Early Changes in Energy Metabolism in the Myocardium Following Acute Coronary Artery Occlusion in Anesthetized Dogs

By Wolfgang Braasch, M.D., Sigmundur Gudbjarnason, Ph.D., Prirpal S. Puri, M.D., Kurt G. Ravens, M.D., and Richard J. Bing, M.D.

ABSTRACT

The tissue content of energy-rich phosphates and glycolytic metabolites and the activity of myocardial enzymes were examined in the dog after producing myocardial infarction by ligating branches of the anterior descending and circumflex coronary arteries. The pattern of systolic fiber movement shown by a strain-gauge assembly differentiated ischemic from nonischemic portions of myocardium. In ischemic muscle, 30 minutes after onset of ischemia, creatine phosphate content fell from 8.0 to 1.4 μmoles/g, ATP content fell from 5.8 to 1.5 μmoles/g, lactate content rose tenfold, and α-glycerophosphate content rose fivefold. The content of energy-rich phosphates and glycolytic metabolites did not change much in nonischemic muscle. The activities of myocardial enzymes were assayed in extracts of tissue samples from ischemic and non-ischemic muscle 5 to 120 minutes after coronary artery occlusion. The activities of aldolase, lactic dehydrogenase (LDH), glyceraldehydephosphate dehydrogenase, α-glycerophosphate dehydrogenase, malate dehydrogenase (MDH), and 6-phosphogluconate dehydrogenase did not change significantly in ischemic muscle during 2 hours of observation. In nonischemic muscle, phosphofructokinase activity increased 75% 5 minutes after coronary occlusion, followed by an increase in activity of isocitrate dehydrogenase, creatinephosphokinase, MDH, and LDH. The enzymatic changes in nonischemic muscle suggest metabolic changes in nonischemic muscle accompanying compensatory hyperfunction and increased energy requirements of surviving muscle.

ADDITIONAL KEY WORDS myocardial ischemia enzyme profile glycolysis energy-rich phosphates myocardial fiber shortening paradoxical systolic fiber lengthening

Previous communications from this laboratory have described the biochemical changes in heart muscle that occur from 5 hours to 10 weeks following coronary occlusion. At 5 hours following myocardial infarction, there occurs an inactivation of glycolytic and oxidative enzymes in infarcted heart muscle and a pronounced increase in the activity of the hexosemonophosphate shunt pathway (1, 2). Examinations of metabolic changes after coronary artery ligation have demonstrated an increase in the tissue content of metabolites from the glycolytic pathway and a diminution of glycogen in the ischemic heart muscle (3-10) compared to normal heart muscle.

In contrast to numerous studies dealing with changes in substrate utilization by the ischemic myocardium (3-16), few papers have described enzymatic changes that occur within the first 2 hours after coronary artery occlusion. At 5 hours following myocardial infarction, there occurs an inactivation of glycolytic and oxidative enzymes in infarcted heart muscle and a pronounced increase in the activity of the hexosemonophosphate shunt pathway (1, 2). Examinations of metabolic changes after coronary artery ligation have demonstrated an increase in the tissue content of metabolites from the glycolytic pathway and a diminution of glycogen in the ischemic heart muscle (3-10) compared to normal heart muscle.

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occlusion. One of these early enzymatic changes is the conversion of the enzyme phosphorylase from the inactive (b) to the active (a) form \((7, 11, 13, 16)\). The purpose of this study was to examine alterations in the activities of various myocardial enzymes and in the tissue content of metabolites in the center and periphery of the ischemic heart muscle and in the nonischemic area of the heart during the first 2 hours after experimental coronary artery occlusion.

**Methods**

Experimental myocardial ischemia was produced in 37 mongrel dogs (15 to 25 kg) under light pentobarbital anesthesia, 25 mg/kg iv, and artificial respiration as described previously \((17)\). Several branches of the left anterior descending and circumflex coronary arteries were ligated, producing an area of ischemia of about 16 to 25 cm\(^2\). The ischemic area was readily recognized because of the bluish color and the paradoxical character of fiber movements.

**DETERMINATION OF LEFT VENTRICULAR FUNCTIONS**

Myocardial fiber movements were registered by a strain-gauge assembly, the detailed description of which has been published previously \((18)\). Briefly, this device consists of two strain-gauge bearing prongs mounted on a flexible stylet which, if required, can be threaded through an intracardiac catheter. From the linear relation between spacing of prongs and strain in the gauges, the curve of fiber movement is inscribed in systole and diastole on a beat-to-beat basis \((10)\). This method has been employed in the present investigation to distinguish the ischemic from the nonischemic portions of the myocardium. It is based on the observations reported previously \((20)\), which indicate that in the ischemic myocardium, the pattern of fiber shortening during systole is replaced by paradoxical fiber lengthening. Strain-gauge bearing prongs of the assembly were directly inserted from the epicardial surface into the left ventricular cavity, and left ventricular pressure was monitored by a Statham PD 31 strain-gauge system and a Sanborn recorder. Left ventricular end-diastolic pressures were recorded at higher sensitivity.

**DETERMINATION OF ENERGY-RICH PHOSPHATES AND METABOLITES**

The early changes in energy-rich phosphates (ATP and creatine phosphate) and products of the glycolytic pathway were studied in nine dogs. After opening the chest through a left thoracotomy, the heart was exposed, and control biopsy samples were obtained from the apex of the left ventricle with a bone rongeur precooled in liquid nitrogen.

The silk ligatures were placed around the branches of the coronary arteries, and at time zero the ligatures were tied producing an instant occlusion of the coronary arteries. At 15, 30, and

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**Figures and Data**

[Graph showing pattern of paradoxical fiber movement in the ischemic myocardium. Curve of fiber length (upper curve) and left ventricular pressure pulse are recorded simultaneously. An upward deflection of the upper curve indicates fiber shortening. After ligation of the regional coronary arteries, the curve of shortening is replaced by curve of fiber lengthening (inverted curve). The nonischemic myocardium continues to show the pattern of fiber shortening with some increase in its amplitude.]
ENERGY METABOLISM IN MYOCARDIAL ISCHEMIA

80 seconds and 3, 10, and 30 minutes following the coronary artery ligation, biopsy samples (50 to 150 mg) were obtained from the central portion of the ischemic area, and care was taken to obtain subsequent samples from uninjured areas of the myocardium, i.e. not from the wound caused by a previous sample. After 30 minutes of coronary occlusion, a biopsy sample was also obtained from the nonischemic posterior wall of the left ventricle. The muscle samples were placed immediately (within 1 to 2 seconds) in a Dewar flask containing precooled Freon. Freon was preferred over liquid nitrogen since it permits more rapid and thorough freezing of the samples. The specimens were then transferred to liquid nitrogen and stored.

After weighing the tissue, the frozen samples were pulverized and homogenized with 1 ml perchloric acid per 100 mg tissue. ATP content was determined according to Adam (21), utilizing the phosphoglycerate kinase (PGK) catalyzed phosphorylation of 3-phosphoglycerate with ATP to yield 1, 3-diphosphoglycerate and ADP. The 1, 3-diphosphoglycerate formed was reduced by glyceraldehyde phosphate dehydrogenase (GAPDH) and NADH to glyceraldehyde-3-phosphate which was trapped as hydrazine (21). Creatine phosphate (CP) was measured by utilizing the reaction CP + ADP C + ATP. The ATP formed was subsequently determined as mentioned above. The recovery of CP was 95% ± 4%.

Lactate and α-glycerophosphate (α—GP) were determined according to Hohorst (22) and pyruvate according to Biicher et al. (23).

The results were expressed in jumoles of tissue; the changes in the ischemic myocardium were then compared with samples taken prior to ligation of the coronary arteries.

DETERMINATION OF ENZYME ACTIVITIES

For the determination of enzyme activity, 28 animals were killed by removing the heart from the anesthetized animal at 5, 30, 60, or 120 minutes after coronary artery ligation. Samples were obtained from the nonischemic posterior wall of the left ventricle; from the center of the ischemic area, which is defined as the one-third of the ischemic area; and from the periphery of ischemic tissue, which is defined as the two-thirds of the infarcted area, representing the ischemic tissue between the normal muscle and the center portion of the ischemic area. The control group consisted of 10 dogs without coronary occlusion.

The tissue sample (1 g wet weight) was homogenized in a glass Potter-Elvehjem tissue grinder and extracted with 5 volumes of 0.1 M phosphate buffer, pH 7.2, containing 1 mM ADP, 10 mM glutathione, and 10 mM EDTA (54) and centrifuged at 100,000 g. The extraction was repeated twice with 4 volumes of buffer, and the combined extracts were used for the assay of enzyme activities.

The enzyme activities were assayed spectrophotometrically as described previously (25) and expressed in pmol of substrate converted to product per minute and per mg of extracted protein. The protein content of the extracts was not significantly affected by 2 hours of ischemia, and the basis of comparison therefore remained unaltered despite the development of edema resulting in a 2 to 4% increase in water content of the tissue. The assays were examined with respect to linear kinetics and optimal substrate conditions for dog heart muscle, and modifications were made in the assay systems for all the enzymes except aldolase and 6-phosphogluconate dehydrogenase (which did not require modifications), assuring optimal assay conditions (1). The enzymes chosen for this

TABLE 1

Serial Hemodynamic Changes in Dogs Examined for Alteration in Tissue Content of Energy-Rich Phosphates

<table>
<thead>
<tr>
<th>Time of biopsy after coronary artery occlusion</th>
<th>LVSP (mm Hg)</th>
<th>LVEDP (mm Hg)</th>
<th>H.R. (beats/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (control)</td>
<td>144 ± 8.0</td>
<td>3.6 ± 0.1</td>
<td>70.9 ± 4.0</td>
</tr>
<tr>
<td>15 sec</td>
<td>150.2 ± 10.0</td>
<td>6.2 ± 1.2*</td>
<td>70.8 ± 4.6</td>
</tr>
<tr>
<td>30 sec</td>
<td>154.6 ± 9.6</td>
<td>7.1 ± 1.0*</td>
<td>78.8 ± 4.5</td>
</tr>
<tr>
<td>60 sec</td>
<td>159.9 ± 10.6</td>
<td>8.2 ± 1.2*</td>
<td>70.5 ± 4.8</td>
</tr>
<tr>
<td>3 min</td>
<td>153.5 ± 5.9</td>
<td>7.4 ± 0.9*</td>
<td>73.5 ± 3.5</td>
</tr>
<tr>
<td>10 min</td>
<td>127.4 ± 8.6</td>
<td>9.4 ± 1.2*</td>
<td>73.8 ± 4.0</td>
</tr>
<tr>
<td>30 min</td>
<td>120.3 ± 9.8</td>
<td>9.4 ± 1.5*</td>
<td>77.8 ± 4.5</td>
</tr>
</tbody>
</table>

The values given are the means ± SE from 9 dogs. LVSP = left ventricular systolic pressure; LVEDP = left ventricular end-diastolic pressure.

*Significant differences from control, P < 0.05.

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Serum! Hi

Time of sampling
5 min
30 min
60 min
120 min

Mean ± SE
Mean ± SE
Mean ± SE
Mean ± SE

LVSP (mm Hg)
132.7 ± 4.8
144.6 ± 5.8
130.5 ± 4.8
125.9 ± 4.5

LVSP (mm Hg)
77.3 ± 5.1
7.6 ± 8.1
6.8 ± 7.8

H.R. (beats/min)
77.3 ± 4.1
87.0 ± 4.3
80.5 ± 4.1

H.R. (beats/min)
78.8 ± 4.1
89.9 ± 6.3
80.2 ± 6.3

LVEDP = left ventricular end-diastolic pressure; LVSP = left ventricular systolic pressure; H.R. = heart rate.

*Significant differences from control P < 0.05.

**Study** represent three metabolic pathways: from the Embden-Meyerhof pathway we determined the activities of fructose-1, 6-diphosphate aldolase, glyceraldehyde phosphate dehydrogenase (CAPDH), phosphofructokinase (PFK), lactate dehydrogenase (LDH), and α-glycerophosphate dehydrogenase (α-GPDH); from the citric acid cycle: malate dehydrogenase (MDH), NAD- and NADP-specific isocitrate-dehydrogenases (NAD-IDH, NADP-IDH), and glutamate oxaloacetate transaminase (GOT); from the hexosemonophosphate shunt: glucose-6-phosphate dehydrogenase (G-6-PDH) and 6-phosphogluconate dehydrogenase (6-PGDH). In addition, the activity of creatine phosphokinase (CPK) was also determined. The enzyme activities observed in the nonischemic posterior wall of the left ventricle and in the periphery and center of the ischemic tissue were compared to the enzyme activities in the normal control group.

**Results**

**Left Ventricular Function**

Figure 1 shows the pattern of systolic fiber movement in the ischemic and nonischemic portions of the myocardium. The curve of fiber shortening obtained before ligation of the coronary arteries had an upward deflection; this curve was inverted when ischemia was induced by ligation of the coronary arteries. The nonischemic myocardium continued to register the curve of fiber shortening with some increase in its amplitude.

The left ventricular systolic pressure showed a moderate fall and the left ventricular end-diastolic pressure a moderate rise (Tables 1 and 2). In none of the experiments included in this report was a marked fall in systolic pressure registered.

**Biopsy Analysis**

The analysis of the tissue content of energy-rich phosphates and the glycolytic metabolites (Table 3) illustrates the marked changes in energy metabolism of the ischemic tissue. Significant diminution in tissue content of the energy-rich phosphates in the ischemic area was evident 30 seconds after coronary occlusion. Thirty minutes after the onset of ischemia, the CP content fell from 7.99 to 1.43 μmoles/g (a decrease of 82%), and the ATP content diminished from 5.80 to 1.50 μmoles/g (a decrease of 74%). Parallel to this marked decrease in tissue content of ATP and CP, there was a rapid increase in the tissue content of lactate and α-GP. During the first 30 minutes of ischemia the lactate content increased tenfold and the α-GP content increased fivefold, but the tissue content of pyruvate did not change significantly. The lactate-pyruvate ratio thus increased, illustrating the increase in glycolytic metabolism accompanying the ischemia. The control samples obtained from the posterior region of the left ventricle 30 minutes after occlusion of the coronary arteries did not differ significantly in metabolite content from normal anterior muscle samples obtained prior to ischemia.
coronary occlusion. This observation indicates that neither the coronary occlusion nor the prolonged anesthesia resulted in a marked reduction of the energy level of nonischemic muscle, particularly since the tissue content of energy-rich phosphates and glycolytic metabolites was not significantly different in normal left ventricular muscle from the anterior and the posterior regions (Table 4). The tissue content of the glycolytic metabolites and the energy-rich phosphates did not change markedly in the nonischemic tissue.

ENZYMATIC CHANGES

The specific activities of enzymes assayed in tissue extracts from the center of ischemic tissue, periphery of ischemic tissue, and nonischemic muscle are illustrated in Table 5. The activities of most of the enzymes from the center of ischemic tissue did not show significant changes during the 2 hours of observations. PFK showed a temporary increase in activity 5 minutes after coronary occlusion, whereas the activity of IDH (NAD and NADP) was significantly elevated 30 minutes after coronary occlusion and remained elevated during the 2 hours of observation. The activity of G-6-PDH was also significantly increased in the center of the ischemic area 2 hours after coronary occlusion. The activity of G-6-PDH was significantly increased in the periphery of the ischemic area 5 minutes after coronary occlusion and remained significantly elevated 30 minutes and 2 hours after onset of ischemia. The activities of NAD-IDH and NADP-IDH were also significantly increased in the periphery of ischemic muscle 1 and 2 hours after coronary occlusion. There were no significant changes in activities of several of the enzymes in the ischemic muscle, such as GAPDH and a-GPDH, and none of these enzymes showed a significant diminution in activity after 2 hours of ischemia. The nonischemic muscle showed, on the other hand, greater alterations in enzyme activities. The activities of PFK, 6-PGDH, NAD-IDH, and MDH increased 5 minutes after coronary occlusion, followed by an increase in activity of aldolase, LDH, NADP-IDH, and CPK 30 minutes after onset of ischemia. Two hours after coronary occlusion, the activities of NAD-IDH, NADP-IDH, MDH, CPK, and LDH were significantly higher in the nonischemic areas of the heart subjected to coronary occlusion compared to normal cardiac muscle (Table 5).

Discussion

Previous studies have shown that a rapid loss of contractile activity in the ischemic myocardium (20, 26) follows coronary artery occlusion. This is followed by a passive distention of the ischemic myocardium during systole. In the nonischemic myocardium, on the other hand, the pattern of systolic contraction persists and may even show an increase in amplitude. Study of the contractile patterns in different regions of the left ventricular myocardium was utilized in the pres-
### TABLE 3

Changes in Energy-Rich Phosphates and Glycolytic Metabolites Following Acute Coronary Artery Occlusion

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>15 sec</th>
<th>30 sec</th>
<th>60 sec</th>
<th>1 min</th>
<th>3 min</th>
<th>10 min</th>
<th>15 min</th>
<th>30 min</th>
<th>Nonischemic tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ATP</strong></td>
<td>Mean</td>
<td>7.99</td>
<td>8.00</td>
<td>3.65*</td>
<td>2.41*</td>
<td>2.24*</td>
<td>1.86*</td>
<td>1.62*</td>
<td>1.45*</td>
<td>8.21</td>
</tr>
<tr>
<td>±SEM</td>
<td>0.70</td>
<td>0.70</td>
<td>0.70</td>
<td>0.35</td>
<td>0.35</td>
<td>0.35</td>
<td>0.35</td>
<td>1.00</td>
<td>0.53</td>
<td>0.98</td>
</tr>
<tr>
<td><strong>CP</strong></td>
<td>Mean</td>
<td>5.80</td>
<td>5.21</td>
<td>4.75*</td>
<td>4.70*</td>
<td>4.27*</td>
<td>3.13*</td>
<td>2.62*</td>
<td>1.50*</td>
<td>4.91</td>
</tr>
<tr>
<td>±SEM</td>
<td>0.16</td>
<td>0.45</td>
<td>0.35</td>
<td>0.19</td>
<td>0.19</td>
<td>0.17</td>
<td>0.15</td>
<td>0.15</td>
<td>0.15</td>
<td>0.43</td>
</tr>
<tr>
<td><strong>Lactate</strong></td>
<td>Mean</td>
<td>3.04</td>
<td>2.77</td>
<td>5.54*</td>
<td>5.65*</td>
<td>12.04*</td>
<td>15.54*</td>
<td>15.54*</td>
<td>20.41*</td>
<td>2.34</td>
</tr>
<tr>
<td>±SEM</td>
<td>0.26</td>
<td>0.46</td>
<td>0.86</td>
<td>0.75</td>
<td>0.53</td>
<td>1.03</td>
<td>0.35</td>
<td>0.23</td>
<td>0.23</td>
<td></td>
</tr>
<tr>
<td><strong>Pyruvate</strong></td>
<td>Mean</td>
<td>0.52</td>
<td>0.39</td>
<td>0.54</td>
<td>0.37</td>
<td>0.43</td>
<td>0.33</td>
<td>0.20</td>
<td>0.10</td>
<td>0.11</td>
</tr>
<tr>
<td>±SEM</td>
<td>0.09</td>
<td>0.07</td>
<td>0.11</td>
<td>0.11</td>
<td>0.06</td>
<td>0.02</td>
<td>0.10</td>
<td>0.11</td>
<td>0.11</td>
<td></td>
</tr>
<tr>
<td><strong>Lactate/pyruvate</strong></td>
<td>Mean</td>
<td>4.18</td>
<td>4.39</td>
<td>18.33</td>
<td>36.44*</td>
<td>34.10*</td>
<td>31.75*</td>
<td>31.75*</td>
<td>31.75*</td>
<td>5.53</td>
</tr>
<tr>
<td>±SEM</td>
<td>0.47</td>
<td>0.68</td>
<td>10.01</td>
<td>12.26</td>
<td>5.52</td>
<td>3.47</td>
<td>3.47</td>
<td>3.47</td>
<td>3.47</td>
<td></td>
</tr>
</tbody>
</table>

The results are expressed in mmol/kg wet weight. n = number of experiments.

*Significant difference from control P < 0.05.
TABLE 4
Tissue Content of ATP, Creatinine Phosphate, and Lactate of the Anterior and Posterior Regions of Normal Left Ventricular Muscle

<table>
<thead>
<tr>
<th></th>
<th>Anterior</th>
<th>Posterior</th>
<th>SE of mean difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATP</td>
<td>5.39</td>
<td>5.53</td>
<td>0.24</td>
</tr>
<tr>
<td>CP</td>
<td>9.25</td>
<td>9.68</td>
<td>0.85</td>
</tr>
<tr>
<td>Lactate</td>
<td>2.16</td>
<td>1.91</td>
<td>0.29</td>
</tr>
</tbody>
</table>

Results are from six dogs and are expressed in pmoles/g wet weight.

The enzymatic changes observed in this study are difficult to interpret because of the numerous factors that can influence the activity of an enzyme, such as concentrations of the substrate, product, cofactors and co-enzymes, allosteric regulators, inhibitor, activator, conformational changes, extractability, etc. Since the enzyme activities were determined in diluted samples under optimal assay conditions, the alterations in activity observed in vitro are probably not the result of changes in substrate or cofactor concentrations. It must also be pointed out that the alterations observed in enzyme activity, as measured in the tissue extract, do not necessarily reflect accurately the alterations in the heart in vivo.

The results reported here indicate that occlusion of coronary arteries, supplying a limited area of the anterior left ventricular wall, is accompanied by metabolic changes in the entire left ventricle, i.e. in the non-ischemic left ventricular muscle as well as in the ischemic tissue. The increased activities of some of the glycolytic (PFK, ALD, LDH) and oxidative (IDH, MDH) enzymes observed in nonischemic areas of left ventricular muscle could be in response to increased energy requirements of the surviving muscle. This hypothesis appears reasonable when we consider that following coronary occlusion, the nonischemic muscle is called upon to perform additional work to compensate for the nonfunctioning ischemic myocardium, as indicated by an increase in its amplitude of contraction. This additional work-load requires increased energy production in nonischemic muscle, which in turn must be met by increased substrate flux through the Embden-Meyerhof pathway and the citric acid cycle. The increase in substrate flux requires an increase in activity of ratelimiting enzymes. The reaction of the nonischemic cardiac muscle to coronary occlusion was illustrated in a significant (75%) increase in the activity of PFK, the rate-limiting enzyme of the Embden-Meyerhof pathway, observed 5 minutes after coronary occlusion. This increase in activity of PFK was followed by an increase in activity of other glycolytic and some oxidative enzymes, particularly NAD-IDH and NADP-IDH (Table 5). The increase in enzyme activity in absence of marked alterations in tissue content of energy-rich phosphates or glycolytic metabolites...
<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Aldolase ($\times 10^{-1}$)</th>
<th>PFK ($\times 10^{-1}$)</th>
<th>C.APDH</th>
<th>a-Gl=DH ($\times 10^{-1}$)</th>
<th>LDH</th>
<th>NAD-IDH ($\times 10^{-1}$)</th>
<th>NADP-IDH ($\times 10^{-2}$)</th>
<th>G-6-PDH ($\times 10^{-5}$)</th>
<th>6-PGDH ($\times 10^{-3}$)</th>
<th>CPK ($\times 10^{-1}$)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>1.69</td>
<td>1.60</td>
<td>Mean</td>
<td>2.07</td>
<td>Mean</td>
<td>0.18</td>
<td>Mean</td>
<td>1.08</td>
<td>Mean</td>
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<tr>
<td></td>
<td>± SE</td>
<td>0.10</td>
<td>0.18</td>
<td>± SE</td>
<td>0.03</td>
<td>± SE</td>
<td>0.36</td>
<td>± SE</td>
<td>0.32</td>
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<tr>
<td>n</td>
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<td>6</td>
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</tr>
<tr>
<td>Mean</td>
<td>2.07*</td>
<td>2.04</td>
<td>1.33</td>
<td>Mean</td>
<td>0.96</td>
<td>Mean</td>
<td>0.49</td>
<td>Mean</td>
<td>0.92*</td>
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<tr>
<td>± SE</td>
<td>0.18</td>
<td>0.03</td>
<td>0.36</td>
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<td>0.92*</td>
<td>Mean</td>
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<td>± SE</td>
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<td>± SE</td>
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<td>± SE</td>
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<td>15</td>
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</table>

*P < 0.05; ±0.1 > P > 0.05.
suggests that the nonischemic muscle may be able to meet the additional energy requirements of the compensatory hyperfunction of the surviving muscle by way of increased aerobic energy metabolism.

The enzyme profile of the center of ischemic tissue did not change markedly for 2 hours following onset of ischemia. The relatively minor changes in enzyme activity in ischemic muscle in the presence of alterations in substrate availability, coenzyme and cofactor concentrations, and biochemical environment (pH) suggests that these factors do not cause a significant alteration in the enzyme profile as measured in vitro, for at least 2 hours. These enzymes also remain resistant to inactivation or degradation in the ischemic environment for this period of time.

The enzyme profile of the periphery of ischemic tissue demonstrates an increase in activity of G-6-PDH, aldolase, NAD-IDH, and NADP-IDH. In this area of ischemia, a greater transport of metabolites and oxygen from nonischemic muscle can be expected than into the center of ischemic tissue, because of the reactive hyperemia. The reaction of the myocardial enzyme profile to ischemia seems thus to be dependent upon the extent of ischemia.

The changes in tissue content of glycolytic metabolites and energy-rich phosphates were predictable in the ischemic tissue, i.e. an immediate decrease in CP and ATP and an increase in lactate and α-GP content of ischemic muscle. The observations are in line with those reported previously (3-15) and reflect the diminished oxidative metabolism but increased glycolytic or anaerobic metabolism of the ischemic muscle.

The more rapid disappearance of CP than of ATP during the first few minutes following coronary occlusion is in line with the role of CP as a pool of high-energy phosphates which serves to regenerate ATP and to maintain an adequate supply of ATP for uninterrupted contractile processes. Absence or marked reduction of oxidative phosphorylation in the ischemic tissue leads to a rapid depletion of the supply of CP and subsequent diminution in tissue content of ATP, resulting in cessation of contractile processes in the ischemic muscle.

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Early Changes in Energy Metabolism in the Myocardium Following Acute Coronary Artery Occlusion in Anesthetized Dogs
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