicardial excitation over infarcted left ventricular myocardium, as well as later breakthrough on right ventricular epicardium, in conjunction with fixed-coupled H deflections of the His bundle electrogram (figure 3). Our detection of early breakthrough in the peri-infarction region is probably attributable to the fact that we recorded simultaneously from 64 epicardial sites instead of using the 26-lead technique used by Klein et al.

Thus, our data support the view that the ventricular conducting system may be involved in the conduction of the impulse from its origin in the infarcted left ventricle to the right ventricle, but not directly in the mechanism of ventricular tachycardia induced by PES. In fact, the interval between the onset of surface lead complexes and His bundle activation (QH) could be as large as 33 msec during uniform ventricular tachycardia with detectable and fixed-coupled H deflections. This conclusion is further supported by our observation that ventricular tachycardia continued when H deflections and the secondary breakthrough on the right ventricle were no longer detected; thus propagation via the conducting system appeared to fail (figure 3). Even so, the occurrence of a second breakthrough at the left ventricular apex (figure 3, D) suggested that Purkinje fibers could still be involved in conducting the impulse, but at a more regional level. Smith et al. suggested that Purkinje tissue might be involved in the propagation of impulses initiated by pacing at endocardial septal locations when the initial areas of subepicardial excitation were large and/or when multiple epicardial breakthroughs were seen.

At an early stage in our study, before epicardial mapping was begun, the occurrence of subendocardial excitation at, or slightly before, the onset of surface lead complexes during ventricular tachycardia suggested to us that tachycardiac impulses might originate distally within the left ventricular conducting system or just beyond its termination in muscle. However, early subendocardial excitation appeared to be the subendocardial breakthrough of wavefronts originating from subepicardial layers, at least in preparation of permanent occlusion with methylprednisolone treatment (see below). Thus, proximity of subendocardial local activity to onset of QRS was not an indication of the site of origin of electrically induced ventricular tachycardia in our studies, unlike in the case of spontaneous ventricular rhythms 12 to 48 hr after coronary occlusion, in which enhanced automaticity in suben-
docardial Purkinje fibers and focal activity in small subendocardial regions play a role.

Role of surviving muscle and morphologic characteristics of the infarct in uniform ventricular tachycardia. The inducibility of uniform ventricular tachycardia was much higher in our preparations of permanent occlusion and methylprednisolone treatment than in our reperfused infarct preparations. By visual examination of slices and use of our simple histochemical staining technique, we found that necrosis made up a significantly greater portion of the left ventricular mass and had a greater transmural extension toward the epicardium in the former than in the latter preparation. However, the volume of necrosis did not appear to be the sole determinant of inducibility of ventricular tachycardia; for instance, there was no significant difference between the subgroup in which uniform ventricular tachycardia had been induced and that in which it had not been within our group of preparations of permanent occlusion and methylprednisolone treatment.

In methylprednisolone-treated permanent occlusion preparations we found, by morphologic examination and transmural recording, that at least two-thirds of the ventricular wall thickness was necrotic. We mapped patterns of excitation that suggested circus movement within the subepicardial muscle layer surviving over necrotic tissue in these preparations. In theory, succession of cycles during reentrant uniform ventricular tachycardia is a continuous process because of the presence of continuous electrical activity in the circuit. With the limitations of a 64-channel recording technique, it was often possible to map only part of the circuit as an arc of slow activity in the periphery of the surviving subepicardial muscle layer. Whenever a virtually complete circuit could be mapped (down to 6 msec between successive cycles of ventricular tachycardia, i.e., 3% of the cycle length of ventricular tachycardia), this bridging activity was found in the center of the depressed region and appeared to be localized along tenuous tracts. Inasmuch as the circus movement could only be partially mapped, there was between ventricular tachycardia cycles a "missed" time interval in the sequence of activity that should have been, in theory, continuous. This missed time interval, which was left unaccounted for by actual recording of activity, measured from 3% up to 64% of the entire tachycardiac cycle. We cannot exclude that this missed activity could have involved intramural or subendocardial tracts which would not have been detected by our 64-channel recording system and our simple morphologic examinations. If the postulated mechanism is the right one, the duration of these
missed time intervals should be consistently reduced by increasing the number of recording electrodes in critical areas.

Thus, the mechanism of uniform ventricular tachycardia in our methylprednisolone-pretreated preparations could be similar to that described by El-Sherif et al.\(^2,3\) in the permanent occlusion preparation without pretreatment. Although we did not use a nontreated control group, comparison between their data and ours suggests that methylprednisolone pretreatment increases the incidence of inducible ventricular tachycardia perhaps without changing the essential features of its mechanism. Guse et al.\(^3\) reported that methylprednisolone treatment produced transmural extension of necrosis toward the epicardium. The same group of investigators reported that patterns of electrical activity were more stable and ventricular tachycardia more sustained in transmural than subendocardial infarction.\(^4\) However, transmural extension of necrosis by methylprednisolone is at variance with the finding of reduction of experimental infarct size by corticosteroids, which has been reported by several groups.\(^11\) On the other hand, others have not been able to obtain a protective effect of methylprednisolone in the clinical\(^28\) or experimental setting\(^29\) after acute myocardial infarction. Lack of a control group of untreated preparations with permanent occlusion in the present study does not allow us to contribute helpful data on this matter.

In reperfused infarct preparations we found patterns of excitation suggesting subepicardial circus movement on the anterior surface of the left ventricle in two instances. In two other uniform patterns of ventricular tachycardia, the pattern of subepicardial excitation was radial and intramural electrical activity preceded or occurred concomitantly with epicardial breakthrough. Activity at these intramural sites was late during sinus rhythm. By visual examination and with the use of TTC staining we could see that the infarct pattern was more spotty in these preparations than in preparations with permanent occlusion. However, we could not delineate intramural tracts of surviving myocardium, as others have done using more refined histologic technique.\(^4,6\) nor could we map intramural circus movement patterns. Although the presence of an alternate mechanism of arrhythmogenesis cannot be excluded, this could reflect the limitation of our 64-channel recording technique to delineate reentrant pathways in three-dimensional myocardium. Thus, we agree with Wit et al.\(^10\) that uniform ventricular tachycardia might not always be attributable to reentry at the subepicardial level and that its origin might be found in intramural layers in some reperfused infarct preparations. Comparison of findings in our reperfused infarct and methylprednisolone-treated permanent occlusion preparations suggests that a layer might be a better substrate than a three-dimensional structure for sustained circus movement tachycardia.

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