Experimental Study of Ischemic Damage to the Cervical Spinal Cord*

YUTAKA SHIMOMURA, M.D.,† SINSUKE HUKUDA, M.D.,‡ AND SYOTARO MIZUNO, M.D.
Department of Orthopedic Surgery, Osaka University Medical School, Japan

The pathogenesis of myelopathies associated with human cervical spondylosis has been the subject of controversy, and no single explanation suffices for all clinical and anatomical findings. Etiological considerations have included such factors in spinal cord damage as direct compression, "anchoring,"¹⁸, ¹⁹, ²⁶, ³⁴, ³⁶, ³⁸, ³⁹ recurrent minor trauma,²⁸, ⁴⁴ and circulatory disturbances.

The fact that in man the neurological level of dysfunction does not always correspond to the level of the main spondyloptic lesions shown by x-ray and that at surgery the cord is seldom found to be compressed has recently interested a number of authors in the importance of vascular factors. Bolton⁷ and Tureen⁸ have pointed out the importance of the vertebral artery as a source of blood supply to the cervical segments of the cord. Bauer, et al.,³ Maslowski,³³ and Hutchinson and Yates⁴⁷ have assumed without actual proof that spondylosis may cause cervical ischemic myelopathy through compression of the vertebral artery.

Tureen,³⁷ Suh and Alexander,⁵⁸ and Herren and Alexander⁶¹ have described the segmental character of the spinal circulation and suggested that the cervical cord is largely dependent for its blood supply on three to five anterior radicular arteries. Woollam and Millen⁶⁴ called attention to the importance of the anterior radicular arteries by emphasizing that the anterior spinal artery is in reality nothing but an anastomotic chain formed by ascending and descending branches of each anterior radicular artery. Störtebeker⁶¹ suggested that the clinical signs of amyotrophic lateral sclerosis in two cervical spondyloptic patients may have been due to a local chronic hypoxemia of the spinal cord and brain stem induced by very slowly progressive partial compression of radicular and/or vertebral arteries. Taylor⁹ noted the similarity between the spinal cord syndromes produced by ligation of the abdominal aorta in cats and the clinical syndromes of cervical myelopathy. He also found compressed radicular arteries in the narrowed foramina, and fibrous perineural root sleeves at surgery, and considered obstruction of the radicular arteries to be the cause of spondyloptic myelopathy.

Mair and Druckman,²¹ on the basis of four autopsy cases of spondyloptic myelopathy, proposed a relationship between the degenerated region of the spinal cord and that supplied by the anterior spinal artery. Logue²⁹ believed that repeated friction injured the anterior spinal artery and caused the myelopathy. Others, however, question these theories by pointing out that the degenerated area of the cord does not correspond to the territory supplied by the anterior spinal artery. Girard, et al.,¹⁹ noted hyaline degeneration of small arterioles in the interior of the cord at autopsy. Breig, et al.,¹⁰ made microangiographic studies of the shape of the cervical spinal cord during neck motion and emphasized the luminal narrowing of the regional intraspinal arteries.

Most of these theories are hypothetical. Wilson and Landry⁶⁹ tried an experimental production of ischemic cervical myelopathy in dogs, but results were disappointing. Thus, an experimental study of cervical ischemic myelopathy seemed justified. Our study deals with an experimental ischemic myelopathy successfully obtained in mongrel dogs in which the vascular factors were clearly related to the localization and extent of the lesion. However, the relationship of the experimental findings obtained in dogs to those

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† Present address: Department of Orthopaedic Surgery, University of Illinois at the Medical Center, 840 South Wood Street, Chicago, Illinois 60680.
‡ Present address: Department of Surgery, Division of Neurosurgery, University of Kentucky, Lexington, Kentucky 40506.
of cervical spondylosis in man is still undetermined.

The Arterial Anatomy of the Canine Cervical Spinal Cord

As in man, the canine cervical spine consists of seven cervical vertebrae; its vertebral artery also arises from the subclavian artery and enters the bony canal at the transverse process of the sixth cervical vertebra. The two vertebral arteries give origin to symmetrical radicular arteries at each segmental level. These enter the spinal canal through the corresponding intervertebral foramina and divide into ventral and dorsal radicular arteries. The ventral radicular arteries, larger than the dorsal, run with the ventral spinal nerve rootlets and join the anterior spinal artery near the midline on the ventral surface of the cord. The dorsal radicular arteries reach the surface of the spinal cord with the dorsal spinal rootlets, where they divide into cranial and caudal branches which form the dorsolateral spinal artery (Fig. 1). On the surface of the cord there is the so-called pial plexus, which, though incomplete, encircles the cord and makes an anastomosis between the ventral and dorsolateral spinal arteries. From these arteries on the surface of the cord many arterioles arise which penetrate the interior of the cord; some supply the white substance while others reach the gray substance where they divide into fine capillaries. The largest penetrating branch is the ventral median fissure artery.

In the dog, the largest anterior radicular artery enters the spinal canal through the intervertebral foramen between C-2 and C-3 on each side. The anterior spinal artery enlarges abruptly at the point of junction with the C-3 radicular arteries and ascends to form an arterial diamond (the cerebrospinal junction) with the basilar artery and the occipito-vertebral arteries. The vertebral artery tapers after sending off the C-3 radicular artery and is distributed to the occipital muscles.

Material and Methods

Experimental Animals. Forty-six adult mongrel dogs were used for experiments; four of them were used as the control group to provide the normal histological sections. Among 42 operated dogs, 11 died during or after surgery and were excluded from further histological examination.

Operative Technique. Through a median longitudinal incision on the ventral surface of the neck, a paratracheal approach to the vertebral artery was carried out under Nembutal. (The right vertebral artery is situated more superficially and is more easily accessible; that on the left is crossed by the thoracic duct, which causes a little difficulty in dissection.) In some cases, muscle attached to the ventrolateral aspect of the C-3 and C-4 vertebrae was partially removed and the ventral wall of the foramen transversarium opened with rongeurs or the electric reamer.

Technique of Sacrifice. Under Nembutal anesthesia, a glass catheter was introduced into the abdominal aorta toward the heart, and after exsanguination, 500 ml of 3% Berlin blue solution were injected. Immedi-

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Fig. 1. Diagram of the arterial system of the canine caudal medulla and cervical spinal cord (redrawn from the article of Wilson and Landry).
Ischemic Damage to Cervical Spinal Cord

TABLE 1
Interference of blood flow through the vertebral artery

<table>
<thead>
<tr>
<th>Ligation Type*</th>
<th>Dog No.</th>
<th>Physical Signs</th>
<th>Sacrifice (postoperative week)</th>
<th>Macroscopic Findings†</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1</td>
<td>2</td>
<td>none</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>A2</td>
<td>3</td>
<td>none</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>A2</td>
<td>14</td>
<td>none</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>A2</td>
<td>42</td>
<td>none</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>A3</td>
<td>4</td>
<td>paresis of the foreleg</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>A3</td>
<td>7</td>
<td>none</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>A3</td>
<td>8</td>
<td>none</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>A3</td>
<td>9</td>
<td>none</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>A4</td>
<td>13</td>
<td>none</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

* See Fig. 2 for diagram of type of artery ligation.
† Histological examination of the spinal cord showed no abnormalities.

ately after this the whole spinal cord and medulla oblongata were excised. When Marchi staining was used, the exsanguination was done under simultaneous irrigation with 500 ml Müller solution through the leg vein and the excised spinal column fixed in the same solution. Among the four normal control dogs, one was sacrificed without injection of the dye, two with it, and the remaining one was used for the Marchi staining.

Preparation of Specimens. Two cylindrical pieces of tissue were dissected from each spinal cord segment after fixation; and embedded in paraffin or celloidin, sectioned, and stained with hematoxylin-eosin, Nissl, and myelin sheath staining (Weil). Sections of 360 µ were also made from the celloidin block in order to make transparent specimens following Spalteholz’s technique.

Results

Interference with Blood Flow through the Vertebral Artery. The vertebral artery was ligated at its origin unilaterally or bilaterally, and another ligation was added at a higher level between the C-3 and C-4 vertebral bodies in a group of animals (Table 1 and Fig. 2 A). All of these animals were able to walk as usual and showed normal reaction to pinprick from the first day after surgery; no abnormal neurological findings were observed in any extremities except for paresis of the foreleg of the operated side in Dog 4. (We suspect this exceptional case had an accidental injury to the nerve root during surgery.) Animals were killed after 1 to 10 weeks; during this interval no abnormal signs were observed.

Macroscopically, the cervical portion of the anterior spinal artery and each ventral radicular artery which anastomoses with it were completely filled with the injected Berlin blue dye, just as in the normal animals; there was no difference between the types of ligation. The translucent sections prepared in Dog 13, which had bilateral upper and lower ligations, showed that all penetrating branches were filled with the dye as in normal dogs, throughout the whole spinal cord.

Microscopic examination showed quite normal nerve cells from the first cervical to the lumbar spinal segments; in the myelin sheath a slight swelling was observed in the peripheral portion of the cervical white matter.

Interference with Blood Flow through the Radicular Arteries. To avoid the possible backflow of blood from muscular branches nourishing the cervical cord through the radicular arteries, a thin polyethylene catheter
Fig. 2. Diagrams indicating the kinds of vascular occlusion. Interruption of blood flow through the vertebral arteries (A), radicular arteries (B), anterior spinal artery (C), and pial plexus (D). (X = position of ligation; solid line = insertion of polyethylene catheter and filling with resin.)

(2 mm in diameter) was inserted into the vertebral artery 2 cm cranial to its origin and up to the level of the lower border of the C-2 vertebra, thus assuring interception of blood flow from the radicular arteries (Fig. 2 B); at the same time the vertebral artery was ligated at its origin. Three animals were operated on one side, while five were done bilaterally (Table 2).

The animals were lying down or staggering on the first day after surgery, but showed prompt reaction to pinprick. During the second or third postoperative day, normal walking ability was regained; the bilaterally

### TABLE 2

**Interruption of blood flow through the radicular arteries**

<table>
<thead>
<tr>
<th>Type of Artery Occlusion*</th>
<th>Dog No.</th>
<th>Physical Signs</th>
<th>Sacrifice (post-operative week)</th>
<th>Macroscopic Findings</th>
<th>Histological Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>B1</td>
<td>15</td>
<td>unstable gait, 1 day</td>
<td>6</td>
<td>C2-5 incompletely filled with Berlin blue dye, right side poorer than left side.</td>
<td>C3-5 ventral and dorsal horn cells slightly pyknotic; slight swelling of the myelin sheaths at the peripheral white matter; right and left sides the same.</td>
</tr>
<tr>
<td>B1</td>
<td>20</td>
<td>none</td>
<td>13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B1</td>
<td>24</td>
<td>unstable gait, 1 day</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B2</td>
<td>16</td>
<td>lying down, 1 day</td>
<td>5</td>
<td>C2-5 incompletely filled with dye; right and left sides the same.</td>
<td></td>
</tr>
<tr>
<td>B2</td>
<td>18</td>
<td>unstable gait, 1 day</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B2</td>
<td>21</td>
<td>lying down, 2 days</td>
<td>13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>B2</td>
<td>25</td>
<td>unstable gait, 1 day</td>
<td>6</td>
<td></td>
<td></td>
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</tbody>
</table>

* See Fig. 2 for diagram of type of artery ligation.
operated cases took a day longer to accomplish this. The animals were killed at intervals varying from 1 day to 13 weeks. Macroscopically, filling of the superficial blood vessels of the cord with dye was incomplete from C-2 to C-6. Transparent specimens (Spalteholz) were made in all of those animals in which the penetrating arterial branches also showed incomplete filling with dye at the C-2 to C-5 levels. In a few cases operated on one side, the dye did not show up well on the same side.

Degenerative changes such as chromatolysis and pyknosis were observed in a few nerve cells in the ventral and dorsal horns at the C-3 to C-5 levels, but necrosis of the cord was not found anywhere. Swelling of the myelin sheath was also noticed at the periphery of the white matter. In Dogs 24 and 25, where the Marchi staining was done, there was no trace of demyelination.

*Interference with Blood Flow through the Anterior Spinal Artery.* It is almost impossible to interrupt the blood flow of the anterior spinal artery directly without causing mechanical damage to the spinal cord, because the artery runs on the ventral surface of the cord in close contact with it. We overcame this difficulty by utilizing the fact that the C-3 ventral radicular artery is a large and main cranial branch of the vertebral artery. About 0.5 ml of cyano-acrylate resin, which polymerizes in the presence of water, was injected through a catheter inserted into the vertebral artery to the level of lower border of the C-2 vertebral body. Most of the resin pushed out of the cranial end of the catheter flowed through the largest C-3 ventral radicular artery into the anterior spinal artery, filling it between the anastomosing site of the bilateral radicular arteries at C-3 and the cerebrospinal junction. The mechanical damage to the cord was negligible (Fig. 2 C). Pure cyano-acrylate resin caused quick polymerization and made the injection with syringe difficult, but dilution of cyano-acrylate resin with dimethylformamide, a solvent of the resin, made it easier. A small quantity of Micropaque was added to obtain x-ray visualization of the extent of filling (Fig. 3). Injection was unilateral in five dogs and bilateral in four (Table 3 and Fig. 4).

At the time of injection most dogs stopped breathing for several seconds, then returned to normal breathing gradually. Opisthotonus, spasmodic stretching of the four extremities, and spastic torticollis were observed in about half the cases. In one animal in which death ensued in spite of all efforts, x-ray showed that the injected resin had reached the level of the medulla oblongata, having passed through the cerebrospinal junction.

On the first day after surgery all dogs were lying down, hardly moving, and giving no reaction to pinprick. On the third or fourth day after surgery, most of the dogs were able to stand but the forelegs were extremely hyperflexed at the carpal joints. On the fifth or sixth day they usually were able to stand and run but their unstable gait remained almost unchanged until the time of necropsy. No difference of symptoms was noticed between the animals that had unilateral and bilateral injections.

The injected resin usually filled the anterior spinal artery up to the cerebrospinal junction; filling with Berlin blue was poor at the C-2 and C-3 segments (Fig. 5). In transparent specimens the dye hardly entered the penetrating branches at the C-2 and C-3 segments.

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**Fig. 3. X-ray demonstrating the anterior spinal artery and C-3 radicular arteries obliterated by the resin.**

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and only poorly into the lower segments down to C-6. Neither the blood vessels of the ventral column nor those of the dorsal and lateral columns of the injected side, which are not ordinarily considered to be supplied by the anterior spinal artery, were filled with the dye. This fact might have been caused by simultaneous obliteration of the vertebral artery of the same side. Latent ischemia of the spinal cord brought about by obstruction of the vertebral artery might be clearly disclosed when obstruction of the anterior spinal artery was added (Fig. 6).

In Dog 26, sacrificed at 24 hours, the ventral horn cells (especially at the inner side of the horn) showed clear degenerative changes at C-1 and C-2, together with slight demyelination in the periphery of the ventral and lateral columns from C-2 to C-5. In the 1-week survivors (Dogs 27, 28, and 29), tissue necrosis, proliferation of glia cells, and newly formed capillaries were observed in the ven-

### TABLE 3

** Interruption of blood flow through the anterior spinal artery **

<table>
<thead>
<tr>
<th>Type of Artery Occlusion*</th>
<th>Dog No.</th>
<th>Days Lying Down</th>
<th>&quot;Hip-Swaying&quot; Gait</th>
<th>Sacrifice (postoperative week)</th>
<th>Diagrams of Histological Findings</th>
</tr>
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<tbody>
<tr>
<td>C1</td>
<td>27</td>
<td>3</td>
<td>yes</td>
<td>1</td>
<td>Fig. 4, top row</td>
</tr>
<tr>
<td>C1</td>
<td>29</td>
<td>3</td>
<td>yes</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>C1</td>
<td>31</td>
<td>4</td>
<td>yes</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>C1</td>
<td>39</td>
<td>3</td>
<td>yes</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>C1</td>
<td>41</td>
<td>4</td>
<td>yes</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>C2</td>
<td>22</td>
<td>4</td>
<td>no</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>C2</td>
<td>26</td>
<td>2</td>
<td>yes</td>
<td>1 day</td>
<td></td>
</tr>
<tr>
<td>C2</td>
<td>28</td>
<td>3</td>
<td>yes</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>C2</td>
<td>36</td>
<td>died immediately after the injection of the resin</td>
<td>no examination</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* See Fig. 2 for diagram of type of artery occlusion.

![Fig. 4. Histological findings of the spinal cord in Dogs 27, 29 (top row), Dogs 31, 39, 41 (second row from top), Dog 22 (third row), Dog 26 (fourth row), and Dog 28 (bottom row).](image)
tral horn and column from C-1 to C-3, and degeneration of ventral and dorsal horn cells to C-6 (Fig. 7). In the 5- and 6-week survivors (Dogs 31 and 39), liquefaction and a subsequent cavitation occurred in the bilateral ventral horns and columns at C-2 and C-3, where the anterior spinal artery was obstructed (Fig. 8); at lower segments there was demyelinization in the periphery of the ventral column and ventral half of the lateral column, particularly in the medial longitudinal fasciculus along the ventral median fissure where degeneration extended as far as the lumbar segments. The staggering gait that lasted until the time of sacrifice might have been due to degeneration of this extrapyramidal tract.

The dorsal horn cells were also degenerated as low as C-8. The fact that Dog 22 survived for 8 weeks with relatively little change of the spinal cord was probably due to the fact that the amount of injected resin was so scanty that it was not sufficient to obstruct the anterior spinal artery. The spinal cord lesions in Dog 41 which survived for 18 weeks were almost the same as those of Dogs 31 and 39 which survived for 6 weeks. This fact suggests that pathological changes in the spinal cord are determined during the first 5 or 6 weeks after arterial obstruction. In none of the cases were changes observed in the lateral pyramidal tract.

Degenerative changes of the dorsal column were not shown by H. & E. or Weil staining, but demyelinization in the fasciculus cuneatus was clearly demonstrated by Marchi stain in some cases surviving more than 1 week. This usually appeared at about C-4, laterally in the fasciculus cuneatus and in close contact with the filaments of the dorsal root. It appeared ipsilaterally in the unilaterally injected cases and on both sides of those injected bilaterally (Fig. 9).

As this degeneration of the Burdach tract made us doubtful of the degenerative changes noted in C-4 dorsal nerve root, the spinal cord of Dog 45 in which the C-5 dorsal nerve root had been severed 2 weeks previously was examined more extensively from C-1 to C-8. Degenerative changes in the Burdach tract were observed at the C-5 segment, in close contact with the dorsal nerve root filaments and moving medially at higher levels in a manner that resembled the degeneration of the dorsal column observed in the cases of obstruction of the anterior spinal artery (Fig. 10). In the dog with severed dorsal nerve root, however, the dorsolateral region of the lateral column (ventral and dorsal spinocerebellar tract) was also demyelinated.

On the contrary these changes in the lateral column were not observed in the animals with obstruction of the anterior spinal artery. Further studies should be conducted to determine whether this degenerative change of the dorsal column was due to the ischemia caused by obstruction of both the anterior spinal artery and the vertebral artery, or the spinal manifestation of the ischemic radiculopathy that occurred in the spinal ganglion or dorsal spinal nerve root.

**Obstruction of Blood Flow to the Pial Plexus.** Unexpectedly, an animal that had been operated on with the purpose of obstructing the anterior spinal artery (Dog 34) developed a right hemiplegia. Necropsy after 4 weeks disclosed resin filling the pial plexus of the right side by way of the C-5 radicular artery. The upper end of the catheter had accidentally only reached this halfway point. A cavity was found in the lateral column of the same side at C-5. In the transparent specimens, resin
FIG. 6. Two transverse sections of the C-2 segment. Top: Dog 29. The anterior spinal artery is obliterated by the resin injected from one side. The invasion of the Berlin blue dye is observed in the posterolateral quadrant of the uninjected side. Bottom: Dog 27. The anterior spinal artery is obliterated by the resin injected from both sides. Almost nowhere is invasion of the dye seen. (Transparent specimen after Spalteholz.)
Fig. 7. Anterior spinal artery occlusion; Dog 29, sacrificed at 1 week. Top: Transverse section of the C-2 segment shows degenerated ventral horn and column on both sides. Bottom: A high-power view of the square area in the top photograph demonstrates proliferation of glia cells and new formation of blood vessels. H. & E.
filled the blood vessels encircling the right lateral column; the arterial branches penetrating into the lateral column consequently were not filled with Berlin blue. There was demyelinization of the right lateral pyramidal tract from C-5 to the lower thoracic segments (Fig. 11).

This observation led to the next experiment, in which a polyethylene catheter with its cranial end closed, but with rows of slits in the side wall, was inserted into one vertebral artery. Resin was injected through this catheter with the purpose of obstructing the pial plexus of the same side through the radicular arteries. Both of these animals (Dogs 43 and 44) developed immediate hemiplegia of the injected side (Fig. 2 D). The resin filling the pial plexus of the injected side could be seen macroscopically. Because the cranial end of the catheter was closed, it was anticipated that resin would be unable to enter the cranium: moreover, x-rays showed no trace of the resin in the brain. Histological findings revealed an extensive necrosis in the lateral column of the injected side; the demyelinization of the lateral pyramidal tract could be followed down to the lumbar segments. Thus, for the first time, degeneration of the lateral pyramidal tract was experimentally produced by obstructing the pial plexus (Table 4 and Fig. 12).

In the more cranially located segments, demyelinization of the fasciculus cuneatus together with the ventral and dorsal spinocebellar tracts was observed, a fact which exactly corresponded with the spinal change seen in Dog 45 in which the dorsal nerve root was severed. We therefore suspect that a complete obstruction of the radicular arteries with resin might produce ischemic degeneration of the cervical nerve roots as suggested in the C-5 dorsal nerve root of Dog 43.

Experiments upon the Toxicity of the Resin. Studies were undertaken to determine the toxic effect of the resin mixture on local tissue and the general condition of the animal.

Experiment 1: Three times the usual injection (1.5 ml) of resin was injected into the lateral saphenous vein of a normal dog under general Nembutal anesthesia. The dog was unable to stand up for 1 day but walked normally beginning with the second day. Necropsy was done at 10 weeks, and the injected vein was examined histologically. There was infiltration of fibrocytes into the resin from the surrounding tissue but no tissue necrosis or cellular reaction around the blood vessel.

Experiment 2: Laminectomy of T-7 and T-8 was done on a normal dog; a small portion of the dura mater was resected, and resin was poured onto the laminectomized site. The animal had an unstable gait for 1 day but then returned to normal. Histological examination of the spinal cord at 1 week showed that the T-7 segment was compressed by the epidural resin mass; slight demyelinization without any change in the nerve cells in the dorsal column was observed. At T-8 the resin adhered tightly to the surface of the cord; in the peripheral white matter vacuolization of the myelin sheath localized to the superficial layer was observed, but the nerve cells were intact (Fig. 13).

We concluded that any toxic effect on the general physical condition subsides in 1 day, and that there is no tissue damage around the blood vessels filled with the resin. If applied locally, the resin caused slight degenerative changes to the spinal cord at the very site of a
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FIG. 9. Anterior spinal artery occlusion; Dog 39, sacrificed at 5 weeks. Top left: Transverse section of C-2 segment indicates demyelination of the ventral columns, cavitation of the ventral horns, and linear demyelination of the Burdach tract of the injected side (arrow). Top right: Transverse section of C-3 segment. The linear demyelination of the Burdach tract comes near to the dorsal nerve filaments (arrow). Lower left: Transverse section of C-8 segment. Demyelination of the ventral column is localized to the medial longitudinal fasciculus (arrow). Lower right: Transverse section of L-5 segment. Demyelination of the medial longitudinal fasciculus is observed extended to the lumbar spinal cord. Marchi staining.

close contact; even this kind of local toxic effect did not extend very deep.

On the other hand, the degenerative change seen with obstruction of the anterior spinal artery or pial plexus extended to the deepest layers, even though the injected resin made no direct contact with the cord, partitioned off by the arterial wall. Moreover, the longer the survival period, the greater the spinal cord damage. We concluded that most of the cord lesions seen in the experiments following obstruction of the anterior spinal artery or pial plexus were due to the poor local blood supply and eventual ischemia.

Discussion

Since in our animals no remarkable histological changes occurred in the spinal cord after obstructing the vertebral artery, we suggest that the role of the vertebral artery as one of the main sources of blood supply to the cervical cord is not as essential as is emphasized by others. Moreover, in our animal experiments, obstruction of blood flow through each radicular artery at its origin had little effect on the spinal cord. The severe degenerative changes reported in human autopsy studies were never encountered. Because of the dif-
observed in our obstruction of the pial plexus, degeneration of the nerve root (ischemic radiculopathy) might occur if the radicular artery was obstructed. Segmental signs could be caused by this sort of ischemic radiculopathy, whereas cord signs are never encountered with obstruction of the radicular arteries. Therefore, we believe the theory of Woollam and Millen, Bradshaw, Störtebecker, Taylor, and others regarding the importance of the radicular artery in the pathogenesis of cervical ischemic myelopathy does not hold true. Because of the anastomoses between the ventral and dorsolateral spinal arteries through the encircling connecting pathway of the pial plexus, localized ischemia of the spinal cord rarely occurs even when the blood supply from the radicular arteries is stopped.

On the other hand, obstruction of the anterior spinal artery produced distinct degeneration of the spinal cord at the levels of the obstruction; degeneration of the ventral and dorsal horn cells, plus demyelinization of the total ventral column, were the main findings. At 4 or 5 weeks, severe changes such as tissue necrosis, liquefaction, and cavitation in the ventral horn and column appeared in the area supplied by the anterior spinal artery. Demyelinization of the medial longitudinal fasciculus extending down to the lumbar segment was another conspicuous finding. It was thus particularly remarkable that we found little or no change in the lateral pyramidal tract.

These experimental results partly explain ischemic myelopathy in the cervical spinal cord. The principal factor in myelopathy seems to be obstruction of the blood vessels on the surface of the spinal cord, including the anterior and dorsolateral spinal arteries and the medullary parts of the radicular arteries and the pial plexus, rather than obstruction of the vertebral arteries or the lateral portions of radicular arteries.

Direct cord compression by a prolapsed disc or osteophyte from the ventral or ventrolateral aspect and the countercompression by the ligamentum flavum from behind must be important parts of the obstructive mechanism. Recently, applying microangiographic technique to human cadavers, Breig, et al., showed filling defects in the arteries on the surface of the spinal cord corresponding to the location of spondylotic ridges. Although they paid little attention to this fact, we consider it

Fig. 10. Unilateral C-5 dorsal nerve root severing; Dog 45. Top: C-2 segment. Center: C-4 segment. Bottom: C-5 segment. Demyelinization of the Burdach tract appears at the C-5 segment and comes more medial at the upper segments (top arrow). The ventral and dorsal spinocerebellar tracts are also demyelinated (center arrow). Marchi staining.

ference in the number of radicular arteries in man and dog, it is always dangerous to draw too positive a conclusion from the animal experiment. Nevertheless, the fact that in our studies all the radicular arteries, unilateral or bilateral, were obstructed strongly suggests that our animal experiments have some pertinence to human spondylotic myelopathy. As
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TABLE 4

Interference of blood flow through the pial plexus

<table>
<thead>
<tr>
<th>Type of Artery Occlusion*</th>
<th>Dog No.</th>
<th>Physical Signs</th>
<th>Sacrifice (postoperative week)</th>
<th>Diagrams of Histological Findings</th>
</tr>
</thead>
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<tr>
<td>D1</td>
<td>34</td>
<td>Hemiplegia of right side</td>
<td>4</td>
<td>Fig. 12, top row</td>
</tr>
<tr>
<td>D1</td>
<td>43</td>
<td>Hemiplegia of right side</td>
<td>3</td>
<td>Fig. 12, center row</td>
</tr>
<tr>
<td>D1</td>
<td>44</td>
<td>Hemiplegia of right side</td>
<td>4</td>
<td>Fig. 12, bottom row</td>
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* See Fig. 2 for diagram of type of artery occlusion.

important proof of our speculation. In the same way, as Kahn suggested, the dentate ligament might exert a mechanical stress that causes obstruction of the pial plexus leading to ischemic demyelinization in the lateral pyramidal tract. Arachnoidal adhesions, which were considered as exerting an anchoring effect on the cord by Nugent, Wilkinson, and Girard, et al., could be another factor that brings about obstruction of the blood vessels on the surface of the cord, which in turn produces ischemic myelopathy.

Although even extensive obstruction of the lateral portion of the radicular arteries did not cause ischemic myelopathy of the cervical cord, the situation may be different in the thoracic or lumbar regions. In fact, several cases have been reported in which central necrosis developed in the thoracic and lumbar spinal cord after surgery of the aorta or a dissecting aneurysm. Here, of course, the anterior spinal artery cannot play the role of an anastomosing channel.

Although there is little doubt as to the effectiveness of the Cloward procedure (anterior decompression and interbody fusion of the cervical spine for cervical spondylosis and cervical disc herniation), there still remain questions as to why those surgical procedures are so effective. Some authors emphasize the removal of an osteophyte; others maintain that simple interbody fusion does the job. Others think that spreading the intervertebral space is important. During the past 3 years, we have performed Cloward's operation successfully in more than 100 cases, many of which showed a postoperative intervertebral space that was unchanged or even narrower than before. Moreover, we often only removed the dorsal longitudinal ligament at the bottom of the drilled hole which exposed the dura mater for decompression of the spinal cord from the front and did not remove lateral osteophytes protruding into the intervertebral foramen; in many of the cases, not only the cord signs but also the segmental signs were much improved.

We believe that the demyelinization following obstruction of the radicular arteries alone is not clear. We consider that Cloward's decompressing procedure improves the blood flow through the anterior spinal artery, and

![Fig. 11. Cervical pial plexus obstruction of one side; Dog 34, sacrificed at 4 weeks. Transverse section of C-5 segment shows the resin filling the pial plexus (top arrow) and cavitation of the lateral column (lower arrow). (Transparent specimen after Spalteholz).](image-url)
Fig. 12. Histological findings of the spinal cord in Dog 34 (top row), Dog 43 (center row), and Dog 44 (bottom row).

Fig. 13. Tissue reaction of the spinal cord against the cyanoacrylate resin. *Top:* Transverse section of T-7 segment. The spinal cord is flattened by compression of the epidural resin, but no remarkable histological changes of the cord is found. *Bottom:* Transverse section of T-8 segment. The resin adheres to the surface of the spinal cord and demyelinization of the white matter is found at the site but does not extend deeper.
Ischemic Damage to Cervical Spinal Cord

consequently through the pial plexus, and that even the blood supply to the nerve roots is increased by this anastomatic compensation; this we believe is why not only the segmental but the cord signs are improved by this relatively restricted anterior decompression.

We therefore emphasize the importance of decompressing the spinal cord anteriorly by Coward's operation, which improves the circulation on the surface of the cord by direct decompression of the anterior spinal artery, and possibly indirectly by the relaxing effect upon the dentate ligament.

In man, thrombosis of the anterior spinal artery also results in degenerative changes and even necrosis in the area supplied. Several autopsy cases have been reported and characteristically showed necrosis of the pyramidal tract and the ventral two-thirds of the cord at the most severely affected segment. On the other hand, in our experiment the main lesion was confined to the ventral third of the cord while the lateral pyramidal tract remained intact; degeneration of the pyramidal tract occurred only after occlusion of the pial plexus on the surface of the lateral column. The extensive necrosis found in the human autopsy cases might have been due either to an extensive thrombosis of the anterior spinal artery or to extension into the pial plexus.

Hemiplegia is usually considered of cerebrovascular etiology, and that due to spinal cord involvement is rare. We produced unmistakable experimental ischemic spinal hemiplegia by obliterating the pial plexus of one side, which strongly suggests the possibility that human spinal hemiplegia may be caused by ischemia. We also suggest that hemiplegia that develops as a direct side effect of angiography of the vertebral artery may be due to obstruction of the pial plexus.

In the present experiments, not only the simple degenerative changes but also liquefaction and subsequent cavitation in the spinal cord were observed. The pathogenesis of syringomyelia is a controversial subject and several combined factors are generally considered as the cause. 6, 16, 21, 37, 41, 43, 47, 53, 60

Netsky, Nelson and Lubin reported cavities at the site of arachnoidal fibrosis and suggested that the vascular disruption resulting from the arachnoiditis might have been the specific cause of the syrinx formation. McLaurin, et al., produced experimental arachnoiditis by injecting kaolin and Pantopaque into the cisterns of dogs; well-defined cavitations developed in the spinal cord after about 5 weeks. Tauber and Langworthy, by application of silk ligatures to the ventral half of the cord, produced cavitation in the ventral portion of the posterior columns; this change was considered due to injury to the anterior spinal artery. Mair and Druckman found cavitation in the cord in one case out of four autopsied having herniated cervical intervertebral discs. Davison and Keschner described two cases showing that atherosclerosis of cord arteries caused cavitation by circulatory interference.

Probably there are multiple factors which cause intramedullary cavitation but there is no doubt that ischemia is a significant one.

Summary and Conclusions

On the basis of animal experiments we conclude that:

1. Obstruction of blood flow through either the vertebral artery or the radicular arteries at their origin has little relationship to cervical ischemic myelopathy.
2. Degeneration of the spinal cord caused by obstruction of the anterior spinal artery alone is limited to the ventral third of the spinal cord and does not extend to the lateral pyramidal tract.
3. The pathogenesis of cervical ischemic myelopathy is intimately concerned with obstruction of the arteries spreading on the surface of the spinal cord, including the anterior spinal artery, medullary parts of the radicular arteries, the pial plexus, and the dorsolateral spinal arteries.
4. Ischemic radiculopathy depends not only on obstruction of the radicular arteries but also on disturbances in blood flow through the anterior spinal artery.
5. Experimental hemiplegia of spinal origin can be caused by obstructions to the pial plexus of the spinal cord.
6. Interference with blood flow through arteries on the surface of the spinal cord has been confirmed as one of the factors causing intramedullary cavitation.

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