The Electrophysiologic Time-Course of Acute Myocardial Ischemia and the Effects of Early Coronary Artery Reperfusion

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SUMMARY
Bipolar potentials were recorded from intramural electrodes located within areas of acute myocardial ischemia in dogs. Alterations in bipolar potential electromotive force (EMF) and local activation times were measured at predetermined intervals up to 12 hours after coronary occlusion. Histochemical stains were used to correlate structural-biochemical changes with sites of electrophysiologic changes. In severely ischemic areas, bipolar potentials lost 50% of their preocclusion EMF within 30 min and 95% within six hours at which time all parameters stabilized. Lesser decreases in bipolar potential EMF were recorded in the peripheral areas of the infarct. Bipolar potential EMF increased at the junction of ischemic and normal myocardium. Activation time was delayed in ischemic areas but no correlation between the magnitude of delay and the degree of tissue ischemia could be established. Coronary reperfusion after 30 min, one hr, two hr and six hr of occlusion resulted in some return in bipolar potential EMF, decreasing as a function of duration between occlusion and reperfusion.

Variation in the degree of ischemia of different zones of injury within an acute myocardial infarction, as well as a different response of those zones to the return of blood flow, was shown.

Additional Indexing Words:
Bipolar potential
Histochemical enzyme stains
Intramural electrodes
Parietal Purkinje system
Purkinje activation
Ventricular activation time

The dysrhythmias accompanying acute myocardial infarction have received much attention in recent years from both the clinician and the experimental investigator.1–8 Several studies employing microelectrode techniques have demonstrated electrophysiologic alterations in the early stages of acute myocardial infarction.6–8 This technique, however, is limited in that only a few myocardial cells are studied and the relationship of activity in them to the electrical events occurring simultaneously in other regions of ischemic myocardium is not known. Epicardial surface electrodes have been used recently in experimental animals and in humans during cardiac surgery to identify areas of myocardial ischemia.9 This latter technique, however, is limited to a two-dimensional study of the area of ischemia and is incapable of differentiating between differing degrees of intramural myocardial ischemic injury. As a result of the limitations of both of these techniques and the relatively small number of previous studies, the alterations in electrophysiology which occur within different regions of an acute myocardial infarction during the first several hours following coronary artery occlusion are poorly understood. In the present study, intramyocardial (intramural) electrodes were used to evaluate early electrophysiologic alterations in acute myocardial infarction. This technique provides for the three-dimensional study of an evolving myocardial infarction because it 1) is capable of distinguishing between regions of ventricular wall which differ in the degree of ischemic injury, 2) allows repeated measurements within the same areas of ischemia throughout the period of study, and 3) is amenable to histologic correlation. This study was designed to characterize the electrophysiologic alterations which occur in ischemic myocardium following acute coronary

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artery occlusion and to establish the electrophysiologic time-course for different regions of an acute myocardial infarction. The effects of coronary artery reperfusion on the electrophysiologic parameters of local ischemic injury after varying intervals of coronary occlusion are also shown.

Methods

Sixteen normal dogs ranging in weight from 15 kg to 22 kg were anesthetized with intravenous sodium pentobarbital, 30 mg/kg. The blood pressure was recorded via a femoral artery catheter and was displayed, along with the lead II ECG, on an oscilloscope. Blood pH was maintained between 7.38 and 7.45 throughout each experiment. After tracheal intubation, a left lateral thoracotomy was performed and the heart was cradled in the pericardium to expose the left ventricle. The main diagonal branch of the anterior descending coronary artery was exposed and a snare was placed around it. The vessel was occluded for 10-15 sec to determine the resultant area of cyanosis and the occlusion was then released. Subsequently eleven intramural, multipoint electrode shafts were placed in regions both within and outside the boundaries of this cyanotic zone. The electrode shafts were placed in three rows across the myocardium approximately 1 cm apart. In any given animal, this method of electrode placement resulted in a variation in the position of different electrode shafts in relation to the central versus the peripheral areas of the cyanotic zone. A reference intramural electrode was placed in the right ventricle.

The recording methods used in this study have been reported in detail previously. Control bipolar electrograms were recorded from electrode terminals located 1 mm apart on each of the eleven electrode shafts. Each electrode shaft had a plastic hub attached just above the level of the most proximal electrode terminal. This resulted in the proximal terminal of each electrode shaft being positioned at the epicardium. The electrode terminals were coupled directly to a set of FET buffer amplifiers with an input impedance of 10^11 ohms and unity gain. The signals were subsequently amplified and recorded on magnetic tape at a speed of 7.5 inches/sec. The frequency response of the system was from 0.1 Hz to 2.5 kHz.

After recording control bipolar electrograms from all intramural electrode terminals and the reference electrode, the coronary artery was occluded and potentials were again recorded at the following intervals after occlusion: 30 min, 1 hr, 2 hr, 3 hr, 6 hr, and 12 hr. In eight dogs, after producing varying intervals of ischemia, the occlusion was released and the bipolar electrograms were recorded up to 12 hr following initial coronary occlusion.

Data were also recorded on photographic paper at a speed of 500 mm/sec. In these recordings, the fast component of the bipolar potential (representing local muscle depolarization) was used to determine local activation time in relation to the constant reference electrogram recorded from the right ventricle. The amplitude of the bipolar potential was then determined by measuring the distance in millimeters from the baseline to the point of maximum positive or negative deflection of the bipolar potential.

The animals were sacrificed at the end of the 12 hr experiments. The block of myocardium containing each electrode shaft was excised and immediately quick frozen with powdered dry ice. The tissue was stained for succinic dehydrogenase activity according to the method of Nachlas et al. and correlations were made between the electrophysiologic changes and the histochecmic sections.

Results

Effect of Coronary Artery Occlusion on Ventricular Activation Time

In each experiment, local activation time within the left ventricular wall prior to coronary artery occlusion was determined in relation to the reference electrogram recorded from the right ventricle. Coronary artery occlusion resulted in a progressive delay in the onset of activation in the area of myocardial ischemic injury (fig. 1). The control curve on the left in figure 1 represents the time of local activation at points along an electrode

![Figure 1](https://example.com/figure1.jpg)

**Figure 1**

*Alteration in local activation time in an area of myocardial ischemia. Bipolar electrograms were recorded from successive electrode terminals 1 mm apart along a single electrode shaft located in a transmural myocardial infarction. Terminal number 1 was located at the endocardium and terminal number 8 at the epicardium. Activation time is plotted in relation to the time of activation of a bipolar reference electrode in the right ventricle. The delay in local activation time with increasing duration of myocardial ischemia was typical of all experiments, although the degree of delay did not always reflect the degree of myocardial ischemic injury.*

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shaft prior to coronary occlusion. Thirty minutes after occlusion, the time of activation of each point was delayed 1-4 msec. This delay has increased at one hour after occlusion. After six hours the subendocardium showed no electrical activity due to advanced ischemia and the epicardial activation was delayed 11 msec. Similar changes in ventricular activation time in areas of myocardial ischemic injury were noted in all 16 experiments.

An attempt was made to establish a correlation between the quantitative changes in activation time and the degree or duration of myocardial ischemia. No consistent quantitative changes could be discerned, however, either on the basis of the duration of coronary artery occlusion or on the position of the monitoring electrode within the ischemic area (i.e., central versus peripheral area of ischemia). For example, in some areas, severe ischemic injury resulted in a delay in intramural activation of 20 msec, whereas other areas with similar degrees of injury exhibited only a 10 msec delay in activation.

**Effect of Coronary Artery Occlusion on Activation of the Purkinje System**

Purkinje activity was recorded frequently by the endocardial terminal of an electrode shaft. This activity occurred as a single, sharp deflection immediately preceding activation of the subendo-

![Figure 2](http://circ.ahajournals.org/)

**Figure 2**

*Preservation of parietal Purkinje System adjacent to subendocardial infarction. The times listed above electrograms represent the duration of coronary artery occlusion. No change in the amplitude of the Purkinje complex (peak to peak deflection) occurred despite its immediate proximity to a severe localized subendocardial infarction which is demonstrated by the large negative bipolar deflection. The progressive loss of the negative bipolar potential electromotive force (EMF) following coronary artery occlusion indicates the presence of subendocardial infarction. (Pj = Purkinje activation; mV = millivolt EMF).*

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Relationship between intramural location and absolute electromotive force (EMF) of bipolar potentials in normal myocardium. The absolute EMF of bipolar potential electrograms in normal myocardium increases as the wavefront moves from endocardium to epicardium. The bipolar potentials recorded at the endocardial level in all 16 animals before coronary artery occlusion are plotted at electrode terminal 1 on the abscissa (mean ± se). The control bipolar potentials recorded at each successive electrode terminal away from the endocardium are plotted at their respective positions on the abscissa (mean ± se).

Endocardium and epicardium. Similar differences in control subendocardial and subepicardial potentials have been reported in the hypertrophied right ventricular wall.\textsuperscript{12}

Myocardial ischemic injury was associated with a decrease in bipolar potential electromotive force (EMF) (fig. 4) except at the junction of ischemic and normal myocardium. The greatest decrease in bipolar potential EMF occurred within the first 30 min after coronary artery occlusion as demonstrated in figure 5. In this case, the electrode shaft was located within a transmural infarct of the free left ventricular wall. Prior to coronary artery occlusion (control curve), the bipolar potential EMF was 9 mV at the endocardium and 37 mV at the epicardium. By 30 minutes after coronary artery occlusion, the bipolar potential EMF had decreased at all terminals along the electrode shaft. As the myocardial infarction evolved, there was a progressive decrease in the bipolar potential EMF so that by 12 hours after coronary occlusion, only a small area in the subepicardium exhibited any measurable electrical activity.

An important variation in the slope of the control curve depicted in figure 5 was noticed early in the course of this experiment. By chance, approximately 20% of the electrode shafts traversed the anterior papillary muscle. Bipolar potentials recorded within the papillary muscle exhibited greater amplitudes than did those recorded at the base of the papillary muscle. A typical example of this observation is shown in figure 6. In this case, the first four terminals of the electrode were located within papillary muscle. This accounts for the lower control bipolar potential EMF at terminal 5 which was located at the junction of the anterior papillary muscle and the free left ventricular wall. Coronary artery occlusion resulted in a transmural infarct involving the anterior papillary muscle as evidenced by the fact that 30 minutes after coronary occlusion, all bipolar complexes exhibited a decrease in amplitude. This decrease was progressive so that by 1 hr after coronary occlusion, only the papillary muscle and the subepicardial area showed any measurable activity. After the 2 hr postocclusion recordings, no electrical activity was present at any of these electrode terminals for the remainder of the 12 hr experiment. The changes in bipolar potential EMF shown in figures 5 and 6 are typical of the results obtained in all 16 experiments.

In each experiment, several electrode shafts were placed in areas of the left ventricle which were not affected by ligation of the anterior descending coronary artery. No decrease in amplitude of the bipolar complexes occurred on any of these electrodes. However, electrode terminals situated at the junction of ischemic and normal myocardium showed an increase in bipolar potential EMF over their control values.

**Anatomic—Electrophysiologic Correlation**

The correlation between the electrophysiologic alterations and the anatomic changes which occurred following coronary occlusion is illustrated in

\begin{figure}
\centering
\includegraphics[width=0.5\textwidth]{figure3.png}
\caption{Relationship between endocardium and epicardium. Similar differences in control subendocardial and subepicardial potentials have been reported in the hypertrophied right ventricular wall.\textsuperscript{12}}
\end{figure}
ELECTROPHYSIOLOGY OF ACUTE ISCHEMIA

Figure 4

Bipolar electrograms recorded from a single transmural electrode shaft before coronary occlusion, 30 min after occlusion, and 30 min after coronary reperfusion (one hour after initial occlusion). Coronary occlusion resulted in a decrease in bipolar potential EMF and a delay in local activation at all points except at electrode sites 1-2 located at the endocardium. Coronary reperfusion resulted in both parameters returning to control levels transmurally. (Bip. ref. = bipolar reference electrogram; EPI = epicardium; mV = millivolts).

Figures 7 and 8. The tissue section in figure 7 was taken in the plane through which one electrode shaft was placed. Identification of the electrode tract was made possible by dipping the electrode shafts into India ink and allowing them to dry prior to placing them into the heart. Diffusion of the India ink into surrounding myocardium was negligible. In this particular case, the ventricular wall was 14 mm thick so that all 14 pairs of electrode terminals were located intramurally, terminal number 1 being on the endocardium and terminal number 15 being on the epicardium.

The tissue section was stained by the histochemical staining techniques mentioned earlier in order to demonstrate more specifically the differing degrees of myocardial ischemic injury. Microscopic examination of the tissue section revealed that approximately the outer one-third of the section was normal myocardium (as in inset B). The inner two-thirds, however, exhibited the changes of myocardial ischemic injury, i.e., 1) swollen mitochondria (seen as fine "dots" or "granules" in inset A), 2) swollen A-Bands, and 3) loss of the diffuse sarcoplasmic-staining reaction as indicated by the example shown in Inset A taken from the endocardium. Separation of the individual myocardial bundles in the injured areas represents fixation artifact and is not a strict criterion of myocardial ischemic injury. Inset C shows a 3 mm area of myocardial injury extending down the electrode tract from the epicardium caused by pressure from the plastic epicardial marker attached to the electrode shaft.

The graph in figure 8 is the electrophysiologic correlate of the tissue plane shown in figure 7. All precoronary occlusion bipolar potential amplitudes were assigned a value of 100% as represented by the horizontal control line in figure 8. The amplitudes...
Progressive loss of bipolar potential electromotor force (EMF) in transmural infarction of free left ventricular wall. Bipolar electrograms were recorded from successive electrode terminals along a single electrode shaft located within the transmural myocardial infarction. Electrode terminal number 1 was located at the endocardium, the terminal number 8 was located at the epicardium. The control curve demonstrates the bipolar potential EMF at each electrode terminal from endocardium to epicardium prior to coronary artery occlusion. The decrease in bipolar potential EMF at each of these terminals following coronary artery occlusion is evident. The overlapping of some portions of the curves from 2-12 hr postocclusion was unavoidable since the changes in bipolar potential EMF were minor after 2 hr of coronary occlusion. The transmural infarction was confirmed histologically.

Figure 5

Transmural infarct involving anterior papillary muscle. Bipolar electrograms were recorded from successive electrode terminals along a single electrode shaft. The first four terminals were located within the anterior papillary muscle. Terminal number 5 was located at the junction of the base of the papillary muscle and the free left ventricular wall. The control (precoronary occlusion) curve demonstrates that the bipolar potential EMF within the body of the papillary muscle is normally higher than that at its base. Coronary occlusion resulted in a transmural infarction involving the anterior papillary muscle as evidenced by the progressive decrease in bipolar potential EMF with increasing duration of myocardial ischemia. The transmural infarction was confirmed histologically.

of the bipolar potentials recorded following coronary artery occlusion were expressed as a percentage of their control values. The subendocardial...
Figure 7

Histochemical stain (for succinic dehydrogenase activity) of a transmural section of left ventricular wall in the plane through which a single electrode shaft had been placed. Arrows mark the position of the electrode shaft. The inner two-thirds of the wall showed ischemic changes histochemically (as in inset A). The outer one-third of the LV wall was normal histochemically (as in inset B) except for a small area near the epicardial surface (inset C) which was damaged by the plastic epicardial hub attached to the electrode shaft.

Electrophysiologic Time-Course of Acute Myocardial Ischemia

The variation in response of different regions of an acute myocardial infarction to acute coronary artery occlusion in eight dogs is demonstrated in figure 9 and in table 1. In figure 9 the area of ischemia was separated into five electrophysiologic
zones with Line A representing the epicenter of the myocardial infarction and successive lines B, C, D, and E representing zones progressively further away from the epicenter of the infarct.

**Alterations in Electrophysiologic Time-Course Following Coronary Reperfusion**

Coronary reperfusion resulted in a return of bipolar potential EMF toward control levels (fig. 4). The magnitude of the response to coronary reperfusion varied depending on 1) the duration of coronary artery occlusion and 2) the location of the recording electrode terminals within the myocardial infarction. The quantitative effect of coronary reperfusion on the voltage time-course of acute myocardial ischemia is shown in figure 10 and table 1. The data shown in figure 10 are not absolutely comparable to the data in figure 9 because the bipolar potentials used to construct each curve in figure 9 were grouped on the basis of the degree of EMF change at 6 hr postcoronary occlusion. Such grouping in the reperfusion graphs of figure 10 was impossible since the coronary occlusion was released before the 6 hr measurement except in the lower right graph. As a result of this inability to reproduce absolutely comparable curves, an effort
### Table 1

Tabulation of Data from which Curves in Figures 9 and 10 Were Constructed

<table>
<thead>
<tr>
<th>Line</th>
<th>Control</th>
<th>30 min</th>
<th>1 hr</th>
<th>2 hr</th>
<th>3 hr</th>
<th>6 hr</th>
<th>12 hr</th>
<th>No. of measurements</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Electrophysiologic Time-course</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>A (0–25%, 6 hr)</td>
<td>100</td>
<td>42.3 ± 3.1</td>
<td>29.7 ± 2.2</td>
<td>19.9 ± 1.9</td>
<td>13.3 ± 1.1</td>
<td>5.6 ± 0.4</td>
<td>3.2 ± 0.5</td>
<td>1715</td>
</tr>
<tr>
<td>B (26–50%, 6 hr)</td>
<td>100</td>
<td>70.8 ± 5.0</td>
<td>60.5 ± 4.4</td>
<td>54.4 ± 3.8</td>
<td>48.7 ± 2.9</td>
<td>39.1 ± 0.7</td>
<td>33.6 ± 4.3</td>
<td>322</td>
</tr>
<tr>
<td>C (51–75%, 6 hr)</td>
<td>100</td>
<td>88.1 ± 1.6</td>
<td>77.5 ± 3.9</td>
<td>77.2 ± 3.2</td>
<td>73.2 ± 3.5</td>
<td>64.1 ± 0.9</td>
<td>47.7 ± 5.3</td>
<td>329</td>
</tr>
<tr>
<td>D (76–100%, 6 hr)</td>
<td>100</td>
<td>97.5 ± 2.9</td>
<td>96.4 ± 3.1</td>
<td>98.5 ± 2.9</td>
<td>94.9 ± 1.9</td>
<td>90.6 ± 0.7</td>
<td>92.1 ± 2.5</td>
<td>574</td>
</tr>
<tr>
<td>E (above 100% 6 hr)</td>
<td>100</td>
<td>111.1 ± 4.1</td>
<td>124.4 ± 5.6</td>
<td>129.8 ± 5.1</td>
<td>120.0 ± 4.4</td>
<td>130.4 ± 3.5</td>
<td>142.2 ± 5.7</td>
<td>511</td>
</tr>
<tr>
<td><strong>Reperfusion After 30 Min Occlusion</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>A (0–50%, 30 min)</td>
<td>100</td>
<td>13.0 ± 1.4</td>
<td>52.9 ± 3.5</td>
<td>50.4 ± 2.9</td>
<td>43.4 ± 3.1</td>
<td>38.0 ± 2.8</td>
<td>46.3 ± 3.0</td>
<td>420</td>
</tr>
<tr>
<td>B (51–70%, 30 min)</td>
<td>100</td>
<td>56.9 ± 3.3</td>
<td>77.5 ± 3.6</td>
<td>67.7 ± 3.3</td>
<td>64.9 ± 3.3</td>
<td>72.7 ± 4.9</td>
<td>78.9 ± 6.0</td>
<td>133</td>
</tr>
<tr>
<td>C (71–99%, 30 min)</td>
<td>100</td>
<td>82.3 ± 1.6</td>
<td>87.3 ± 5.2</td>
<td>80.8 ± 4.1</td>
<td>77.7 ± 4.4</td>
<td>86.8 ± 4.6</td>
<td>93.3 ± 6.1</td>
<td>203</td>
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<tr>
<td>D (above 100% 30 min)</td>
<td>100</td>
<td>116.1 ± 4.4</td>
<td>102.7 ± 9.2</td>
<td>93.9 ± 8.9</td>
<td>95.2 ± 8.7</td>
<td>99.8 ± 6.8</td>
<td>104.6 ± 7.7</td>
<td>114</td>
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<tr>
<td><strong>Reperfusion after 1 Hr Occlusion</strong></td>
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<td></td>
</tr>
<tr>
<td>A (0–50%, 1 hr)</td>
<td>100</td>
<td>39.8 ± 2.6</td>
<td>21.3 ± 1.9</td>
<td>34.9 ± 2.4</td>
<td>38.4 ± 2.5</td>
<td>35.5 ± 2.3</td>
<td>32.0 ± 2.1</td>
<td>482</td>
</tr>
<tr>
<td>B (51–70%, 1 hr)</td>
<td>100</td>
<td>73.6 ± 6.2</td>
<td>60.8 ± 2.0</td>
<td>45.1 ± 6.9</td>
<td>51.1 ± 8.2</td>
<td>49.0 ± 9.0</td>
<td>78.9 ± 10.0</td>
<td>63</td>
</tr>
<tr>
<td>C (71–99%, 1 hr)</td>
<td>100</td>
<td>95.5 ± 1.9</td>
<td>87.5 ± 0.8</td>
<td>88.7 ± 1.9</td>
<td>88.7 ± 1.7</td>
<td>78.0 ± 2.2</td>
<td>78.5 ± 2.3</td>
<td>364</td>
</tr>
<tr>
<td>D (above 100% 1 hr)</td>
<td>100</td>
<td>107.3 ± 1.6</td>
<td>105.9 ± 1.4</td>
<td>97.3 ± 2.7</td>
<td>97.7 ± 3.2</td>
<td>91.2 ± 3.6</td>
<td>90.5 ± 4.0</td>
<td>245</td>
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<tr>
<td><strong>Reperfusion after 2 Hr Occlusion</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>A (0–50%, 2 hr)</td>
<td>100</td>
<td>37.3 ± 3.5</td>
<td>19.0 ± 1.9</td>
<td>18.3 ± 2.5</td>
<td>24.5 ± 2.6</td>
<td>23.2 ± 2.5</td>
<td>23.4 ± 3.0</td>
<td>567</td>
</tr>
<tr>
<td>B (51–70%, 2 hr)</td>
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<td>74.3 ± 3.2</td>
<td>61.5 ± 1.0</td>
<td>55.8 ± 3.1</td>
<td>59.2 ± 3.9</td>
<td>55.9 ± 3.4</td>
<td>62.3 ± 4.6</td>
<td>189</td>
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<tr>
<td>C (71–99%, 2 hr)</td>
<td>100</td>
<td>97.1 ± 5.2</td>
<td>82.2 ± 1.5</td>
<td>71.3 ± 5.9</td>
<td>66.7 ± 6.8</td>
<td>63.9 ± 5.5</td>
<td>69.4 ± 4.5</td>
<td>182</td>
</tr>
<tr>
<td>D (above 100% 2 hr)</td>
<td>100</td>
<td>129.9 ± 6.9</td>
<td>133.1 ± 9.7</td>
<td>118.6 ± 9.7</td>
<td>115.3 ± 16.9</td>
<td>101.9 ± 10.2</td>
<td>108.5 ± 15.1</td>
<td>56</td>
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<tr>
<td><strong>Reperfusion after 6 Hr Occlusion</strong></td>
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</tr>
<tr>
<td>A (0–25%, 6 hr)</td>
<td>100</td>
<td>49.2 ± 7.3</td>
<td>40.6 ± 6.5</td>
<td>34.7 ± 5.4</td>
<td>31.8 ± 5.4</td>
<td>14.7 ± 1.9</td>
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<td>B (26–50%, 6 hr)</td>
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<td>79.8 ± 4.5</td>
<td>69.6 ± 4.3</td>
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<td>66.7 ± 3.4</td>
<td>38.3 ± 1.4</td>
<td>54.6 ± 4.0</td>
<td>189</td>
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<tr>
<td>C (51–100%, 6 hr)</td>
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<td>87.5 ± 2.2</td>
<td>83.7 ± 1.9</td>
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<td>D (above 100% 6 hr)</td>
<td>100</td>
<td>114.9 ± 5.6</td>
<td>119.5 ± 7.3</td>
<td>115.8 ± 6.8</td>
<td>117.5 ± 4.4</td>
<td>125.5 ± 4.6</td>
<td>120.4 ± 4.2</td>
<td>77</td>
</tr>
</tbody>
</table>

Control bipolar potential electromotive force (EMF) is expressed as 100% regardless of the absolute amplitude prior to coronary artery occlusion. All values recorded thereafter are expressed as a percent of control (mean ± se). The values used to construct figure 9 appear under "Electrophysiologic time-course." The values used to construct the reperfusion curves of figure 10 appear under the appropriate headings. The method of grouping the changes in bipolar potential EMFs for each curve of each graph appears in parentheses in the left column of the table. "Number of Measurements" refers to the number of bipolar potentials measured to construct each curve.
Figure 10

Effects of coronary artery reperfusion at various intervals after coronary occlusion on bipolar potential EMF. These curves prior to coronary artery reperfusion are not absolutely comparable to the curves of figure 9 (see text for discussion) but they do demonstrate an over-all beneficial effect of coronary artery reperfusion after up to 6 hr of coronary artery occlusion.

was made to construct curves in figure 10 prior to coronary reperfusion which were comparable to the early portions of the curves in figure 9. Such grouping of the EMF changes prior to coronary artery reperfusion permitted a qualified evaluation of the effects of early coronary reperfusion on the electrophysiologic time-course of acute myocardial ischemia. Due to the smaller number of animals included in the reperfusion studies, the curves of figure 10 represented different ranges than did the curves of figure 9. Therefore, only four curves were constructed for each graph in figure 10.

It is apparent from figure 10 that the greatest quantitative response to coronary reperfusion occurred in those areas which demonstrated the greatest change in bipolar potential EMF following coronary artery occlusion (lines A). The degree of recovery was less dramatic in all zones of the myocardial infarction when coronary occlusion was maintained for more than 30 minutes. However, in figure 9, each point on Lines A-D is lower than the point immediately preceding it (except points 4 and 7 on line D). This indicates a progressive decline in bipolar potential EMF in all areas of the myocardial infarction except in the most peripheral areas (line E). In contrast, after coronary reperfusion, virtually all points in figure 10 show an increase over each preceding point, indicating a reversal or cessation in the progressive decline in EMF in the involved myocardium. All the minute areas of myocardium monitored by the electrode terminals did not respond to coronary artery reperfusion but these graphs show a beneficial over-all result of coronary artery reperfusion after up to 6 hr of coronary occlusion.

Table 1 represents the data from which figures 9 and 10 were constructed. The standard errors were omitted from the reperfusion graphs in the interest of clarity but do appear within the table. The manner in which the bipolar potentials were
grouped to form each line in each graph appears in parentheses in the left column of Table 1.

Discussion

The present study was designed to evaluate the electrophysiologic alterations which occur in ischemic myocardium following acute coronary artery occlusion. A critical analysis of certain of these alterations provided a means of characterizing several important aspects of an evolving myocardial infarction.

Effect of Coronary Artery Occlusion on Local Activation Time

Acute coronary artery occlusion resulted in a delay in the onset of activation within the area of myocardial ischemic injury (fig. 1). This delay in local activation time in an evolving myocardial infarction progressed with time, indicating that the velocity of wavefront propagation through ischemic myocardium is related to the degree of local ischemic injury. Such intramyocardial conduction abnormalities have been shown previously to be important in the genesis of ventricular arrhythmias following acute myocardial infarction. Of particular interest is the fact that no such abnormalities of conduction were detected in the Purkinje system, located immediately adjacent to a severe subendocardial infarction. The significance of the small potential preceding Purkinje activation after coronary artery occlusion in figure 2 is not known. Regardless of the origin of this small potential, the magnitude of injury to the Purkinje system was negligible in comparison to the injury caused to the underlying subendocardium following coronary artery occlusion. These findings support previous studies in which the Purkinje system survived in areas adjacent to subendocardial infarctions of several weeks' duration. Whether the Purkinje system has a lower oxygen requirement or is adequately oxygenated by intracavitary blood remains a problem for further investigation.

Effect of Coronary Artery Occlusion on Bipolar Potential EMF

The nonuniformity of tissue injury within an acute myocardial infarction has been documented histologically and electrophysiologically. The importance of this inhomogeneity of ischemic injury in the origin of ventricular arrhythmias has been shown. However, differing degrees of ischemic injury within a myocardial infarction have not been quantitated in a manner such that the evolution of the different zones of injury could be studied over several hours in the same heart. The documentation of such a time-course for different zones within an acute myocardial infarction becomes important if one wishes to evaluate the benefit of potentially therapeutic interventions on the course of an evolving myocardial infarction.

The present study again demonstrates the nonuniformity of myocardial ischemic injury following acute coronary artery occlusion (fig. 9). This variation in response to acute coronary artery occlusion was quantitated by measuring the changes in bipolar potential EMF recorded from the area of myocardial ischemia. Histochemical studies of the involved myocardium confirmed that the degree of change in bipolar potential EMF was related to the geometry of the myocardial infarction (figs. 7 and 8). The greatest decrease in bipolar potential EMF occurred in the epicenter of the myocardial infarction. Lesser decreases in bipolar potential EMF occurred in the more peripheral zones of the infarct. The bipolar potential EMF increased at the junction of ischemic and normal myocardium.

The curves in figure 9 suggest a graded response within the region of ischemia to acute coronary artery occlusion. This graph, however, is not intended to imply that myocardial ischemic injury is graded uniformly from the anatomic periphery to the anatomic epicenter of an infarct. For example, on a given electrode shaft, adjacent bipolar electrograms frequently responded differently to acute coronary artery occlusion. This variation in response to coronary artery occlusion of adjacent intramural electrograms reflects the severe degree of inhomogeneity that is present within an area of myocardial ischemic injury.

In this study, the area of ischemic injury was divided into five zones from the epicenter to the periphery of the myocardial infarction with each zone representing a different degree of myocardial injury (lines A through E, figure 9). Such a division is arbitrary since there may be an infinite number of "zones" between the epicenter and the periphery of a myocardial infarction. However, the demonstrable number of "zones" is dependent upon the sensitivity of the technique used to quantitate the degree of ischemic injury. Although histochemical stains were used in this study to demarcate the central and peripheral zones of myocardial ischemia, it is apparent that these stains are not as sensitive to the degree of myocardial ischemic injury as are the electrophysiologic parameters measured. For example, inset C in figure 7 shows a small area of
subepicardial injury (caused by the plastic hub on the electrode shaft) which appears histologically comparable to the ischemic subendocardium. However, the decrease in bipolar potential EMF in this subepicardial area was not as great as the decrease which occurred in the subendocardium (figure 8). The reason for this apparent discrepancy is that histochemical stains are capable of demonstrating only two orders of ischemic injury. In contrast, the decrease in bipolar potential EMF in an area of ischemic injury varied from 1% to 100% of control EMF, thereby providing a more sensitive means of assessing changes in local ischemic injury.

One factor other than myocardial ischemic injury which could decrease the bipolar potential EMF is a change in waveform orientation. For example, if the waveform became more tangential to the electrode terminals following coronary artery occlusion (e.g., in those areas immediately surrounding the infarct), the maximum potential difference between the two recording electrode terminals would be decreased even though the dipole moment across the waveform remained the same. However, we observed an increase in bipolar potential EMF at the junction of ischemic and normal myocardium (figures 7 and 8) and no change in EMF in the normal areas surrounding the infarct. Also, figure 4 demonstrates a decrease in bipolar potential EMF with no coincident alteration in waveform orientation. Therefore this theoretical possibility was not a significant factor in the bipolar potential alterations shown in this study.

Effect of Early Coronary Artery Reperfusion on Bipolar Potential EMF

Some of the limitations in comparing the graphs in figure 10 to the graph in figure 9 have been mentioned. Despite these limitations, certain valid comparisons can be made between the two figures. For example, it is reasonable to assume that Line A in the 30-minute reperfusion graph of figure 10 would have been 15% or less at 12 hours after coronary artery occlusion if the intervention of coronary artery reperfusion had not been introduced. This conclusion is based on the fact that the loss of EMF in the epicenter of a myocardial infarction was progressive if coronary artery occlusion was maintained (Line A, figure 9). Likewise, the peripheral zones of myocardial ischemia appear to return toward normal after coronary artery reperfusion at 30 minutes (Lines B and C). It is interesting also that following coronary artery reperfusion at 30 minutes, the slope of Line D is reversed, indicating that the altered electrophysiological parameters of local ischemic injury were returning toward normal. Inspection of figure 10 indicates that coronary artery reperfusion after 30 minutes of coronary occlusion stopped and reversed the progression of myocardial ischemic injury. Coronary reperfusion after 1 hour, 2 hours, and 6 hours of coronary occlusion effectively stopped the decline in bipolar potential EMF but did not reverse the process. These data may bear an important relationship to the recent studies of Mundth et al. and Sanders, et al. who have demonstrated the feasibility of immediate myocardial revascularization in selected cases of cardiogenic shock accompanying acute myocardial infarction.

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References


The Electrophysiologic Time-Course of Acute Myocardial Ischemia and the Effects of Early Coronary Artery Reperfusion

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