Lactate accumulation in spinal cord tissue following trauma was determined to ascertain the role and magnitude of ischemia. High thoracic and low thoracic laminectomies were performed on each of nine rhesus monkeys. The lower exposed cord was traumatized with a calibrated blow of 300 gm cm. The upper exposed cord served as a nontraumatized control. At time intervals of 1.5 min to 48 hrs after trauma, both cord segments were removed and assayed for lactic acid. Lactate in nontraumatized segments averaged 3.64 mM/kg tissue, with a range of 2.20 to 4.95. Lactate in traumatized segments removed in from 1.5 min to 12 hrs from six monkeys averaged 5.50 mM/kg tissue, with a range of 4.32 to 6.46. Lactate in traumatized segments from three monkeys 18 to 40 hrs after trauma averaged 4.07 mM/kg, with a range of 3.20 to 5.18. This finding supports the concept that ischemia plays a role early in the traumatic process in spinal cord injury.

Key Words: spinal cord ischemia · spinal cord injury · lactate
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rapid excision of two 1.5 to 2.5 cm segments of spinal cord, each weighing approximately 0.4 to 0.7 gm. At predetermined time intervals after injury (1.5, 15, and 30 min, and 1, 2, 12, 18, 24, and 48 hrs) the dura was incised, and then the traumatized lower thoracic segment was excised followed 5 min later by the nontraumatized upper-thoracic segment. All cord segments were frozen in liquid nitrogen immediately after excision, and surgical hemostasis was carried out in the wound bed.

Monkey 10, which served as a nontraumatized control to assess the effect of excision of a segment upon lactate accumulation in a distant spinal cord area, was subjected to laminectomies and excision of spinal cord tissue in accordance with the above model. Each sample was dropped intact and frozen into 6% weight per volume (W/V) perchloric acid and homogenized in preweighed glass homogenizers. Lactate determinations were performed on the aqueous extract by a lactic dehydrogenase method.* Spectrophotometric determinations (Beckman Spectrophotometer DU-2) of the conversion of nicotinamide adenine dinucleotide (NAD) to reduced nicotinamide adenine dinucleotide (NADH) were used for the final measurements.

Results

Grossly, all traumatized segments appeared to be pale immediately after injury. Within minutes, pia-arachnoid hemorrhages were evident. By 30 min and thereafter, swelling was also apparent.

Lactate in the nontraumatized segments excised from Monkeys 1–9 averaged 3.64 millimoles (mM)/kg tissue, with a range of 2.20 to 4.95. Lactate in traumatized segments excised from Monkeys 1–6 (1.5 min to 12 hrs post-trauma) averaged 5.5 mM/kg tissue, with a range of 4.32 to 6.46. In each of these animals there was a definite significant rise in lactate values in the traumatized segment (Table 1, Fig. 1). Traumatized segments excised from Monkeys 7–9 (18 to 48 hrs post-trauma) had lactate values averaging 4.07 mM/kg with a range of 3.20 to 5.18 (Table 1, Fig. 1). In these animals there was no rise in the lactate of traumatized versus nontraumatized segments.

In control monkey No. 10 the lower thoracic segment lactate value was 3.70 mM/kg and the upper thoracic lactate was 4.73 mM/kg.

Four animals (Monkeys 6–9) were allowed to awaken between the administration of trauma and the excision of tissue, and all exhibited flaccid paraplegia. The initial results in Monkey 3 showed a considerably elevated control lactate as well as an even greater lactate level in the traumatized segment. Because the initial high lactate value in the control segment may have represented pre-existing hypoxia, it was repeated. Both results are indicated in Table 1, but only the repeated values are included in Fig. 1.

Discussion

This experimental model of localized trauma to the spinal cord allowed each monkey to serve as its own control. This virtually eliminated the possibility that changes in spinal cord lactate were due to variations between individual monkeys.

Results from control monkey No. 10 indicated: 1) the caudal lower thoracic segment did not have an intrinsically higher lactate value than the cephalad upper thoracic segment, and 2) the effect of excising the lower

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**Table 1**

Lactate accumulation in traumatized vs nontraumatized spinal cord tissue (mMoles lactic acid/kg spinal cord tissue)

<table>
<thead>
<tr>
<th>Monkey No.</th>
<th>Time Post Trauma</th>
<th>Lactate In Traumatized Segment (mM/kg)</th>
<th>Lactate In Non-traumatized Segment (mM/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.5 min</td>
<td>5.92</td>
<td>3.38</td>
</tr>
<tr>
<td>2</td>
<td>15 min</td>
<td>6.46</td>
<td>4.18</td>
</tr>
<tr>
<td>3</td>
<td>30 min</td>
<td>4.32</td>
<td>3.56</td>
</tr>
<tr>
<td>4</td>
<td>1 hr</td>
<td>(*7.12)</td>
<td>(*6.49)</td>
</tr>
<tr>
<td>5</td>
<td>2 hr</td>
<td>5.72</td>
<td>2.20</td>
</tr>
<tr>
<td>6</td>
<td>12 hr</td>
<td>6.20</td>
<td>3.60</td>
</tr>
<tr>
<td>7</td>
<td>18 hr</td>
<td>3.80</td>
<td>4.56</td>
</tr>
<tr>
<td>8</td>
<td>24 hr</td>
<td>5.18</td>
<td>4.95</td>
</tr>
<tr>
<td>9</td>
<td>48 hr</td>
<td>3.24</td>
<td>3.36</td>
</tr>
</tbody>
</table>

* Initial lactate measurement for 1st 30 min, which may have represented preexisting hypoxia; repeat measurement was a lower value and is given above. (See “Results.”)

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Thoracic segment 5 min before the upper thoracic segment might, in fact, have caused some elevation of lactate in the latter. In our traumatized preparations, however, the lower thoracic segment was excised first and was generally higher in lactate than the upper thoracic segment. There is evidence, in cerebral tissue, that an insult to one area of the cerebrum can cause a vascular disturbance in distant areas. The possibility of this type of distant vascular effect was reduced in our experiments because of the fact that the two areas of the spinal cord in question had unrelated main vascular supply sources. It was also possible, of course, that the more cephalad portion of the spinal cord had intrinsically higher lactate values, but the experimental design in this case made such a possibility of little importance.

In contrast to Monkey 10, Monkeys 1-6 showed elevation of spinal cord tissue lactate in the traumatized segment, in spite of the fact that the traumatized segment was excised before the nontraumatized segment. It may be concluded that trauma to the spinal cord results in elevated levels of lactic acid. Although this elevation is not as high as that seen in anoxic spinal cord after circulatory arrest, it is significant in that the elevation is consistent.

This conclusion provides a baseline for further studies in spinal cord trauma. Localized spinal cord cooling, for example, has been found to be of benefit in the experimental animal after localized cord trauma. Further studies of this sort and others can now be correlated with lactate analysis for a more complete understanding of the pathological process.

Further, the finding that lactic acid increases after spinal cord trauma supports the hypothesis that ischemia plays some role in the pathological process. Lactic acid is known to increase in other tissues during ischemia. The accumulation of lactate during ischemia is presumably caused by: 1) some degree of hypoxia to the tissues resulting in conversion from aerobic to anaerobic metabolism, and 2) poor perfusion of tissues resulting in inadequate "washout" of accumulating lactate. Wagner, et al., presented evidence that localized spinal cord trauma results in mechanical distortion of blood vessels with some slowing of flow at the site of the injury. Spinal cord edema observed within minutes after the injury may also have contributed to ischemia by reduction in blood flow. Angiographic studies have revealed marked slowing of circulation in localized areas of edematous brain, and histological studies of gray matter in cerebral edema have shown stasis of the microcirculation.

Return of lactate values to near or below control values in Monkeys 7-9 indicates a change in the pathological process after the first 12 hrs following injury and suggests that hypoxia is important only in the initial stages of reaction to injury. It is possible that there was a readjustment of circulation to the traumatized area with reutilization of aerobic glycolytic pathways and washout of lactic acid. If circulatory recovery did occur, however, it was not manifested clinically because all monkeys remained paraplegic and the traumatized segment continued to demonstrate marked swelling. It is also possible that a dilution of tissue contents by edema fluid accounted for the reduction in lactate levels, but we do not believe this is the cause of the reduction. Obviously, the observed change in lactate levels in traumatized spinal cord tissue beginning 12 to 18 hrs after trauma requires further investigation.

Summary

Two spinal segments were exposed by laminectomy in 10 monkeys, and in nine of them the lumbar segment was traumatized. Both segments were then assayed for lactic acid after the cord had been in situ for...
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graded time periods. Immediately after trauma (up to 12 to 18 hrs), all traumatized spinal cord showed an elevation of lactic acid over nontraumatized segments. Thereafter, lactic acid in traumatized segments re-approximated those values seen in nontraumatized segments. It has been concluded that tissue ischemia, with resultant decreased oxygenation and perfusion, plays a significant role in the pathological processes involved in spinal cord injury. The reapproximation of lactate values beginning 12 to 18 hrs after injury requires further investigation.

References

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