Reentrant ventricular arrhythmias in the late myocardial infarction period

Interruption of reentrant circuits by cryothermal techniques

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ABSTRACT Both sustained and nonsustained ventricular tachycardias were reproducibly induced in dogs 3 to 5 days after ligation of the left anterior descending coronary artery. Isochronal maps of ventricular activation were constructed from close bipolar electrograms recorded from the entire epicardial surface and selected intramural sites by a computerized multiplexing technique. The electrophysiologic data were correlated with the anatomic characteristics of the infarction. The induced tachycardias were due to reentrant activation in the surviving epicardial layer overlying the infarction. Cooling or cryoablation was applied to localized epicardial sites along the reentrant circuit to reversibly or permanently interrupt reentrant activation. The reentrant circuit could be consistently interrupted when cooling or cryoablation was applied to the distal part of the common reentrant wave front proximal to the site of earliest reactivation. Localized cooling of the site of earliest reactivation usually failed to interrupt reentry because the common reentrant wave front reactivated other sites close to the original reactivation site. Before interruption of reentry, cooling resulted in characteristic changes in conduction of the reentrant wave front. The study (1) fulfills Mines’ criteria that circus movement reentry is the mechanism of the induced rhythms in this canine experimental model and (2) identifies the critical site along the reentrant circuit at which cryothermal ablation (or surgical interruption) of reentrant activation could be successfully accomplished.


WE HAVE SHOWN that ventricular arrhythmias induced by programmed stimulation in dogs 1 to 5 days after infarction are due to reentrant circuits located in the surviving, although electrophysiologically abnormal, thin epicardial layer overlying the infarction. These electrophysiologic-anatomic correlative studies provide strong evidence for circus movement reentry. However, to establish the mechanism as reentrant, the reentrant circuit should be interrupted at one point to produce termination of reentrant activation. The present study was conducted to fulfill Mines’ criteria for proving the presence of circulating excitation and to identify the critical site along the reentrant circuit at which interruption of reentrant activation could be successfully accomplished. For this purpose, we used reversible cooling and/or cryoablation of localized areas of the epicardial surface of the reentrant circuit.

Methods

In 18 mongrel dogs weighing 15 to 20 kg the left anterior descending coronary artery was ligated just distal to the anterior septal branch. Details of the surgical technique have been described. The dogs were reanesthetized with sodium pentobarbital (30 mg/kg iv) 3 to 5 days after coronary artery ligation and received supplemental doses as required. Each animal was ventilated with room air through an endotracheal tube with a Harvard positive pressure pump, and in each a jugular vein was cannulated for the administration of fluids. Electrocardiographic lead II and femoral blood pressure were continuously monitored on an Electronics for Medicine DR10 electrophysiologic recorder. To slow the sinus rhythm, stimulation of the right or left vagosympathetic trunk was accomplished by delivery of 0.5 msec square-wave pulses of 1 to 10 V intensity at a frequency of 10 to 20 Hz through two Teflon-insulated silver wires (0.012 inch in diameter). The heart was exposed through a left thoracotomy and cradled in the opened pericardium. Ventricular pacing was achieved via two fine Teflon-insulated stainless steel wires (0.005 inch in diameter) inserted by a 21-gauge hypodermic needle into the right ventricular wall. Both regular pacing and programmed premature stimulation were performed with a programmable digital stimulator (model DTU-101 MVA, Bloom Associates, Ltd.). The stimulator delivered rectangular pulses of variable duration (usually 2 to 5 msec)
twice diastolic threshold with an accuracy up to a 1 msec interval. Details of the stimulation protocol were described previously. In each experiment, a stimulation protocol was selected that resulted in the induction of a reproducible monomorphic ventricular rhythm. The protocol varied from one experiment to the other and will be detailed in Results.

Once a reproducible ventricular rhythm was established, 62 simultaneous bipolar electrode recordings were obtained with a sock electrode. A higher density of electrodes (approximately 6 to 10 mm between pairs) covered the area of the infarction and the border zones, and a lower density (approximately 15 mm) covered the remaining surface of the heart. In some experiments a patch electrode was also used to obtain epicardial recordings at a closer interelectrode distance (4 mm). Intramura1 recordings were obtained with specially designed 21-gauge needles. Details of the recording techniques, the mapping system, and the methods for construction of epicardial isochronal maps were previously reported.

After termination of the electrophysiologic study, the anatomic locations of intramura1 recording sites were determined and correlated with epicardial recording sites by inserting short clipped needles at selective sites. The anatomic features of the infarction were first determined by gross examination. The heart was then cut transversely at 0.5 cm intervals and the sections were stained by the nitroblue tetrazopium (NBT) macroscopic enzyme-mapping procedure. A tridimensional outline of the infarction was then constructed and correlated with the recorded electrograms. For histologic examination, tissue blocks were fixed in acetate-buffered neutral 10% Formalin, embedded in paraffin, and cut at a thickness of 5 to 7 μm. The sections were stained with hematoxylin and eosin.

Cryothermal techniques. The cryothermal system was a Spemnley-Amoils BMS 411 cryo unit. This apparatus regulates the flow of nitrous oxide through the tip of the cryoprobe. The cryoprobe used in the study (No. 7107) had a flat tip 12 mm in diameter. Local epicardial temperature could be measured by a thermocouple at the tip of the probe, and intramura1 temperature could be measured by a needle thermistor. For reversible interruption of reentrant activation, the myocardial temperature at a localized epicardial site was reduced to between −5° and +5° C for 10 to 30 sec. Different epicardial sites were tested, and the effects of transient epicardial cooling on ventricular activation patterns were analyzed. To achieve cryoablation, the temperature at the tip of the cryoprobe was reduced to between −55° to −65° C for 2 min. Sometimes transient cooling of two contiguous sites was performed, in which case the probe was rapidly moved to the second site to achieve local cooling before the effects of cooling on the first site had expired. Alternatively, cryoablation was applied to one site, and transient cooling was applied to a contiguous site.

Results
A reproducible monomorphic ventricular rhythm could be induced by programmed stimulation in 16 of 18 dogs. In three dogs the reentrant circuit could not be completely identified on the epicardial surface. In these dogs cryothermal interruption of possible reentrant activation was not tried. In the remaining 13 dogs, isochronal mapping successfully identified an epicardial reentrant circuit. Of these dogs, programmed stimulation reproducibly initiated a sustained monomorphic ventricular tachycardia (lasting for more than 1 min) in three, two morphologically distinct sustained ventricular tachycardias in one, and short runs of a monomorphic ventricular rhythm (2 to 10 beats) in nine. The rate of the induced ventricular rhythms ranged from 240 to 360 beats/min. Cryothermal interruption of the reentrant circuit could be consistently accomplished in each of the 13 dogs. The results from these experiments are presented here.

Figure 1 illustrates electrocardiographic recordings from one of the experiments in which a sustained monomorphic ventricular tachycardia was reproducibly induced by programmed stimulation. Figure 1, A, shows the control recording. Pacing was applied to the base of the right ventricle at a basic cycle length (S1-S1) of 360 msec. Two premature stimuli (S2 and S3) were introduced at a coupling interval of 200 and 190 msec, respectively, and initiated a sustained ventricular tachycardia at a cycle length of 190 to 200 msec. Figure 1, B to D, illustrates three separate episodes of reversible termination of the tachycardia by cooling. As shown in figure 1, B, the tachycardia cycle length slightly increased to 220 msec before termination. More marked lengthening of the last one or two tachycardia cycles occurred before termination (figure 1, C and D). Figure 1, recordings E and F, were obtained after cryoablation of reentrant activation. The tachycardia could not be induced by a programmed stimulation protocol similar to that used at control (figure 1, E) or by a more aggressive stimulation protocol (figure 1, F).

Figures 2 to 6 illustrate the effect of reversible cooling at different epicardial sites along the reentrant circuit during ventricular tachycardia from the same experiment. The left side of figure 2 illustrates the isochronal map of the control reentrant circuit and selected epicardial electrograms. The isochronal map was drawn at 20 msec intervals. The reentrant circuit had a characteristic figure of 8 activation pattern. It consisted of two separate arcs of functional conduction block (represented by the heavy solid lines) and two circulating wave fronts. The two wave fronts joined into a common wave front that conducted slowly between the two arcs before reactivating an area on the septal border of the infarction. The cryoprobe (shaded circle) was applied to the earliest reactivation site. At this site, represented by electrogram 23, the slow common reentrant wave front first reexcited myocardial zones on the other side of the arcs of conduction block. Electrogram 23 preceded the onset of surface QRS by 30 msec. The right side of the figure illustrates the isochronal map of the reentrant circuit after cooling and the effect of cooling on selected local electrograms. Cooling resulted in conduction block between
EL-SHERIF et al.

site 24, located along the distal part of the common reentrant wave front, and the early reexcitation site 23. Before cooling, electrogram 23 had two components. The first was a low-amplitude slow deflection approximately synchronous with the activation potential at site 24 and represented a passive far field or electrotonic potential and the second was a larger, relatively sharp potential that represented the moment of local activation. When cooling induced conduction block between sites 24 and 23, the electrotonic potential was still recorded synchronous with the activation potential at site 24. On the other hand, the activation potential at site 23 was markedly delayed and occurred after the onset of the surface QRS. The isochronal map after cooling showed significant changes in the position of the upper arc of conduction block and the clockwise-directed wave front. However, the common reentrant wave front still reexcited site 18 on the proximal border of the arc of block. This site was adjacent to the original site of early reactivation (site 23). Thus, cooling the original site of early reactivation did not interrupt the reentrant circuit but rather resulted in a shift of the early reexcitation site. Conduction of the common reentrant wave front to the new reexcitation site (site 24 to site 23) and resulted in a 20 msec increase in the tachycardia cycle length.

Figure 3 shows recordings obtained when the cooling probe was applied over the epicardial site of the upper arc of conduction block and the clockwise-directed circuit. The control map and selected electrograms are shown on the left. The right side of the figure shows the epicardial activation maps of two consecutive reentrant beats after cooling. As in figure 2, localized cooling of this epicardial site failed to terminate reentrant activation but rather resulted in a slight (15 to 20 msec) lengthening of the tachycardia cycle length. Cooling also resulted in significant alteration of the upper arc of conduction block and the clockwise-directed circuit. A relatively slow common reentrant wave front still reexcited the more distal site 18. During control mapping, electrograms 24 and 29 showed both electrotonic and activation potentials. Cooling resulted in 2:1 block at sites 24 and 29. During the blocked beat only the electrotonic potential was recorded (marked by asterisks). Other electrograms (23, 25, and 30), recorded slightly distant from the site of cooling, showed alternation of electrogram configuration. The 2:1 conduction block after cooling is represented on the epicardial maps as a zone of conduction

FIGURE 1. Electrocardiographic recordings from an experiment in which a sustained monomorphic tachycardia was reproducibly induced by programmed stimulation. A, Control recording. B to D, Three separate episodes of reversible termination of the tachycardia by cooling. E and F, Failure to initiate the tachycardia after cryoablation of the reentrant circuit. See text for details.
block around the site of the cryoprobe during alternate beats of the tachycardia.

Figure 4 shows that when cooling was applied to the distal part of the common reentrant wave front, the reentrant circuit was interrupted. At this site the width of the reentrant wave front enclosed between the two arcs of functional conduction block narrowed considerably. The control map and selected electrograms are shown on the left. Electrographic recordings on the right illustrate the termination of the reentrant tachycardia after cooling, and the two maps on the right illustrate the epicardial activation pattern during the last two cycles of reentrant activation. During control mapping, the conduction time between proximal electrode site 25 and the more distal site 24 was 33 msec. Before termination of the tachycardia, an incremental beat-to-beat increase of the conduction time between sites 25 and 24 occurred and was associated with equal increases in the tachycardia cycle length. When conduction block developed between the two sites, the reentrant circuit was interrupted, and electrogram 24 recorded an electrotonic potential but not a local activation potential. This was represented on the isochronal map by an arc of conduction block (heavy solid line) that joined the two separate arcs of conduction block into one.

Figure 5 illustrates another termination of the reentrant circuit when cooling was applied to approximately the same site as shown in figure 4. Epicardial and intramural recordings were obtained from needle electrodes inserted at site 25 proximal to the cryoprobe and at site 24 within the cooled zone. Needle electrode recordings were also obtained from site 18 in the normal zone to the right of the septal border of the infarc-
el-Sherif et al.

At each site the most proximal needle electrode recorded from the superficial 1 mm epicardial layer. This electrogram was synchronous with that obtained from the epicardial sock electrode in the immediate vicinity. Four intramural recordings were obtained from levels 2, 4, 6, and 8 mm below the epicardial surface. Recordings at the 6 mm level are not shown in the figure. Control recordings are shown on the left panel. Synchronous electrical potentials denoting myocardial activation were recorded up to 2 mm below the epicardial surface at sites 25 and 24, and intramural recordings at the 4, 6, and 8 mm levels below the surface revealed low-amplitude broad deflections consistent with cavity potentials. On the other hand, needle recordings at site 18 showed almost simultaneous activation of epicardial and intramural sites. The intramural recordings were consistent with the anatomic characteristics of the infarction, which showed a layer of surviving epicardium 1 to 3 mm thick overlying a core of infarcted myocardium that extended to the endocardial surface. This is shown in the photograph of the stained section of the heart at the level at which intramural needles at sites 18 and 24 were inserted (bottom of left panel). Intramural recordings after cooling application are shown in the right panel, and the two maps on the bottom of the right panel illustrate the last two cycles of reentrant activation. The figure shows that cooling resulted in lengthening of the last two cycles of the tachycardia to 260 msec compared with 200 msec during the control recording. This was exclusively accounted for by increased conduction delay between sites 25 and 24. The conduction delay and conduction block between the two sites occurred in a tangential direction across the thickness of the surviv-

FIGURE 3. Same experiment as in figures 1 and 2. The effects of reversible cooling when the cryoprobe (shaded circle) was applied over the epicardial site of the upper arc of conduction block and the clockwise directed circuit. The control map and selected electrograms are shown on the left and the maps of two consecutive reentrant beats after cooling are shown on the right. Localized cooling of this site failed to terminate reentrant activation but resulted in a shift in the site of early reexcitation and a slight lengthening of the tachycardia cycle length. The electrograms on the right show the occurrence of 2:1 block at sites 24 and 29 after cooling. See text for details.
ing epicardial layer. Conduction across the perpendicular (epicardial-endocardial) axis remained synchronous. The temperature gradient across the surviving myocardial layer during epicardial cooling as measured by a needle thermistor only varied by 2° to 8° C.

Figure 6 illustrates the effects of cooling applied to a wider, more proximal part of the common reentrant pathway. The cryoprobe was sequentially applied to two contiguous epicardial zones. Cooling of either zone alone failed to interrupt the tachycardia, but when both zones were cooled the tachycardia was terminated. Termination was associated with alternation of the tachycardia cycle length. Both the alternate short and long cycles were longer than in the control recording, and marked lengthening of the last cycle before termination occurred. The three isochronal maps represent, from left to right, the control map and the last two cycles of the tachycardia before termination, respectively. Analysis of epicardial electrograms showed that the alternation of the tachycardia cycle length was due to alternation of conduction delay between electrode sites 25 and 24. Conduction block resulting in termination of reentrant activation occurred between these two sites. The conduction time between the two sites (10 mm apart) during the last cycle of the tachycardia was 220 msec, which reflects a conduction rate of 4.5 cm/sec. Alternation of electrogram configuration was also seen in several recordings from within and around the cooled zone.

Figure 7 illustrates electrocardiographic recordings from another experiment in which a nonsustained monomorphic ventricular tachycardia (cycle length, 200 to 220 msec) was reproducibly induced by a single premature beat (S₁-S₂ at 380 msec and S₁-S₃ at 200 msec). The control recording is shown in figure 7, A. The recording in figure 7, B, was obtained after localized epicardial cooling to 0° C was applied for 20 sec. The premature impulse could only initiate a single beat with markedly prolonged coupling (380 msec compared with 180 msec for the first reentrant beat during control recording in figure 7, A). The recording in figure 7, C, was obtained after 30 sec of cooling at 0° C and shows that S₂ stimulation failed to initiate the reentrant tachycardia.

The recordings in figure 8 were obtained during the

![Figure 4](http://circ.ahajournals.org/)

**FIGURE 4.** Same experiment as in figures 1 to 3. Interruption of the reentrant circuit when the cryoprobe (shaded circle) was applied to the distal part of the common reentrant wave front. The control map and selected electrograms are shown on the left. Electrographic recordings on the right illustrate the termination of reentrant tachycardia after cooling, and the two maps on the right illustrate the epicardial activation pattern during the last two cycles of reentrant activation. See text for details.
same experiment and illustrate the position of cryo-probe application and the changes in the reentrant circuit after cooling. The left side of the figure shows the control map of the S₂-stimulated beat. During S₂ stimulation a continuous arc of functional conduction block developed with two circulating wave fronts, one traveling clockwise around the upper end of the arc and the other counter clockwise around the lower end. The two wave fronts joined to form a slow common wave front that reactivated normal myocardial zones on the proximal side of the arc of block to initiate the first reentrant beat. The earliest reactivation zone is represented by the dotted line. The bottom recordings on the left are selected epicardial electrograms during S₁-S₂ stimula-

![Figure 5](https://circ.ahajournals.org/)

**FIGURE 5.** Same experiment as in figures 1 to 4. Another termination of the reentrant circuit when the cooling probe (shaded circle) was applied to the distal part of the common reentrant wave front. Epicardial (EPI) and intramural needle recordings were obtained from site 25, 24, and 18. Control recordings are shown on the left, and recordings after cooling are shown on the right. A photograph of the stained section of the heart at the level at which intramural needles at sites 18 and 24 were inserted is shown on the bottom of the left panel. The two maps on the bottom of the right panel illustrate the last two cycles of reentrant activation. See text for details.
tion and the first two reentrant beats. Electrogram 6 represented the earliest site of reactivation after S_2 stimulation, and electrogram 12 represented the earliest reactivation site during subsequent reentrant beats. Cooling was applied to the distal part of the common reentrant wave front (electrode site 9) immediately proximal to the site of earliest reactivation. The center map represents the S_2-stimulated beat after cooling at 0°C for 15 sec. S_1 initiated only a single reentrant beat with a coupling interval of 270 msec (compared with 170 msec during control recording). The selected electrograms at the bottom of the map show that cooling resulted in marked widening of electrogram 9 during S_1 stimulation but only slight widening of surrounding electrograms 6, 12, 13, and 7. However, during S_2 stimulation sites 6 and 12 showed conduction block (or possibly markedly slowed conduction). This event reflected lengthening of the effective refractory period at sites 6 and 12 after cooling, since the S_1-S_2 cycle length remained unchanged from that in the control recording. On the map, this was represented by a shift of the arc of conduction block to a position proximal to sites 6 and 12. Cooling also resulted in conduction block around the cooled zone (site 9), and in marked conduction delay in epicardial zones immediately adjacent to the cooled zone (between sites 18 and 13 as well as

**FIGURE 6.** Same experiment as in figures 1 to 5. Effects of cooling a more extensive area of the proximal part of the common reentrant pathway (shaded circles). Cooling resulted in cycle length alternation and marked lengthening of the last reentrant cycle before termination. The three isochronal maps represent, from left to right, the control map and the last two cycles of the tachycardia before termination, respectively. The alternation of conduction delay and final conduction block occurred between sites 25 and 24. The zigzag line represents very slow conduction. See text for details.
between 13 and 7). The common reentrant wave front was forced to conduct at a slower speed in epicardial zones located between the original arcs of functional conduction block and the cooling-induced zone of block. This accounted for the marked lengthening of the coupling interval of the reentrant beat. Eventually, the slow wave front reactivated a normal myocardial zone (site 64) adjacent to the original site of earliest reactivation (site 6). The subsequent turnaround of reentrant activation was blocked around site 13 (not shown in the figure). This explained the occurrence of a single reentrant beat after S₂ stimulation. The map on the right represents the S₂-stimulated beat after cooling was applied at 0° C for 30 sec. The premature beat failed to initiate a reentrant rhythm. The map shows that the upper clockwise-directed wave front blocked at the right border of the cooled zone (sites 18 and 13). However, the lower counterclockwise-directed wave front continued to conduct between two zones of functional conduction block before eventually being blocked as it approached the cooled zone. The electrograms on the bottom of the map show that site 13 was activated after site 14. This represented a reversal of the direction of activation at these two sites compared with that in the control map, in which site 14 was activated after site 13.

In seven experiments, when the original reentrant circuit was interrupted by cryoablation, a more aggressive programmed stimulation protocol (two or three successive premature beats or short bursts of rapid pacing) could still induce ventricular rhythms with different QRS morphologic features; in three of these dogs ventricular fibrillation was induced. Some of these rhythms could be shown to be due to an epicardially located reentrant circuit different from the control circuit. The recordings in figure 9 were obtained during one of these experiments. During control recording, a single premature impulse (S₁-S₂, 380 msec and S₁-S₂, 200 msec) reproducibly induced short runs (3 to 5 beats) of a monomorphic rhythm (positive QRS in lead II). The epicardial isochronal map in figure 9, A, shows that the S₂-stimulated beat resulted in a continuous arc of functional conduction block and two circulating wave fronts around the upper and lower ends of the arc. A broad common reentrant wave front reactivated an area on the proximal side of the upper septal border of the arc (marked by the dotted line) to initiate the first reentrant beat. Cryoablation was applied to the epicardial zone in which the common reentrant wave front reactivated normal myocardium (shaded circle in A) and resulted in complete conduction block around the site of the cryoprobe. After cryoablation, the S₂-stimulated beat failed to initiate a reentrant rhythm (figure 9, B). In figure 9, C, a second premature beat (S₃) was introduced and resulted in a short run (3 to 5 beats) of a monomorphic ventricular rhythm with negative QRS in lead II. The epicardial map shows that S₃ resulted in a longer arc of conduction block. The common reentrant wave front conducted slowly in a basal to apical direction before reactivating myocardial sites on the lateral apical zone of the infarction (marked by the dotted line) that initiated the first reentrant beat. The slower conduction of the reentrant wave front and the longer pathway explained the longer coupling interval of the first reentrant beat with negative QRS (270 msec) compared with the first beat with positive QRS in figure 9, A (170 msec). The reentrant circuit could only be interrupted when

**FIGURE 7.** Electrocardiographic recordings from another experiment showing A, the initiation of a nonsustained monomorphic tachycardia after a single premature beat (S₂) and B, the effect of localized epicardial cooling to 0° C for 20 sec. The premature impulse could only initiate a single beat with markedly prolonged coupling compared with that in control. C, After 30 sec of cooling, premature stimulation failed to initiate a reentrant rhythm.
cryoablation was applied to an approximately $12 \times 20$ mm area of the common reentrant wave front immediately proximal to the reactivation site (shaded circles). This resulted in conduction block around the cryoablated area, and $S_1$-$S_2$-$S_3$ stimulation failed to induce the reentrant rhythm (figure 9, D).

Discussion

Effects of cooling on the reentrant circuit. Moderate cooling results in a marked increase of the duration of the ventricular action potential without marked changes in the resting potential. The change in duration results particularly from a decreased slope of phase 2 and from the consequent increase in the duration of phase 2. However, if ventricular myocardium is cooled sufficiently, resting potential is decreased and excitability is diminished or blocked. In the in vivo canine heart, cooling of the normal ventricular epicardial layer results in lengthening of the effective refractory period of the cooled region with consequent cycle length–dependent conduction delays and conduction block. Because of the nature of reentrant activation, it was not possible in the present study to analyze in a systematic fashion the effects of cooling on the effective refractory period of the surviving epicardial layer in which the reentrant circuit was located. However, some of our observations, particularly in epicardial zones immediately proximal to the arc of functional conduction block, suggest lengthening of the effective refractory period of cooled zones (figure 8). It could be assumed that during self-sustained reentrant activation, the wave front will move at the maximum velocity permitted by the state of recovery (i.e., the duration of the effective refractory period) of the myocardium. Any lengthening of the effective refractory period of a localized but critically located myocardial zone along the reentrant pathway will be directly reflected in changes in conduction. In the present

![Figure 8](http://circ.ahajournals.org/)

**FIGURE 8.** Same experiment as in figure 7. Effects of cooling the part of the common reentrant wave front (shaded circle) immediately proximal to the area of earliest reactivation (dotted line). The control map of the $S_2$ beat and selected epicardial electrograms are shown on the left. The center map represents the $S_2$ beat after cooling at $0^\circ$ C was applied for 15 sec; $S_2$ initiated only a single reentrant beat with a longer coupling interval. The map on the right represents the $S_2$ beat after cooling was applied for 30 sec and illustrates failure of $S_2$ to initiate a reentrant rhythm. See text for details.
study, it is probable that cooling-induced lengthening of the effective refractory period of localized zones of the epicardial layer in which the common reentrant wave front was located did result in slowing of conduction and/or conduction block. Because the reentrant circuit was located in a 1 to 3 mm thick epicardial layer with reduced myocardial blood flow12 overlying a core of necrotic myocardium, cryoprobe application to the epicardial surface resulted in sufficient cooling across the entire epicardial layer. Before cooling, reentrant

FIGURE 9. Recordings from another experiment. A, Control recordings. A single premature beat (S2) induced 3 beats of a monomorphic rhythm with positive QRS in lead II. The map of S2 shows the site of earliest reactivation (dotted line) on the upper paraseptal border of the infarction (interrupted line). B, After cryoablation of the epicardial site of the common reentrant wave front adjacent to the zone of earliest reactivation (shaded circle in A), S2 failed to initiate the reentrant rhythm. C, A second premature beat (S3) succeeded in inducing 4 beats of a monomorphic rhythm with negative QRS in lead II. The S3 map shows the site of earliest reactivation (dotted line) on the lateral apical border of the infarction. After cryoablation of the distal part of the common reentrant wave front (shaded circles), S3 failed to induce the reentrant rhythm.
activation advanced in a horizontal direction in the thin epicardial layer, with activation being almost synchronous in the epicardial-to-endocardial axis. Cooling-induced conduction delay and conduction block of the common reentrant wave front also occurred in the horizontal direction (figure 5). Due to this electrophysiologic-anatomic characteristic of the common reentrant wave front, conduction velocity of the wave front before and after cooling could be estimated with reasonable accuracy. Cooling could result in a marked decrease of conduction velocity (as low as 4.5 cm/sec as in figure 6). This suggests the possibility that reentrant circuits with very small dimensions can occur in canine ischemic myocardium if conduction velocity is markedly reduced; also, in a large reentrant circuit most of the conduction delay may occur in a small localized zone. This latter observation may explain, in part, some of our earlier findings of wide gaps in epicardial activation during potentially reentrant rhythms in the same canine model.\(^1\)\(^2\) Because of the limited resolution of our epicardial recordings, it is quite possible that small epicardial zones with very slow conduction were missed.

The common reentrant wave front and the critical area for interruption of reentrant activation. The present study has demonstrated that reentrant activation can be successfully interrupted when cooling or cryoablation is applied to the part of the common reentrant wave front immediately proximal to the zone of earliest reactivation. At this site, the common reentrant wave front is usually narrow and is surrounded on each side by an arc of functional conduction block. On the other hand, localized cooling at the site of earliest reactivation usually failed to interrupt reentry. The common reentrant wave front usually broke through the arc of functional conduction block to reexcite other sites close to the original reactivation site without necessarily changing the overall reentrant activation pattern. Usually, however, the reentrant cycle length increased by 10 to 30 msec. As explained previously,\(^2\) earliest reexcitation will occur at the first site on the proximal side of the arc of block at which the effective refractory period is slightly shorter than the conduction time around the arc. If cooling results in lengthening of the refractory period of this site, the slow common wave front may still be able to reexcite a contiguous site. If this site has a longer effective refractory period compared with that of the original reexcitation site, slight lengthening of the reentrant cycle length may occur.

Recent clinical studies have advanced the notion of an earliest site of ventricular activation during possible reentrant rhythms. At this site, electrograms — mostly on the endocardial side — were recorded 2 to 48 msec before the onset of the surface QRS complex.\(^13\) Surgical excision of this site was reported to have resulted in termination of the ventricular tachycardia.\(^15\) In the present study, electrograms representing the earliest reactivation site preceded the surface QRS by 10 to 40 msec. However, application of cooling to this site usually failed to interrupt reentrant activation. On the other hand, electrograms representing the distal portion of the common reentrant wave front, the area from which the reentrant circuit could be consistently interrupted, preceded the surface QRS by 40 to 80 msec. It is possible that the anatomic-electrophysiologic characteristics of reentrant circuits in these clinical studies were significantly different from reentrant circuits in the present canine model. However, another plausible explanation is that the surgical excision in these studies was in fact extensive and included, in addition to the site of earliest reactivation, parts of the area of the common reentrant wave front. Supporting this possibility is the finding in the present study that the reentrant circuit could also be interrupted at a more proximal and broader part of the common reentrant wave front if cooling or cryoablation were applied to a more extensive area (figure 6). The main advantage of cryoablation is that the resulting cryolesion is a localized and sharply demarcated homogeneous scar.\(^15\) It is obvious that in order to minimize the area of the cryolesion, precise localization of the site from which the reentrant circuit could be successfully interrupted must be accomplished.

Proving reentry as the mechanism of an arrhythmia. The early studies of Mayer,\(^16\) Mines,\(^3\) and Garrey\(^17\) have clearly established that circulating excitation could be initiated in simple rings of excitable tissue. The criteria for proving the presence of circulating excitation as established by Mines are (1) an area of unidirectional block must be demonstrated. (2) The movement of the excitatory wave should be observed to progress through the pathway, to return to its point of origin, and then to again follow the same pathway. (3) ‘‘The best test for circulating excitation is to cut through the ring at one point. If impulses continue to arise in the cut ring, circus movement as a cause can be ruled out.’’\(^13\) Surprisingly enough, no single arrhythmia in a mammalian heart has been demonstrated, to date, to fulfill all of Mines’ three criteria for definite proof of reentry.\(^18\) The present study, by satisfying all of Mines’ three criteria, establishes that circus movement reentry is the mechanism of the observed tachyarrhythmias. The study also demonstrates that the configuration of the reentrant circuit in the mammalian ventri-
icles (and most probably in the atria as well) is significantly different from that originally described in simple rings of excitable tissue. These rings resembled in a substantial way the anatomic substrate of the preexcitation syndrome in the human heart in which a large part of the pathway is made of excitable bundles that are not connected to adjacent atrial and ventricular myocardium. In these rings, as well as in the preexcitation syndrome, a single simple circulatory wave could be established. The circuit could be interrupted with ease by cutting at any point along the insulated excitable bundles (either the normal or accessory AV pathways), but most probably not at the less well-defined atrial or ventricular connections of these pathways. On the other hand, there are no such insulated excitable bundles in the ventricles (or atria) at large but rather an interconnected syncytial structure. The reentrant circuit here has a figure of 8 activation pattern whereby two circulating wave fronts advance in a clockwise and counterclockwise direction, respectively, around two zones (arcs) of unidirectional block. The zones of conduction block are either purely functional (i.e., cycle length-dependent) or are composed of both organic (anatomic) and functional block. The two circulating wave fronts coalesce into a common reentrant wave front that conducts between the two zones of block before reexciting myocardium on the other side of the zones of block. The reentrant circuit could be successfully terminated only from localized areas along the common reentrant wave front. It should be emphasized that the localization of the reentrant circuit in a thin epicardial layer in the present study is only a reflection of the particular anatomic features of this infarction. Depending on the distribution of the pathologic features of the myocardium, reentrant circuits could also be expected to be located in the subendocardial and intramyocardial zones. However, irrespective of the anatomic localization of the circuit, its configuration probably has to conform to the figure of 8 model.

In summary, the present study has provided the necessary evidence for circus movement reentry in the mammalian ventricle in accordance with Mines’ standard criteria. The study has also identified the critical site along the reentrant circuit at which cryothermal (or surgical) interruption of reentrant activation could be successfully accomplished.

References
Reentrant ventricular arrhythmias in the late myocardial infarction period. Interruption of reentrant circuits by cryothermal techniques.
N El-Sherif, R Mehra, W B Gough and R H Zeiler

Circulation. 1983;68:644-656
doi: 10.1161/01.CIR.68.3.644

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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