Electrophysiology of Coronary Reperfusion

A Mechanism for Reperfusion Arrhythmias

DAVID K. MURDOCK, M.D., JEROD M. LOEB, PH.D., DAVID E. EULER, PH.D.,
AND WALTER C. RANDALL, PH.D.

SUMMARY To gain insight into the mechanisms of reperfusion arrhythmias, we studied ventricular automaticity and conduction characteristics in 35 dogs during 10 minutes of left anterior descending coronary artery (LAD) occlusion and subsequent reperfusion. The frequency of ectopic activity reached a maximum within the first 6–8 minutes after LAD occlusion and then declined, leading to an ectopia-free quiescent period. The arrhythmias after occlusion were marked by prolonged ischemic zone conduction times as measured from local bipolar plunge electrodes while marked fractionation of electrical activity was recorded from specially constructed composite epicardial electrodes. The quiescent period was characterized by a loss of marked fractionation of electrical activity from composite recordings and a progressive decrease or complete loss of electrogram amplitude from plunge electrodes. Reperfusion was characterized by a rapid improvement in both the ischemia-induced conduction delay and amplitude on the local bipolar electrogram. However, the composite electrode recorded a return of the marked fractionation of electrical activity associated with a return of arrhythmias.

Ventricular automaticity during reperfusion (50.6 ± 6.0 beats/min) was assessed in five dogs with complete atrioventricular block and was not significantly different from control preocclusive automaticity (47.6 ± 5.8 beats/min). In addition, reperfusion at a heart rate of 220 beats/min was associated with increased frequency and severity of arrhythmias compared with those at a heart rate of 150 beats/min.

We conclude that the early ischemic arrhythmias result from conduction slowing through the ischemic zone establishing reentrant pathways, while the quiescent period is a manifestation of further conduction suppression so that reentrant pathways become blocked. Reperfusion of this electrically unresponsive tissue results in a nonhomogenous improvement in conduction that transiently restores the conditions necessary for reentry.

IN 1943 Harris and Rojas first demonstrated a specific time course for ventricular arrhythmias during acute ischemia. After coronary occlusion, they noted a progressive increase in the frequency of ectopic activity that reached maximal intensity within 6–10 minutes and then abated, resulting in a relatively ectopia-free quiescent period. Ventricular fibrillation, when present, was limited to the early arrhythmic period. These investigators also demonstrated that reperfusion of acutely ischemic myocardium also gave rise to a rapid increase in ectopic activity, leading frequently to ventricular fibrillation. The malignant potential of coronary reperfusion has since been demonstrated by several investigators.

Several studies using both specially constructed composite electrodes and bipolar electrodes have demonstrated a close relationship between the extent of desynchronization of electrical activity during acute ischemia and ventricular arrhythmias. The desynchronization of electrical activity is believed to represent marked slowing and inhomogeneity of conduction through the ischemic zone. This finding, coupled with the failure to demonstrate enhanced automaticity, suggests a reentrant mechanism for the early ischemic arrhythmias.

Although reentry is generally considered the mechanism for the early occlusive arrhythmias, the etiology for the reemergence of arrhythmias with reperfusion of ischemic myocardium remains unclear. With the concept of coronary artery spasm firmly established, the functional components necessary to produce reperfusion arrhythmias are readily available in the clinical setting. Furthermore, since most cases of sudden death do not demonstrate occlusive coronary disease, a reperfusion mechanism involving relaxation of coronary artery spasm was recently suggested.

This study was undertaken to examine the cause of reperfusion arrhythmias. Specifically, we examined conduction characteristics in acutely ischemic and reperfused myocardium using both local electrodes and specially constructed composite electrodes. We also analyzed ventricular automaticity during reperfusion and the effect of heart rate on reperfusion arrhythmias.

Methods

Experiments were performed on 35 mongrel dogs of either sex ranging in weight from 13–25 kg. The dogs were anesthetized with intravenous sodium pentobarbital, 30 mg/kg body weight, and mechanical ventilation was provided through auffed endotracheal tube via a Bird Mark 7 respirator. The femoral artery was isolated and cannulated to monitor arterial pressure. The heart was exposed through a left lateral thoracotomy and a pericardial cradle constructed. The

From the Department of Physiology, Loyola University of Chicago, Stritch School of Medicine, Maywood, Illinois.

Supported by NIH grant HL08682.

A preliminary report of this work has appeared in abstract form in Federation Proceedings 37: 1101, 1978.

Address for correspondence: David K. Murdock, M.D., Department of Physiology, Loyola University Medical Center, 2160 South First Avenue, Maywood, Illinois 60153.

Received January 16, 1979; revision accepted July 25, 1979.

Circulation 61, No 1, 1980.
left anterior descending coronary artery (LAD) was dissected free below the first diagonal branch and myocardial ischemia was produced with an atraumatic vascular occluder. Heart rate was maintained at 150–180 beats/min via right atrial or ventricular pacing with stimuli 2 msec in duration and 4–8 V delivered from a Grass S5 stimulator.

Local ischemic zone conduction times were measured in 20 dogs subjected to right atrial pacing. In 14 dogs the LAD was occluded for 5 minutes and epicardial mapping with a bipolar exploring electrode was instituted to identify areas of conduction delay. After release of the occlusion, four or five close bipolar electrodes were inserted into the subepicardium in the regions in which conduction delay was identified. An additional one or two electrodes were inserted into the subendocardium. In six other dogs, four or five electrodes were inserted randomly into the subepicardial and subendocardial regions of the ischemic and border zone. Each electrode consisted of two stainless-steel, teflon-insulated wires (0.003 in. in diameter) threaded through a 25-gauge hypodermic needle. The needle was used to plunge the wires into the myocardium and was then removed after the wires were in place.

In 10 additional dogs with right atrial pacing, a large bipolar composite electrode was sutured to the epicardium in the area supplied by the LAD. The construction of this electrode has been described elsewhere.18 The resulting electrode had two terminals and consisted of 12–15 contact points covering an area of myocardium 2 × 3 cm². A similar electrode was sewn to a nonischemic area.

All electrograms were amplified with Grass P511 preamplifiers with a low-frequency cutoff of 30 Hz and displayed along with a lead II ECG on a Beckman 612 strip recorder or a Grass Model 7 polygraph at paper speeds of 25–200 mm/sec. Selected electrograms and a lead II ECG were recorded on a Tetronix 5111 storage oscilloscope at sweep speeds of 20 msec/cm for photographic purposes.

Ventricular automaticity was assessed in five dogs during reperfusion after complete atrioventricular (AV) block was produced by injecting formalin into the AV node according to the technique described by Loeb et al.19 The chest was then closed and the animal allowed to recover. Seven to 10 days after the initial surgery, the dogs were reanesthetized and prepared in the same way as the other dogs, except that heart rate was maintained by right ventricular pacing.

Experimental Protocol

Local conduction times were measured through 10 minutes of ischemia and continuously during reperfusion. After LAD occlusion, progressive delay of the local electrogram within the ischemic zone was manifested as an increase in the time between onset of the QRS complex of the standard lead II ECG and the R wave of the local electrogram. This time was measured in milliseconds at 10 minutes of ischemia from recordings at paper speeds of 200 mm/sec. The amount of ischemic delay in each local electrogram immediately before reperfusion (10 minutes of ischemia) was normalized and percent of maximal ischemic conduction delay at 5 and 10 seconds of reperfusion in each electrogram was determined for both the subendocardium and subepicardium. The mean ± SEM of these normalized values was calculated. The mean and range of conduction delay in these regions was also determined. After release of the occlusion, the electrodes were repositioned and at least 30 minutes was allowed before additional conduction times were obtained.

Conduction delay on the composite electrogram appeared as a fractionation of the electrogram. A tracing of the composite electrogram at 100 mm/sec was obtained at each minute of ischemia and throughout reperfusion. Representative tracings were obtained from the early arrhythmic period, the subsequent quiescent period and during reperfusion for each dog.

In dogs with complete AV block, ventricular automaticity was measured after the temporary cessation of ventricular pacing. Control automaticity was assessed immediately before occlusion. Then, ischemia was produced and the dogs were paced at 150 beats/min through 10 minutes of ischemia. Occlusion was released simultaneously with cessation of pacing, providing an assessment of automaticity during reperfusion. The mean ± SEM of the atomatic rates was calculated. The t test for paired data was used to compare the rates.

The five dogs with complete AV block were also used to study the effect of heart rate on reperfusion arrhythmias. In each dog, additional occlusions were instituted with heart rate held constant at 150 beats/min during the ischemic period. After 10 minutes of ischemia, the heart rate was either maintained at 150 beats/min during reperfusion or increased to 220 beats/min 15 seconds before reperfusion. To rule out the possibility that repeated occlusions caused the effects of heart rate on reperfusion arrhythmias, the order in which we studied automaticity, 220 beats/min and 150 beats/min during reperfusion, was varied in each dog.

If ventricular fibrillation intervened during ischemia, the experiment was terminated. However, if ventricular fibrillation occurred only during reperfusion, defibrillation was accomplished with a 20-J DC pulse applied directly to the heart. At least 30 minutes were allowed before additional studies were undertaken.

Results

Arrhythmias

Ventricular ectopic activity occurred in the 10-minute period of coronary occlusion in 31 of 35 animals. The frequency of ectopic activity generally reached a maximum within the first 6–8 minutes and then declined. Ventricular fibrillation, when present, was noted during the period of maximum ectopic activity. Twenty-seven of 35 dogs survived the 10-minute period of ischemia. In each of these dogs, occlusive arrhythmias were generally absent or greatly di-
minimised by 10 minutes of ischemia. A reemergence of ectopic activity was noted in 20 of 27 dogs after release of the occlusion. The severity of these reperfusion arrhythmias varied from two or three ectopic beats to ventricular fibrillation. Reperfusion arrhythmias never occurred without occlusive arrhythmias. However, occlusive arrhythmias did not guarantee the presence of reperfusion arrhythmias. When arrhythmias were present during reperfusion, the onset was always noted within the first 10 seconds of release of the occlusion and usually within the first 5 seconds.

Automaticity and Effect of Heart Rate

The five dogs with complete AV block showed no significant difference in ventricular automaticity between the preischemic and reperfused state. The rate of the idioventricular pacemaker immediately before occlusion was 47.6 ± 5.8 beats/min and was unchanged (50.6 ± 6.0 beats/min) during reperfusion ($p > 0.05$).

Although the severity of arrhythmias varied from dog to dog, heart rate had a consistent effect on the intensity of reperfusion arrhythmias. Figure 1 shows a typical experiment illustrating the effect of heart rate on reperfusion arrhythmias. When heart rate was maintained at 150 beats/min during reperfusion, arrhythmias appeared in three of the five dogs tested. Ventricular fibrillation was not observed in these dogs at this rate. However, when the pacing rate was increased to 220 beats/min 15 seconds before reperfusion, arrhythmias appeared in all five dogs, with ventricular fibrillation in three of these five. When pacing was terminated simultaneously with reperfusion, allowing for a slow idioventricular rhythm to appear, no arrhythmias appeared. The order in which the heart rate studies were performed could be altered without affecting the general outcome; i.e., more rapid heart rates always potentiated reperfusion arrhythmias, while slower heart rates had a protective effect.

Local Conduction Studies

Conduction time measurements using close bipolar electrodes were attempted in 20 animals. Measurements were excluded from seven dogs due to ventricular fibrillation during either occlusion (five dogs) or reperfusion (two dogs). In the other 13 dogs, 142 bipolar electrograms were monitored through 10 minutes of ischemia and 10 seconds of reperfusion. One hundred eighteen of these local electrograms were from subepicardial sites and 24 were from subendocardial sites. Conduction delay was measurable at 10 minutes of ischemia in 80 of the 118 electrograms recorded from the subepicardial site and 10 of the 24 electrograms from the subendocardium. For the electrodes showing delay, the mean delay at 10 minutes of ischemia was 24.4 msec (range 5–55 msec) for the subepicardium and 6.3 msec (range 2–14 msec) for the subendocardium.

Within 5 seconds of reperfusion, the maximal ischemic delay had decreased to 40.3 ± 2.6% in the subepicardium and 16.6 ± 10.2% in the subendocardium. By 10 seconds of reperfusion, only 10.2 ± 1.6% of maximum delay appeared in the subepicardium and no delay was observed in the subendocardium.

Electrograms that did not demonstrate delay with ischemia also showed no delay with reperfusion. Furthermore, reperfusion never resulted in an increase in the ischemia-induced conduction delay. In every
case, the conduction delay resulting from ischemia rapidly returned to control with reperfusion. This improvement began almost immediately and was progressive with each beat until control values were again achieved. We could even demonstrate a small but definite improvement in conduction in each of the electrodes from the two dogs that fibrillated within 3 seconds of reperfusion.

Progressive loss of electrogram amplitude prevented the measurement of conduction delay at 10 minutes of ischemia in 25 of the 118 epicardial electrograms. Figure 2 illustrates this phenomenon and shows the reemergence of delayed electrical activity during reperfusion in regions without identifiable electrical activity at 10 minutes of ischemia.

Composite Electrode Studies

Composite electrodes were used in 10 dogs to allow a qualitative assessment of conduction during ischemia and reperfusion. Eight of these 10 dogs survived a 10-minute period of ischemia. Six of the surviving dogs demonstrated reperfusion arrhythmias.

Conduction slowing on composite electrograms was manifest by a progressive fractionation of the electrogram, resulting in delayed electrical activity. This was only seen in electrograms recorded from the ischemic site. The degree of fractionation was always closely correlated with ectopic activity. Thus, after occlusion of the LAD, the amount of fractionation increased and became maximal during the early arrhythmic period and then declined along with the arrhythmias as ischemia progressed. Reperfusion led to a dramatic reemergence of delayed electrical activity and a simultaneous return of arrhythmias. This course of events is illustrated in figure 3. Panel A was recorded immediately before occlusion. The composite electrogram at this time consisted of a discrete narrow complex, indicating uniform, rapid conduction over all the contact points. Panel B was recorded at 7 minutes of ischemia during the arrhythmic period. The third paced beat was followed by a premature complex on the ECG, while the corresponding composite electrogram revealed extensive fractionation with delayed electrical activity spanning the entire interval between the paced beat and the premature ectopic beat. At 9 minutes of ischemia (panel C) the arrhythmias abated and extensive fractionation of the composite electrogram was no longer observed. Panel D was recorded during reperfusion. The occlusion was released at the arrow in the upper trace. The seventh paced beat was followed by a single ectopic beat while the ninth paced beat was followed by a short run of ventricular tachycardia. The corresponding electrograms (arrows in lower trace) demonstrated increased delayed, fractionated electrical activity compared with the period immediately preceding reperfusion (first three cycles of panel D). This reemergence of delayed electrical activity occurred before the onset of the arrhythmias and during the period of ventricular tachycardia, continued to span the electrical diastolic interval. After ectopic activity subsided, the electrogram rapidly resumed its preocclusive configuration.

In figure 3 the nature of the delayed, fractionated electrical activity during reperfusion was not clear. It was difficult to determine whether the electrical activity represented delayed depolarization activity and thus true delayed conduction, or merely electrogram T wave. However, additional experiments showed that the reemergence of delayed electrical activity represented true depolarization activity, as illustrated in figure 4. Panel A was recorded immediately before occlusion and again a discrete narrow electrogram

![Figure 2](http://circ.ahajournals.org/doi/abs/10.1161/01.CIR.61.1.178?journalCode=circ)

**Figure 2.** The establishment of delayed conduction in regions in which no electrical activity was identifiable at 10 minutes of ischemia. Each panel is an oscilloscope trace of a lead II ECG and three bipolar electrograms recorded from different regions of the subepicardium. Panel A was recorded immediately before occlusion. Panels B and C were recorded at 5 and 8 minutes of ischemia. Note the increase in conduction delay and progressive decrease in electrogram amplitude with continued ischemia so that by 10 minutes (panel D) no intrinsic deflections could be identified. However, by 5 seconds of reperfusion (panel E) the intrinsic deflections of the electrograms have reemerged and each again demonstrates conduction delay when compared with control panel A. With progressive reperfusion (panel F), conduction continues to improve and the electrograms return to control.
Figure 3. Conduction characteristics during ischemia and reperfusion using a composite electrode. Each panel is a lead II ECG (above) and a composite electrogram (below). Ischemia was characterized by an initial marked fractionation of the composite electrogram which maximized during the arrhythmic period (panel B, third complex). However, with progressive ischemia, arrhythmias abated and extensive electrogram fractionation was no longer observed (panel C). Reperfusion was characterized by a sudden increase in fractionation of the composite electrogram (panel D), which corresponded with a return of arrhythmias. See text for details.

Figure 4. The reemergence of delayed, fractionated electrical activity during reperfusion. Each panel consists of a lead II ECG (above) and a composite electrogram (below). Note that the composite electrogram shows delayed, fractionated electrical activity during the arrhythmic period (panel B), disappearance of fractionation during the quiescent period (panel C) and a reemergence of delayed, fractionated electrical activity with reperfusion (panel D). Furthermore, as shown in the lower trace of panel D, the newly emerged delayed electrical activity moves toward the intrinsic deflection of the electrogram with progressive reperfusion, indicating this electrical activity results from depolarization of slow conducting tissue and not electrogram T wave. See text for details. Pacemaker artifact precedes each p wave.
complex was evident. At 4 minutes of ischemia (panel B), the arrhythmic phase was present and the second paced beat was followed by two ectopic beats. The electrogram of the paced beat, immediately before the ectopic beats, showed continuous fractionation that spanned the interval between the paced and ectopic beats. At 9 minutes of ischemia, the early arrhythmic period subsided and very little delayed, fractionated electrical activity was observed.

Panel D is a divided but continuous trace of the reperfusion period. The occlusion was released at the arrow in the upper trace and within 2 seconds, a short run of ventricular tachycardia occurred. The electrogram preceding each set of ectopic beats revealed the presence of delayed electrical activity that was not present during the late ischemic period. This was seen most clearly in the tenth and sixteenth cycles, where a small electrical spike (arrows) preceded ectopic activity. In the lower trace, ectopic activity was absent and the presence of newly emerged delayed electrical activity was even more apparent on the electrogram. These electrical spikes (marked in each subsequent cycle by a small arrow) revealed a progressive movement toward the intrinsic deflection of the electrogram with reperfusion. This was demonstrated by a decrease in the coupling interval (shown under the electrogram) from 200 msec to 120 msec over 16 beats. The coupling interval was measured between the onset of the intrinsic deflection of the composite electrogram and the peak of the indicated electrical spike. The fact that the newly emerged electrical spikes moved toward and eventually converged with the intrinsic deflection of the electrogram with reperfusion, is consistent with the notion that these spikes represented a reemergence of depolarization activity arising from regions of slowly conducting tissue.

Discussion

After the work of Harris and Rojas,1 numerous investigators have confirmed malignant ventricular arrhythmias appearing within the first few minutes of occlusion and gradually diminishing with progressive ischemia.4, 5, 14 Scherlag et al.14 demonstrated that the early occultive arrhythmias were exacerbated by rapid atrial pacing and were abolished during vagally induced atrial arrest, leading these investigators to discount enhanced automaticity as the mechanism responsible for the early occultive arrhythmias. Recently, several studies have shown marked slowing and fractionation of conduction through acutely ischemic myocardium, establishing the prerequisites for reentry.11-14

Although reentry is generally regarded as the most plausible explanation for the early occultive arrhythmias, the mechanisms underlying the re-emergence of arrhythmias with reperfusion are less clear. Experiments on the role of enhanced automaticity during reperfusion have yielded conflicting results. In dogs with complete AV block, Levites et al.8 studied the idioventricular pacemaker rate and the effects of sudden termination of a 30-second period of rapid ventricular pacing on the time for ventricular escape to occur as indices of ventricular automaticity. Neither of these parameters showed evidence of enhanced automaticity during reperfusion after 15 minutes of ischemia. However, in a more recent study, Penkoske et al.9 demonstrated an accelerated idioventricular rate in vagally arrested cats reperfused after 35 minutes of ischemia. Furthermore, they noted that rapid atrial pacing suppressed the arrhythmias of reperfusion and concluded that enhanced automaticity may play a role in the initiation of reperfusion arrhythmias. However, since the idioventricular rates (188 beats/min) were not sufficient to account for the arrhythmias (250-300 beats/min), they concluded that other mechanisms for the arrhythmias could also have been operative.

In the present study, we saw no evidence for enhanced automaticity. When pacing was terminated simultaneously with reperfusion, the result was a slow idioventricular escape rhythm that was not significantly different from the preocclusive rate. Furthermore, faster heart rates (220 beats/min) potentiated the arrhythmias of reperfusion, while slower rates had a protective effect. Thus, we found that the arrhythmias of reperfusion behaved similarly to the arrhythmias of early ischemia with respect to varying heart rate. Since faster pacing rates would be expected to suppress automatic foci,20 our results suggest that mechanisms other than enhanced automaticity account for the reperfusion arrhythmias observed in dogs after short periods of ischemia, in agreement with the work of Levites et al.8 The reasons for the discrepancy between the present findings and those of Penkoske et al.9 are not clear but may be due to differences in species, anesthesia or duration of ischemia.

Since reentry is dependent upon slow, nonuniform conduction, we analyzed the nature of conduction during ischemia and reperfusion. We observed significant ischemic zone conduction delay in the subepicardium (mean 24.4 msec, range 5-55 msec) while only minimal delay appeared in the subendocardium (mean 6.3 msec, range 2-14 msec). This is consistent with the work of Scherlag et al.,14 who compared the electrograms of the subendocardial, subepicardial and intramural layers. They found the greatest delays in the subepicardial layers and inferred that reentry occurs in that region. This presumably results from the additive effects of slow conduction through deeper intramural layers as well as the subepicardial layers themselves.

The conduction delay that occurs as a consequence of ischemia is promptly abolished with reperfusion. In cats subjected to 35 minutes of ischemia, Penkoske et al.9 demonstrated that within 60 seconds of reperfusion, conduction time from the endocardial to the mid-myocardial regions of the ischemic zone returned to control while the residual delay in the epicardial region markedly improved. We also demonstrated a prompt reversal of the ischemia-induced conduction delay. In every experiment, a rapid return toward normal conduction was observed on the local bipolar elec-
trograms such that by 10 seconds of reperfusion only 10.2% of the ischemia-induced delay was observed in the subepicardium and no delay was observed in the subendocardium. Regardless of the region sampled or the amount of delay observed during ischemia, a further delay of conduction was never observed during reperfusion.

The composite electrode, with its multiple contact points, has proved to be a valuable method for detecting areas of markedly delayed conduction by recording delayed, fractionated electrical activity.\(^4\) The recording of delayed, fractionated electrical activity from the epicardium in the present study always correlated well with the time course of arrhythmias. Thus, as shown in figures 3 and 4, the early arrhythmic period was marked by delayed, fractionated electrical activity that spanned the interval between the paced and ectopic beats, while the quiescent period demonstrated little fractionation. Reperfusion led to a dramatic reemergence of fractionated electrical activity, which was associated with a return of arrhythmias. Furthermore, the newly emerged electrical complexes moved toward the intrinsic deflection of the electrogram with progressive reperfusion (fig. 4). This indicates that this electrical activity resulted from a reemergence of slow conducting wave fronts. Thus, as conduction within the reperfused tissue improved, less and less delayed activity was recorded. Delayed electrical activity, spanning the interval between paced and ectopic beats, is strongly suggestive of a reentrant mechanism.\(^8\)

In the present experiments, the frequency of ectopic activity reached a maximum within the first 6–8 minutes and then declined, leading to an ectopia-free quiescent period by 10 minutes of ischemia. Scherlag et al.\(^4\) attributed the onset of the quiescent period to a paradoxical improvement in conduction delay with progressive ischemia such that sufficient delay to sustain reentry was no longer present. They reported electrograms that displayed less conduction delay at 30 minutes of ischemia than during the early arrhythmic period. However, since the arrhythmic period is generally over in 10–15 minutes,\(^1\) any mechanism that causes a decline in arrhythmias should manifest itself by this time. In the present study, an improvement in the ischemia-induced conduction delay on bipolar electrograms was never observed after the termination of the arrhythmic period. Instead, a progressive decrease in electrogram amplitude occurred, which in many cases continued until no electrical activity was recorded (fig. 2).

In the intact porcine heart, Downar et al.\(^7\) demonstrated that ischemia led to a decrease in the upstroke velocity and amplitude of epicardial transmembrane action potentials, which often continued to total unresponsiveness of the fiber. Thus, in the present study, electrodes that recorded a complete loss of amplitude during ischemia were probably positioned in areas in which a severe depression or unresponsiveness of fibers had occurred as a result of ischemia. The decrease in amplitude of the bipolar electrograms and the disappearance of delayed, fractionated electrical activity on the composite electrograms suggest that the quiescent period results not from an improvement in conduction, but rather from a further deterioration of tissue responsiveness with resultant block of reentrant pathways. Since reperfusion promptly restores electrical activity in fibers rendered unresponsive by ischemia,\(^7\) it is likely that reperfusion may also transiently reestablish the conditions necessary for reentry. In the present study, reperfusion at 10 minutes of ischemia resulted in the reemergence of delayed, fractionated electrical activity in the composite electrograms (figs. 3 and 4) along with an increase in the amplitude of delayed electrical complexes in the close bipolar electrograms (fig. 2). Thus, it appears that reperfusion reestablishes slow conduction through severely depressed regions, allowing reentrant pathways to form again, resulting in the reemergence of ectopic activity.

We did not record composite electrograms from the endocardium or middle layers of the myocardium, so fractionated activity may have resulted in reentrant excitation during ischemia or reperfusion in these regions as well as the epicardium. However, since conduction delay increases from endocardium to epicardium during ischemia,\(^14, 22\) the amount of delayed, fractionated activity necessary to produce reentry would probably be found in the more superficial layers. The precise localization of the reentrant pathways responsible for both ischemia and reperfusion arrhythmias will require further investigation.

References

Characteristics of Reflection as a Mechanism of Reentrant Arrhythmias and Its Relationship to Parasystole

CHARLES ANTZELEVITCH, PH.D., JOSÉ JALIFE, M.D., AND GORDON K. MOE, M.D., PH.D.

SUMMARY A model of "reflection" was developed in a sucrose gap preparation of Purkinje fibers. In this preparation, a driven impulse on the proximal side of a sucrose gap is electrotonically transmitted after a delay to the tissue distal to the gap. When the delay is long enough, electrotonic transmission in the reverse direction over the same blocked segment can reexcite the proximal segment. Frequency-dependent alterations of patterns of ectopic activity were qualitatively similar to those of a parasystolic model and to those described in previous in vivo demonstrations presumed to represent circus movement reentry. Moderate changes of frequency or in the degree of block were shown to convert a manifest bigeminal rhythm to a trigeminal or more complex rhythm with or without intervening periods of silence. Our observations suggest that reflection and parasystolic pacemaker activity are examples of a continuous spectrum of ectopic impulse generation.

ECTOPIC IMPULSE FORMATION in cardiac tissue must be caused either by reentry or pacemaker activity, but each mechanism has subclasses. The term reentry usually implies a circuit — one-way block in one of two parallel pathways permits passage of an impulse over one pathway, and a retrograde passage of the same impulse, after a conduction delay, over the other pathway. But another kind of reentry, to which the term "reflection" has been applied,1,2 can be readily demonstrated in isolated bundles of cardiac tissue. For example, in a false tendon in which an area of depressed conductivity has been induced by current pulses of long duration, as in the experiments of Wennemark et al.,3,4 or by the impedance of a sucrose gap,5 a driven response at one end of the fiber may induce a response beyond the area of block, but only after a delay so long that recovery of excitability has already occurred in the driven side, permitting a recurrent response (or reentry) of the driven end. Reflected responses have been observed in Purkinje fiber preparations exposed to high K+ by Wit et al.1 They also appear to occur in cultured strands of chick heart tissue.6

The term reflection has previously been used to describe reentry in a linear bundle of conducting tissue, with the implication that a circuitous pathway at the microscopic level might be responsible.5,2 In the context of the present study, electrotonic transmission across an inexcitable segment of tissue is more likely than a microcircuit in the depressed area, particularly in the sucrose gap experiments. This possibility was suggested to us by C. Mendez (personal communication), and has been briefly considered by Cranefield.3

Pacemaker activity is, of course, an inherent property of the specialized conducting tissue of the ventricle, requiring only the protection of entrance block to permit its occasional expression in the form of parasystolic arrhythmias, or a sufficient elevation of its intrinsic frequency to become the dominant pacemaker, as in an episode of ventricular tachycar-
Electrophysiology of coronary reperfusion. A mechanism for reperfusion arrhythmias.
D K Murdock, J M Loeb, D E Euler and W C Randall

_Circulation_. 1980;61:175-182
doi: 10.1161/01.CIR.61.1.175

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1980 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/61/1/175.citation

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org//subscriptions/