Dissimilarities in the Electrophysiological Abnormalities of Lateral Border and Central Infarct Zone Cells after Healing of Myocardial Infarction in Cats

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SUMMARY. We studied the characteristics of an electrophysiological border zone detected after healing of experimental myocardial infarction in cats. Thirty-two isolated left ventricles were studied in tissue bath 2–7 months after distal left coronary artery ligation. Action potentials were recorded from endocardial ventricular muscle cells in normal, lateral border and central infarct zones. Action potential duration was prolonged in central infarct zone cells, while action potentials of lateral border zone cells had the shortest duration. Ventricular muscle cells in the border zone also had lower resting potential, action potential amplitude and Vmax. Slowly rising action potentials (Vmax < 20 V/sec) were noted in central infarct zone cells, but more consistently in border zone cells. Functional refractory period of cells in central infarct zone was significantly longer than that recorded from border and normal zone cells. Post-repolarization refractoriness occurred in the majority of border zone cells. Failure of a border zone cell to respond to a premature stimulus during repetitive activity was observed in ten of the 22 preparations in which repetitive activity could be induced. Furthermore, when the coupling interval between driving and premature stimuli was shortened, border zone cells were first to fail to be excited by the premature stimulus. These data indicate that conduction was impaired in the border zone, whereas normal conduction was still possible in central infarct and normal areas. The electrophysiological abnormalities in the endocardial lateral border zone cells of the healed myocardial infarction appear to be the most severe, and the border zone may play an important role in chronic electrophysiological instability observed both in situ and in vitro (Circ Res 51: 486–493, 1982)

DURING acute ischemia and early infarction, a border zone composed of damaged but viable myocardium surrounding a central zone of irreversible injury or infarction has been identified ultrastructurally (Cox et al., 1968; Page and Polimeni, 1977; Kloner et al., 1979), histochromically (Fishbein et al., 1980), and electrophysiological (Kléber et al., 1978; Anderson et al., 1980). Hearse et al. (1977), in a recent study of acute ischemia in the dog, described a border zone of reduced blood flow, elevated lactate, and sharply decreased high energy phosphate content. A gradual change in electrical potential from normal to ischemic tissues has been observed in acutely ischemic pig hearts (Kléber et al., 1978). Anderson et al. (1980) demonstrated marked variations in electrophysiological responses developed in normal, border, and infarct zones after acute coronary occlusion. Although these studies have generated considerable information on the characteristics of border zone cells in acute experimental ischemia, few data are available on the border zone of healing or healed myocardial infarction. There are indications that injury at the border zone persists during the healing process after infarction. For instance, the overall characteristics of the border zone do not change after reperfusion (Janse et al., 1979), and lipid accumulation persists in border zone cells 72 hours after acute myocardial infarction (Page and Polimeni, 1977; Kloner et al., 1979). Fishbein et al. (1980), using histochemical techniques, demonstrated that the border and central infarct zones continuously change in size and character up to 72 hours after acute coronary occlusion in the rat.

We have developed an experimental myocardial infarction model in the cat which maintains electrophysiological abnormalities after complete healing of infarction (Myerburg et al., 1977; Myerburg et al., 1982a, 1982b). The present study was designed to determine whether an electrophysiological endocardial border zone persists 2 months or longer after acute myocardial infarction in the cat. Our data indicate that a surviving endocardial border zone over the lateral borders of the infarct zone can be detected after healing of myocardial infarction, and that its characteristics differ from those reported during acute ischemia and early infarction.

Methods

Adult conditioned domestic cats (2.3–3.2 kg), anesthetized with sodium pentobarbital (30 mg/kg, ip), were used in this study. Acute myocardial infarction was created by single-stage ligation of 2 or 3 distal tributaries of the left anterior descending and left circumflex coronary arteries which predictably produced infarcts 5–15% of the left ventricular muscle mass; these techniques are described in detail elsewhere (Myerburg et al., 1977). A 6-lead electrocardiogram was recorded prior to the thoracotomy and before and after ligation of the coronary arteries. Surgical
mortality was less than 15%, and the cats were maintained in a colony for 2-7 months. Cardiac rhythm was determined during anesthesia by electrocardiogram 15-30 days prior to terminal study. On the day of terminal studies, the healed myocardial infarction (HMI) cats were anesthetized with sodium pentobarbital (20-30 mg/kg, ip), and the electrocardiogram was again recorded. After thoracotomy, hearts were removed and then dissected in cool, oxygenated Tyrode's solution of the following composition (mm): NaCl = 129, NaHCO3 = 20, dextrose = 5.5, KCl = 4.0, NaH2PO4 = 1.8, MgCl2 = 0.5, CaCl2 = 2.7; pH = 7.35.

Preparations of left ventricle obtained by techniques previously reported (Myerburg et al., 1977) were mounted, endocardial surface up, with stainless steel pins, to the bottom of a Lucite tissue bath. Warmed (37°C) Tyrode's solution equilibrated with 95% O2-5% CO2 superfused the tissue at a rate of 10 ml/min. Driving stimuli at cycle lengths ranging from 500 to 1000 msec were delivered to the left bundle branch through Teflon-coated silver wire electrodes, 0.01 inch (0.254 mm) in diameter. Pulse duration was 3 msec and current intensity was 1.5 times diastolic threshold.

Whereas visible scars were almost always present over the infarcted areas, surface electrograms also were used to delineate areas of electrophysiological abnormality (Bassett et al., 1976; Myerburg et al., 1977). Surface electrogram was recorded through fine silver wire bipolar electrodes, 0.01 inch (0.254 mm) in diameter, differentially amplified and displayed on a dual beam oscilloscope screen.

After identification of endocardial areas with abnormal surface electrogram recordings, transmembrane potentials of ventricular muscle cells from specific regions of interest were recorded using standard microelectrode techniques previously reported in detail (Myerburg et al., 1972). The glass microelectrodes filled with 3 M KCl (resistance 10-30 MΩ) were connected through Ag-AgCl junctions to high impedance electrometers with input capacity neutralization (Bioelectric Instruments, NFI). The amplifier outputs were recorded through fine silver wire bipolar electrodes, 0.01 inch (0.254 mm) in diameter, differentially amplified and recorded on film. Action potentials were recorded from endocardium overlying and bordering areas of healed myocardial infarction and from normal areas in the same heart. There were instances of difficult impalement, particularly in areas close to the center of the infarction. This may be due to interstitial fibrosis, which interferes with microelectrode manipulation.

Grids (6-12 mm2) were constructed to provide a consistent sampling technique to sample cells from normal, border, and central infarct myocardial tissues. This sampling technique was reported in detail elsewhere (Myerburg et al., 1977, 1982a, 1982b). Depending on the interelectrode distance (0.5-1.0 mm), 12-30 cells distributed evenly among the three zones were sampled within each recording grid. Premature stimuli were delivered to various sites on the endocardial surface both to measure functional refractory period and to initiate sustained ventricular activity. Premature stimuli (S2) were delivered at 2.0 times late diastolic threshold strength after every eighth drive stimulus (S1).

Functional refractory period was defined as the minimum interval between response (R1) to S1 stimulus and the earliest elicited propagated response (R0) to premature S2 stimulus (Myerburg et al., 1970a). In experiments in which initiation of sustained ventricular activity was attempted, premature stimuli were delivered to sites on 1- to 2-mm grids overlying the healed infarction and surrounding tissues. S1-S2 intervals were systematically varied, as was the intensity of S2 (from 2 to 10 times diastolic threshold).

Action potential characteristics measured from photographic records included resting potential (RP), overshoot (OS), action potential amplitude (AP amplitude) and maximum rate of rise of phase 0 depolarization (Vmax). Action potential duration at 50% and 90% repolarization (APD50 and APD90) and functional refractory period were measured on-line (Myerburg et al., 1970b; Gelband et al., 1970). Vmax was electronically differentiated, using a calibrating signal of known voltage (20-30 μV) and duration (Bigger et al., 1968).

The left ventricular preparations were fixed in 10% neutral-buffered formaldehyde after electrophysiological studies, and sections were obtained from control and infarcted areas. Paraffin-embedded sections (5 μm thick) were stained with Masson's trichrome and hematoxylin and eosin. Data are expressed as mean values ± SE. For comparisons of the differences between mean data from central infarct, border, and normal zones, an analysis of variance was employed (Steel and Torrie, 1960). In all cases, P < 0.05 was considered significant.

Results

Thirty-two cats with experimental myocardial infarction were studied 2-7 months after undergoing coronary artery ligation. Pale retracted scars were distinctly visible on the endocardial surface of the left ventricle in nearly all preparations. The infarctions involved the base of the anterior papillary muscle, plus variable involvement of the apex and the inter-papillary portion of the free wall of the left ventricle. In some preparations, the base of the posterior papillary muscle and lower septum were also infarcted. Histologically, subendocardial scars were observed in all preparations (Fig. 1). At the periphery of the scar, interdigitation between surviving muscle cells and scar tissue often was observed. The surviving bands of subendocardial fibers overlying the infarction scars appeared histologically normal, as did the subendocardial cells overlying the lateral “border zone” of interdigitation.

Thirteen of the 32 HMI cats (41%) had in situ ventricular ectopic activity during either or both of the monitoring periods described above, while the remaining cats were free of arrhythmias. All 13 arrhythmic cats had premature ventricular contractions, and four of them also had more complex arrhythmias including ventricular trigeminy and recurrent ventricular tachycardia (Fig. 2). Automatic activity also occurred in 26 of the 32 isolated ventricular preparations in tissue bath. In comparison, none of the control noninfarcted cat preparations required cycle lengths shorter than 800 msec to overdrive automatic activity. There appeared to be a direct correlation between arrhythmias in situ and automatic activity in the tissue bath. Eleven HMI cats that demonstrated in situ arrhythmias required drive cycle lengths of 630 msec or less to overdrive spontaneous activity in the tissue bath. Conversely, of the six preparations that did not require cycle lengths shorter than 1000 msec to overdrive automatic activity in vitro, none demonstrated in situ arrhythmias.

Action potentials were recorded at the maximum cycle length permitting capture. Figure 3 shows representative records from three preparations driven at cycle lengths of 630, 800, and 1000 msec. The recordings are from endocardial cells overlying normal, lateral border, and central infarct areas. APD50 and
FIGURE 1. Histopathology of healed myocardial infarction. The histological section, obtained from a cat killed 3 months after myocardial infarction, was stained with Masson's trichrome. Note the dense scar formed in the infarcted area. At the periphery of the scar, interdigitation between surviving muscle cells and scar tissues was observed. This area represents the border zone between healed infarction and presumably normal tissues.

APD_{90} are noted next to each action potential. Consistently, action potentials of lateral border zone cells were characterized by short APD_{50} and APD_{90}. In contrast, cells overlying the central infarct generated action potentials with long APD_{50} and APD_{90}, compared to those recorded in normal and border zones. Similar patterns of action potential configuration abnormalities (i.e., prolonged action potential duration in central infarct zone cells and shortened action potential duration in border zone cells) occurred at other drive cycle lengths (from 500 to 1000 msec).

Figure 4 illustrates representative action potentials recorded at 12 sites within a sample grid (12 mm²) straddling areas of infarct and surrounding normal tissues from a left ventricular preparation 3 months after infarction. For each site, the action potential shown corresponds to the second cell layer recording. Action potentials of configuration similar to those recorded from normal, nonoperated cat hearts (Myerburg et al., 1977) were noted at the normal zone of the infarcted heart (sites A-1, A-3, A-4, B-1, C-1). Prolonged action potentials were recorded in the central infarct zone (sites C-2, C-3, C-4) of the same preparation. For example, APD_{90} of a central infarct zone cell (site C-2) was 210 msec, while that of a normal zone cell (site A-1) was 128 msec. However, other action potential characteristics (RP, Os, AP amplitude, and V_{max}) were similar in cells of the normal and central infarct zones. As the electrode was moved away from the central infarct area into the border zone (sites A-2, B-2, B-3, B-4), action potential duration shortened dramatically. In addition to the abnormally shortened APD_{50} and APD_{90}, action potentials recorded in the endocardial lateral border zone had a lower RP, AP amplitude, and V_{max}. In other hearts, action potentials with slow upstroke velocity (V_{max} ≤ 20 V/sec) were also recorded in border zones, less frequently in central infarct zones, but never in normal zones. Action potential properties of cells in the normal, lateral border, and central infarct zones at various stimulus cycle lengths are summarized in Table 1. Data from each preparation were compiled from recordings from at least three sampling grids (6-12 mm²). Over 70% of the cells in a given region exhibited the electrophysiological properties that were representative of that region.

Premature stimuli were used to determine functional refractory periods of cells in the normal, lateral border, and central infarct zones at basic driving cycle lengths of 500, 630, and 800 msec. An average of 15 cells per preparation, distributed evenly among the three zones, were monitored on the endocardial sur-
CAT 293 - 6 Months After M.I.

CAT 365 - 3 Months After M.I.

CAT 474 - 6 Months After M.I.

FIGURE 2. Representative ECG rhythm strips. Selected ECGs demonstrate spontaneous ventricular ectopic activity in three of the experimental cats. The abnormalities include single premature ventricular beats (cat 293), trigeminy (cat 365), and recurrent ventricular tachycardia (cat 474). The calibration represents 0.20 sec.

face of the remaining 26 preparations. Table 2 summarizes the functional refractory period data from cells of normal, lateral border, and central infarct zones, recorded during stimulation at various basic cycle lengths. Functional refractory period of cells in central infarct zone was significantly longer than that recorded from cells in lateral border and normal zones, at all three drive cycle lengths. This is consistent with the action potential duration data (APD_{50} and APD_{90} were longest in central infarct zone cells). However, there was no significant difference between the functional refractory period of normal and border zone cells, even though action potentials of border zone cells were of significantly shorter duration. In the majority of endocardial lateral border zone cells studied, full repolarization was attained before the cells could respond to a premature stimulus.

![Figure 3](image_url)

FIGURE 3. Representative recordings of transmembrane action potentials from normal, border, and central infarct zones of healed myocardial infarction. Action potential durations printed adjacent to each action potential recording were measured at 50% repolarization (APD_{50}) (top number) and 90% repolarization (APD_{90}) (bottom number). Panels A, B, and C demonstrate data recorded from preparations driven at cycle lengths of 630 msec (A), 800 msec (B), and 1000 msec (C). Note that the border zone cells consistently demonstrate the shortest action potential duration, while cells overlying the central infarct show prolongation of action potential duration. Horizontal calibration = 50 msec, vertical calibration = 20 mV.

![Figure 4](image_url)

FIGURE 4. Cellular electrophysiology of normal, border, and infarct zone cells 3 months after myocardial infarction (MI). The surface of the MI is indicated by the shaded area. The grid overlaps the border between infarct zone and surrounding normal areas. The interelectrode distance between impalements was 1.0 mm in both directions (i.e., A-C, 1-4) and the recordings in the grid represent the second impalement from the surface of the preparation at each site. The schematic and grid illustrated are not in scale to one another. In addition to the short action potential duration, the action potential of ventricular muscle cells recorded in the border zone (A-2, B-2, B-3, B-4) had a lower resting potential amplitude and V_{max}. Recordings from the central infarct zone (C-2, C-3, C-4) demonstrate a prolongation of action potential duration, compared to that recorded in normal zone cells (A-1, A-3, A-4, B-1, C-1). See Table 1 for summary of electrophysiological data. Cycle length of stimulation = 630 msec. Horizontal calibration = 50 msec, vertical calibration = 20 msec.
Multiple sites of stimulation were used in attempting to initiate sustained ventricular activity (i.e., a train of repetitive responses of up to 1 minute in duration) or repetitive response (i.e., 1-5 repetitive depolarizations). These repetitive activities could be induced by delivering a premature stimulus at central infarct or border zone sites. In 22 of the 32 HMI preparations, sustained ventricular activity or repetitive response was induced. In normal cat preparations, sustained ventricular activity was never induced by similar pacing technique, and we only observed repetitive responses in three normal preparations. In normal cat preparations, stimulus to a premature stimulus during repetitive activity was observed in 10 of the 22 preparations in which repetitive activity could be induced. In other instances, such as the experiment demonstrated in Figure 5 (panels C and D), premature responses were recorded from cells in normal (V-1), border (V-2), and central infarct (V-3) zones when the stimulus coupling interval of S1–S2 was sufficiently long. However, as shown in Figure 5C, the greatest delay of activation by the premature stimulus occurred at a cell (V-2) within the lateral border zone, while premature activation of the recording site (V-3) within the central infarct zone was delayed to a lesser degree. When S1–S2 coupling interval was shortened (Fig. 5D), border zone cells were the first to fail to be excited by a premature stimulus. This may indicate that impaired conduction through the border zone occurred after premature stimulation while normal conduction was still possible in central infarct and normal areas.

### Table 1

<table>
<thead>
<tr>
<th>CL (msec)</th>
<th>Zone</th>
<th>Resting potential (mV)</th>
<th>Overshoot (mV)</th>
<th>Action potential amplitude (mV)</th>
<th>APD&lt;sub&gt;90&lt;/sub&gt; (msec)</th>
<th>APD&lt;sub&gt;90&lt;/sub&gt; (msec)</th>
<th>V&lt;sub&gt;max&lt;/sub&gt; (V/sec)</th>
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<tr>
<td>500 (6)</td>
<td>N</td>
<td>79.5 ± 0.7</td>
<td>25.3 ± 0.4</td>
<td>104.7 ± 0.9</td>
<td>84.8 ± 5.8</td>
<td>110.9 ± 13.7</td>
<td>167.0 ± 22.8</td>
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<td></td>
<td>B</td>
<td>72.7 ± 2.3†</td>
<td>22.2 ± 1.3†</td>
<td>94.4 ± 3.8†</td>
<td>62.5 ± 8.6†</td>
<td>92.2 ± 16.6†</td>
<td>115.8 ± 16.5†</td>
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<tr>
<td></td>
<td>I</td>
<td>81.1 ± 1.1†</td>
<td>27.4 ± 0.9</td>
<td>108.5 ± 1.7</td>
<td>104.7 ± 7.7*</td>
<td>135.3 ± 17.8*</td>
<td>168.3 ± 15.5*</td>
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<tr>
<td>630 (13)</td>
<td>N</td>
<td>81.0 ± 0.8†</td>
<td>26.0 ± 0.4</td>
<td>107.5 ± 1.0</td>
<td>92.7 ± 5.6</td>
<td>135.0 ± 6.8‡</td>
<td>156.2 ± 8.6</td>
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<tr>
<td></td>
<td>B</td>
<td>74.6 ± 1.3‡</td>
<td>24.8 ± 0.8‡</td>
<td>99.8 ± 2.0‡</td>
<td>64.8 ± 5.7‡</td>
<td>111.7 ± 8.3‡</td>
<td>134.9 ± 11.1‡</td>
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<td></td>
<td>I</td>
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<td>26.7 ± 0.5</td>
<td>108.6 ± 1.4</td>
<td>110.4 ± 5.4*</td>
<td>163.0 ± 7.6*</td>
<td>157.8 ± 10.3</td>
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<tr>
<td>800 (7)</td>
<td>N</td>
<td>78.3 ± 0.6</td>
<td>23.9 ± 1.0</td>
<td>102.2 ± 1.0</td>
<td>88.7 ± 6.5</td>
<td>130.2 ± 4.8</td>
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<td></td>
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<td>70.8 ± 2.0†</td>
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<td>70.2 ± 8.3†</td>
<td>106.1 ± 5.9†</td>
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<td>I</td>
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<td>25.1 ± 0.5</td>
<td>103.5 ± 2.0</td>
<td>120.1 ± 6.0*</td>
<td>166.1 ± 8.7*</td>
<td>146.2 ± 11.0</td>
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<td>26.1 ± 1.3</td>
<td>106.5 ± 2.5</td>
<td>98.1 ± 3.9</td>
<td>144.1 ± 4.2‡</td>
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<tr>
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<td>134.8 ± 10.9†</td>
<td>195.9 ± 16.1‡</td>
<td>142.3 ± 17.1</td>
</tr>
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</table>

* Significant differences from normal, via analysis of variance (P < 0.05).
† Significant differences from normal, via analysis of variance (P < 0.05).
‡ Significant differences from CL (500 msec), via analysis of variance (P < 0.05).

### Table 2

<table>
<thead>
<tr>
<th>CL (msec)</th>
<th>Normal zone (msec)</th>
<th>Border zone (msec)</th>
<th>Infarct zone (msec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>500 (6)</td>
<td>155.6 ± 10.4</td>
<td>160.5 ± 14.4†</td>
<td>186.9 ± 12.4*</td>
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<tr>
<td>639 (13)</td>
<td>168.0 ± 8.0</td>
<td>174.6 ± 8.8†</td>
<td>190.0 ± 10.6*</td>
</tr>
<tr>
<td>800 (7)</td>
<td>167.0 ± 13.9</td>
<td>164.0 ± 15.9†</td>
<td>204.7 ± 18.7*</td>
</tr>
</tbody>
</table>

* Significant differences from normal, via analysis of variance (P < 0.05).
† Significant differences from normal, via analysis of variance (P < 0.05).
Discussion

Little is known of the long-term electrophysiologic alterations in different zones of damaged cardiac tissue healed after experimental coronary artery ligation and resultant myocardial infarction. The present study demonstrates that there are dissimilar types of long-term action potential abnormalities recorded from central infarct zone cells and lateral border zone cells in cats after healing of infarction. Pockets of surviving endocardial border zone cells of healed myocardial infarction show significant reduction in resting potential, action potential amplitude, and V_max of endocardial lateral border zone cells. In panel C, the basic cycle length driving the preparation was 630 msec, and a premature stimulus was delivered at an S1-S2 interval of 159 msec to the left bundle branch. At this coupling interval, premature responses were initiated in all three cells. However, at a shorter coupling interval of 111 msec (Panel D), premature response to S2 occurred only at the normal (V-1) and central infarct (V-3) zone sites. Horizontal calibration = 100 msec; vertical calibration = 40 mV.

The increased nonuniformity in repolarization of normal, lateral border, and infarct zone cells could result in potential differences between the cells of two or three zones at any given time. This may give rise to intramyocardial current of sufficient magnitude to induce reexcitation of cells and account for the long-term abnormalities of cardiac rhythm in situ and electrical instability in vitro observed in this study. However, the low electrical resistance of the normal syncytium of myocardium does not favor a marked difference in potentials between contiguous areas (Mendez et al., 1969; Han, 1971; Sasyniuk and Mendez, 1971), and a gradual voltage gradient across infarct regions would not favor the development of sufficient current to induce reexcitation. Our finding that the shortest action potential duration was in the endocardial lateral border zone demonstrates that voltage gradients are not necessarily gradual in damaged myocardium.

The present study demonstrated that the duration of refractoriness of normal and infarct zone cells was consistent with their action potential durations and that infarct zone cells had the longest functional refractory period. However, the functional refractory periods of the lateral border zone cells often outlast the action potentials. This phenomenon has been reported in isolated His-Purkinje fibers excised after several hours of coronary artery occlusion (El-Sherif et al., 1974; Lazzara et al., 1975). Downar et al. (1977) also observed postrepolarization refractoriness in in-
tact porcine heart during acute ischemia. The time-dependent factor of refractoriness (Gettes and Reuter, 1974) may play a more prominent role in the recovery of excitability of border zone cells and may account for the fact that the refractoriness exerts the actual potential duration.

Hoffman and Rosen (1981) indicated that a properly timed premature stimulus may initiate reentrant excitation if the premature impulse is blocked at a certain site. As shown in this study, such a circumstance could arise in the border zone site when the preparation was stimulated rapidly. As the coupling interval of the basic and premature stimuli was reduced, premature activation of the recording site within the border zone occurred progressively later than it finally failed to respond. Impaired conduction into the lateral border zone also was observed during sustained ventricular activity induced by premature stimuli. Gettes and Reuter (1974) demonstrated that with resting potential similar to that obtained in border zone cells, shortening of the stimulus coupling interval caused progressive reduction in Vmax. Since conduction of impulses is related to the magnitude of action potential upstroke (Vassalle, 1977), conduction failure observed at certain sites in the border zone during sustained ventricular activity (rapid responses) could be related to the low resting potential and Vmax of its cells. It has been postulated that sustained ventricular activity in this model might result from reentrant excitation (Myerburg et al., 1982b). Our present observations suggest that the surviving endocardial lateral border zone may be a possible site of unidirectional block and may contribute to reentry. Horowitz et al. (1980) also identified the surviving border of previous infarctions as the site of origin of recurrent ventricular tachycardia observed in patients with chronic ischemic heart disease.

Although the initial damage to lateral border zone cells may be less than that to cells in central ischemic area, electrophysiological abnormalities caused by ischemia appear to persist in the border zone well beyond the early phase of myocardial infarction. Furthermore, electrophysiological abnormalities in the lateral border zone cells of the healed infarction appear to be the most severe. This is in contrast to the characteristics of the border zone cells during acute ischemia and early infarction (Cox et al., 1968; Fishbein et al., 1980). However, the role which the border zone plays in chronic electrophysiological instability persisting after healing of a myocardial infarction remains to be determined.

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