Lactate accumulation in primate spinal cord during circulatory arrest

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In rhesus monkeys subjected to circulatory arrest, studies were made of the relationship of lactate production in the spinal cord to the duration of circulatory arrest and magnitude of lactate accumulation, and the results were compared to the magnitude of rise in cerebral tissue lactate. Both high and low thoracic laminectomies were performed on each of eight rhesus monkeys. Spinal cord tissue was excised for lactate assay at the upper laminectomy as a control, and a second tissue specimen was excised at the lower laminectomy site at time increments of 30 sec to 30 min after circulatory arrest. Tissue was excised from each site without circulatory arrest in one monkey and showed negligible increase in lactate production, indicating that excision of tissue itself does not result in increased lactate. Nonanoxic samples from seven monkeys averaged 4.60 millimoles (mM)/lactate/kg tissue, with a range of 2.22 to 6.49. Postcirculatory arrest samples from these monkeys averaged 11.10 mM lactate/kg tissue, with a range of 3.62 (at 30 sec) to 14.33 (at 10 min). Anoxic spinal tissue lactate was elevated above controls in each instance, and tissue lactate peaked between 5 to 10 min after circulatory arrest and remained stable with mild fluctuations beyond that time. Thus, the spinal cord responds to circulatory arrest much as cerebral tissue, but with some delay in the accumulation of lactic acid.

Key Words: spinal cord, lactate, anoxia, ischemia, circulatory arrest

Lactate is known to accumulate in animal tissues as a result of anoxia. Lactate elevation has been quantitated in cerebral tissue following circulatory arrest and has been shown to increase in cerebral tissue after death, but such determinations have not been made on spinal cord tissue. This study explores the biochemical background for the chemical observation that, following profound central nervous system anoxia, the spinal cord tolerates anoxia better than the brain.

Methods and Materials

Eight rhesus monkeys weighing 3 to 5 kg were anesthetized with sodium pentobarbital (30 mg/kg). They were intubated for monitoring of end expiratory percent CO₂ and application of positive pressure ventilation to keep percent CO₂ at or below 4.5. Heart rate and rhythm were monitored by electrocardiogram (EKG), and arterial blood pressure was obtained via left femoral artery catheterization. These were displayed simultaneously on a Sanborn polygraph-oscilloscope combination.

Laminectomies were performed at the upper and midthoracic area. The dura was opened, and a control spinal cord sample 1.5 to 2.5 cm in length and weighing approximately 0.4 to 0.7 gm was excised from the
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upper thoracic area by sharp dissection. Tissue was immediately frozen in liquid nitrogen and surgical hemostasis carried out in the wound bed. Seven monkeys (Nos. 2–8) underwent exposure and preparation in accordance with the above model. At 5 min after excision of the control segment from the upper thoracic area, circulation was rapidly arrested by intravenous sodium pentobarbital injection (500 mg) in Monkeys 2–6; in Monkeys 7 and 8, air (100 cc) was injected into the left femoral vein.

Time of circulatory arrest was determined by cessation of voluntary respirations, absence of blood pressure, and cardiac fibrillation or arrest. At predetermined time increments after arrest (30 sec, 3, 5, 10, 20, 30 min), midthoracic cord segments were rapidly excised and frozen in liquid nitrogen. One monkey (No. 1) served as a timed control. Two samples of nonanoxic spinal tissue were excised in the locations described above to determine the effect of both excision alone and location of biopsy site on spinal tissue lactate accumulation.

Each sample was placed intact and frozen into 6% weight per volume (W/V) perchloric acid and homogenized in a preweighed glass homogenizer. Lactate in the aqueous extract was determined by a lactate dehydrogenase method. Spectrophotometric determination (Beckman Spectrophotometer DU-2) of the conversion of nicotinamide adenine dinucleotide (NAD) to reduced nicotinamide-adenine dinucleotide (NADH) was used for the final measurement.

All monkeys also had laminectomy and excision of spinal cord tissue from the lower thoracic area approximately 5 min before beginning the present study. This cord segment was used in another related study.

Results

Specimens from control monkey No. 1 showed an increase of 0.77 mM lactate/kg tissue in the midthoracic segment (at 5.50 mM/kg) as compared to the upper thoracic segment (at 4.73 mM/kg) when no circulatory arrest was present (Table 1, Fig. 1). Lactate values in anoxic cord segments excised from the midthoracic area of Monkeys 2–8 at previously mentioned time increments after circulatory arrest averaged 11.10 mM/kg tissue with a

<table>
<thead>
<tr>
<th>Monkey No.</th>
<th>Lactate Control Segment, Upper Thoracic (mM/kg)</th>
<th>Time Of Anoxia</th>
<th>Lactate In Anoxic Segment, Midthoracic (mM/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4.73</td>
<td>0</td>
<td>5.50</td>
</tr>
<tr>
<td>2</td>
<td>3.38</td>
<td>30 sec</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>4.95</td>
<td>3 min</td>
<td>7.80</td>
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<tr>
<td>4</td>
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<tr>
<td>5</td>
<td>4.18</td>
<td>10 min</td>
<td>14.33</td>
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<td>15 min</td>
<td>13.99</td>
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<td>7</td>
<td>3.27</td>
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<td>12.00</td>
</tr>
<tr>
<td>8</td>
<td>2.22</td>
<td>30 min</td>
<td>14.00</td>
</tr>
</tbody>
</table>

Legends:
- Control
- Time (Minutes) Anoxia
- No Anoxia

Fig. 1. Spinal cord lactate accumulation in eight monkeys.
range of 3.62 (at 30 sec) to 14.33 (at 10 min). It can be seen (Table 1, Fig. 1) that the elevation of tissue lactate in the anoxic segments peaked between 5 and 10 min but remained stable, with mild fluctuations, beyond that time.

**Discussion**

Possible metabolic consequences of excision of spinal cord tissue alone were reduced by the minimal change observed between lactate values of the two samples in Monkey 1. As a result, spinal cord tissue from Monkeys 2–8 could be used as an autogenous control. Elevations of tissue lactate values between two samples from the same monkey in this study then cannot be attributed either to sectioning of the cord or to individual variability between monkeys, but must be due to an inhibition of aerobic carbohydrate metabolism as a result of circulatory arrest.

In general, tissue anoxia is known to produce elevation of lactate levels. This lactate accumulation is due to conversion from aerobic to anaerobic glucose metabolism. Anaerobic metabolism is known to be only 2/3 as efficient as aerobic metabolism in terms of energy production. In addition to rapid utilization and depletion of oxygen and conversion to anaerobic metabolism, circulatory arrest and death are known to cause further lactate accumulation because of negligible "washout" of lactate due to lack of tissue perfusion. The central nervous system depends primarily on the metabolism of glucose for energy production and has been shown to be rapidly sensitive to the effects of anoxia, death, and circulatory arrest with rapid accumulation of lactic acid.

The findings in this study indicate that the spinal cord is somewhat more resistant to anoxia than brain tissue, as indicated by the extent of lactate accumulation. These results can be compared to a prior study of cerebral lactate accumulation where lactate accumulated to near peak levels between 2 and 5 min, as compared to the peak observed at 5 to 10 min in the spinal cord.

This study shows that tissue lactate accumulates in anoxic spinal cord, rapidly reaching a peak at 5 to 10 min following circulatory arrest (Table 1, Fig. 1). From these results it can be concluded that spinal cord tissue responds to circulatory arrest much as the more completely studied cerebral tissue but with some delay in accumulation of lactic acid. This is of clinical importance because studies of lactic acid accumulation in cerebral tissues have indicated a correlation between the prognosis for tissue survival and elevation of tissue lactate, although such a correlation has been denied by others.

**Summary**

Spinal cord tissue from seven rhesus monkeys was assayed for extent of lactate accumulation prior to and during total arrest of circulation. All anoxic samples showed elevation of lactic acid over control values. Spinal tissue lactate was markedly elevated within 5 min and reached a peak by 10 min. This elevation, when compared to that in cerebral tissue, was delayed, indicating a relatively greater resistance of spinal cord tissue to anoxia.

**References**


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