Experimental chronic compressive cervical myelopathy

OSSAMA AL-MEFTY, M.D., H. LOUIS HARKEY, M.D., ISAM MARAWI, M.S.,
DUANE E. HAINES, PH.D., DUDLEY F. PEELER, PH.D., HARVEY I. WILNER, M.D.,
ROBERT R. SMITH, M.D., HOWARD R. HOLIDAY, M.D., JOSEPH L. HAINING, PH.D.,
WILLIAM F. RUSSELL, M.D., BRENT HARRISON, M.D. AND TROY H. MIDDLETON, M.D.

Department of Neurosurgery, Loyola University Medical Center, Maywood, Illinois; Departments of Neurosurgery, Anatomy, and Radiology, University of Mississippi Medical Center, and Basic Science Research Laboratory, Veterans Administration Medical Center, Jackson, Mississippi; and Department of Radiology, Harper Hospital and Wayne State University School of Medicine, Detroit, Michigan

A canine model simulating both cervical spondylosis and its results in delayed progressive myelopathy is presented. This model allowed control of compression, an ongoing assessment of neurological deficits, and evaluation using diagnostic images, frequent electrophysiological tests, local blood flow measurements, and postmortem histological examinations. Subclinical cervical cord compression was achieved in 14 dogs by placing a Teflon washer posteriorly and a Teflon screw anteriorly, producing an average of 29% stenosis of the spinal canal. Four dogs undergoing sham operations were designated as controls. Twelve of the animals undergoing compression developed delayed and progressive clinical signs of myelopathy, with a mean latent period to onset of myelopathy of 7 months.

Spinal cord blood flow studies using the hydrogen clearance method showed a significant transient increase in blood flow immediately after compression and a decrease before sacrifice. Somatosensory evoked potential studies indicated progressive deterioration during the period of compression. Magnetic resonance images revealed intramedullary changes. Histological studies showed abnormalities overwhelmingly within the gray matter, including changes in vascular morphology, loss of large motor neurons, necrosis, and cavitation. Axonal degeneration and obvious demyelination were rarely seen. The most profound morphological changes occurred at the site of greatest compression. It is proposed that a momentary arrest of microcirculation occurs during extension of the neck because of loss of the reserve space in the compromised spinal canal. This microcirculatory disturbance is predominant in the watershed area of the cord and mainly affects the highly vulnerable anterior horn cells, leading to neuronal death, necrosis, and eventual cavitation at the junction of the dorsal and anterior horns. Additional supportive evidence of this hypothesis was derived from the literature.

Key Words: cervical spondylosis • cervical myelopathy • spinal cord compression • magnetic resonance imaging • somatosensory evoked potentials • dog

Myelopathy due to chronic compression of the spinal cord is often encountered in cases of cervical spondylosis, ossification of the posterior longitudinal ligament, spinal stenosis, and cervical disc herniation. The pathophysiology of chronic compression myelopathy, however, remains controversial and the two hypotheses about its etiology (vascular and mechanical) do not explain a number of discrepancies existing in studies of myelopathy.1,3,11,12,17,19,24,31,33,37,38,48,52,53,59,60,67,68,71,72,74,77,78,81,83 Although several excellent experimental studies have been reported,5,38,32,47,51,64,70,73,81,84 they are deficient in a number of areas: 1) these studies are acute or subacute in design and the animals are usually sacrificed either shortly after compression or at a maximum of 6 months; consequently, they lack the chronic nature that is the hallmark of this disease; 2) none of these studies measured spinal cord blood flow (SCBF) after prolonged compression; 3) the spinal cord was compressed either anteriorly or posteriorly, thus failing to mimic the clinical disease; 4) in some studies, the main blood supply was ligated or hypotension was induced, thereby overshadowing the effects of pure compression; 5) some studies used a compressive device of increasing mass, producing acute compression once the mass reached a critical volume; 6) most studies lacked a mechanism for spinal cord decompression; and 7) clinical observations of intramedullary cystic necrosis and cavitation seen on magnetic resonance (MR) images or delayed computerized tomography (CT) myelography in patients with spon-
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A canine model for myelopathy has been previously reported in which subclinical compression, or "maximum tolerable compression," was induced by an anteriorly placed metal screw. This model provided invaluable information about the additive effects of multiple levels of compression and ischemia. Our experiment is a modification of this model and was designed to include: 1) prolonged simple compression simulating the chronic nature of chronic compressive myelopathy; 2) spinal canal compromise by anterior and posterior devices simulating cervical spondylosis; 3) Teflon compressive devices (screw and washer) allowing CT and MR images without artifactual interference; and 4) SCBF measurements.

Materials and Methods

Animal Preparation

Eighteen mongrel dogs (11 female and seven male), weighing an average of 20 kg each (range 14 to 28 kg), were used for this study. Animals with chondrodystrophic features were excluded. The animals were tested for disease and observed by a veterinarian for a minimum of 2 weeks before being included in the study. Computerized tomography scans with intrathecal contrast enhancement were obtained for each animal to determine the diameter and area of the cervical canal and cord (Fig. 1). The baseline neurological evaluation and somatosensory evoked potentials (SSEP's) were documented. Each animal was neurologically normal at the outset of the study.

Fourteen animals underwent subclinical cervical cord compression produced by narrowing the cervical canal with Teflon devices implanted anteriorly and posteriorly. An additional four animals underwent a sham operation identical to that of the animals with spinal cord compression ("compressed animals") but without placement of compressive devices. At an average of 45 weeks after compression (range 35 to 50 weeks), six animals underwent decompressive surgery during which the anterior device was removed. All animals were sacrificed within 18 months of the initial surgical procedure. Throughout the study, they were maintained under normal caging conditions in the central laboratory animal facility under veterinary care and supervision, according to the "Institutional Animal Care and Use Guidelines."

During the study period, neurological testing was performed biweekly. Testing included observation of the animal's posture and voluntary movement, the wheeze, hopping, and placing reactions, and withdrawal and stretch reflexes. Spinal cord blood flow was measured using a modified H2 clearance technique before and after compression and before sacrifice. Evoked potentials were recorded during each surgical procedure and at least monthly until sacrifice. An MR image was obtained for all animals at least 24 weeks after compression, and another image was obtained for 10 of the animals before sacrifice. A 1.5-tesla magnet was used in all animals with the following factors: for TR-weighting (TE 20 msec, TR 800 msec, slice thickness 3 mm) and for TR-weighting (TE 30 or 80 msec, TR 2000 msec, slice thickness 3 mm). After the animals were sacrificed, spinal cord microangiograms were obtained by photographing the entire harvested segment of the cord. In addition, axial sections 3 mm thick at the C-3, C-4, C-5, and C-6 vertebral levels were photographed for each animal.

Histopathological Study

The spinal cords were inspected for evidence of external compression. The positions of the screw and washer were identified, and the penetration of the screw was assessed in relation to the position of the washer.

The spinal cords were prepared for histological evaluation at the light microscopic level, and all sections were studied to identify cell loss, the degree of demyelination, evidence of axonal degeneration, necrosis and/or cavitation, and changes in the morphology of blood vessels. Samples were taken at the level of maximum compression, from two segments above, and from at least one segment below the level of compression. Stains were selected that would provide the maximum amount of information. Paraffin-embedded tissues were cut at 10 μm and stained with hematoxylin and eosin, and Luxol fast blue-cresyl violet. Sections prepared with a modification of the Weil stain for myelin were cut at 25 μm.

Cord samples cut in frozen section at 50 μm were impregnated with a modification of the Fink and Hei-

![Fig. 1. Precompression computerized tomographic myelogram demonstrating measurements of cross sections of the spinal cord and canal and their relationship in Dog 7. The area within the spinal canal surrounding the spinal cord (arrows) is the reserve space.](image-url)
mer selective silver method to demonstrate the presence or lack of degenerated axons in the white and gray matter. The glial fibrillary acidic protein with fluorescein tag method was used to identify glial responses. Because of the fixation technique used, this method presented only limited information for our study.

Surgical Procedure

Compression. All surgical procedures were performed under sterile conditions. The animals were anesthetized with an intramuscular injection of 2.5 mg acepromazine and 250 mg ketamine-HCl. They were intubated and allowed to breathe spontaneously. Anesthesia was maintained throughout the procedure with intravenous administration of sodium pentobarbital. Arterial and venous catheters were inserted into the femoral artery and vein, respectively, and an intravenous drip of lactated Ringer’s solution was maintained throughout surgery. The arterial catheter was connected to a pressure transducer that monitored blood pressure and heart rate. Blood gas and hematocrit levels were measured throughout the procedure, and broad-spectrum antibiotics were administered perioperatively.

Using x-ray film: equipment, the C-5 lamina was exposed. The ligamentum flavum and one side of the inferior aspect of the lamina were removed. Spinal cord blood flow was measured using the modified H2 clearance method previously described. The platiniized electrode was placed in the spinal cord through the dura perpendicular to the surface of the cord at a point midway between the midline and the lateral boundary of the cord. The electrode was advanced to a depth of 2 mm in the spinal cord. The reference electrode was secured to the spinous process.

A Teflon washer (1.5 mm thick, 8 mm in diameter) (Fig. 2) was inserted into the cervical canal parallel to the lamina, compromising the canal by 15%. Somatosensory evoked potentials were recorded before and after the washer was inserted. The incision was temporarily closed and the animal was turned to a supine position.

The anterior body of the C-5 vertebra was exposed through a standard anterior cervical approach and confirmed radiographically. A hole 6 mm in diameter was made with a power drill in this anterior body. The posterior longitudinal ligament was removed and the dura exposed. The depth of the defect was measured with a micrometer and the hole was tapped to receive a Teflon screw (7 mm in diameter, 25 mm long, pitch 1.2 mm/turn) (Fig. 2). The maximum tolerable compression was obtained by advancing the screw in small increments while SSEPs were recorded. The first SSEP change was considered an indicator of maximum tolerable compression. If no SSEP changes occurred, the screw was advanced until a total of 35% of the spinal canal diameter was compromised.

The animals were monitored postoperatively in a recovery area. Intravenous fluid infusion was continued and an analgesic (subcutaneous butorphanol tartrate (0.3 mg/kg) was administered for pain as needed. After full recovery, the dogs were transferred to the caging area within 36 hours.

Sacrifice. At the end of the experiment, all animals were sacrificed. The survival period averaged 62 weeks (range 44 to 77 weeks). Anesthesia and preparation were similar to those for prior surgical procedures; the previous laminotomies were exposed and a final measurement of SCBF was obtained. The animal was then turned to a supine position, and both common carotid arteries were ligated. An intravenous injection of 10,000 U heparin was given to each animal. The thorax was opened and the descending aorta clamped. Total blood replacement with heparinized normal saline was achieved through a left ventricular catheter and right atrial drainage. Cardiac arrest occurred during the saline perfusion. Then 1 or 2 liters of a 20% barium sulfate and 10% buffered formalin solution was perfused until the vessels were saturated.

The spinal cord was removed via a laminectomy from the C-2 through C-7 vertebrae, and the level of compression was recorded on the roots. The cord was then suspended in formalin for microangiography and histological evaluation. A block of the cervical column at the level of compression was also removed and preserved in formalin.

Results

The neurological, radiological, electrophysiological, blood flow, and pathological findings were reviewed independently, each by an expert colleague. The data compiled from all categories were reviewed by two investigators for correlation.

Neurological Findings

Twelve of the 14 animals with a compressed spinal cord eventually developed clinical signs of myelopathy. The mean latency period of all 18 animals between compression and onset of myelopathy was 34 weeks. The earliest signs of myelopathy appeared at 17 weeks,
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while the latest appeared at 76 weeks. The two animals that did not develop myelopathy before sacrifice were found not to have cord compression at the postmortem examination. Two of the four animals undergoing the sham operation developed signs of mild myelopathy and were found to have significant cord compression secondary to epidural scar formation (Fig. 3). Neurological deficits were progressive in nature and degree, with the order of onset being placing, hopping, gait disturbance, and withdrawal reflex in 12 of the 14 animals developing deficits. No stretch reflex abnormalities or sphincter disturbance occurred.

Somatosensory Evoked Potentials

The SSEP data were assessed for changes in latency and amplitude of the first negative (N1) and second positive (P2) peaks and in the relationship between these two peaks. Because of several technical and biological factors that produced a wide variability in the data, only trends in the latencies and amplitudes of the SSEP's could be correlated with the onset of neurological deficits. Nevertheless, SSEP's tended to deteriorate in progressive fashion, paralleling the gradual loss of neurological function. These changes usually preceded or coincided with the appearance of neurological deficits.

Perusal of the N1 latency scores indicated an apparent increase of N1 latencies in many of the animals during the period of compression. This trend is emphasized in each subject by smoothing the curve illustrating latencies using the fourth-order polynomial. Of the 14 animals with spinal cord compression, 12 had apparent increases in the differences between N1 and P2 latencies (N1 - P2 latency) during the period of compression.

**Spinal Cord Blood Flow**

Data concerning SCBF were available for analysis in all but one of the animals. Measurement of the SCBF was analyzed before compression, immediately after compression, and at the end of compression (the value obtained at sacrifice or before decompression). The results were analyzed using Tukey's range test with Student modification at a simultaneous error rate of \( \alpha = 0.05 \). The analysis revealed a statistically significant increase in SCBF immediately after compression and a significant decrease in SCBF when the postcompression values were compared with the final SCBF values. When baseline SCBF measurements were compared with those of final blood flow values, a trend toward a decrease in blood flow emerged; however, the differences were not statistically significant (Fig. 4). There were too few sham-operated animals to statistically compare their SCBF findings with those of the compressed group.

**Imaging Data**

Preoperative CT scans revealed the following measurements: sagittal diameter of the spinal canal, mean 10 mm (range 9 to 11 mm); sagittal diameter of the spinal cord, mean 6.5 mm (range 5 to 8 mm); area of the spinal canal, mean 87.2 sq mm (range 64 to 106 sq mm); and area of the spinal cord, mean 48.3 sq mm (range 40 to 55 sq mm).

The screw failed to penetrate the spinal canal in two animals. In five animals there was clear laterality with the screw compressing only one-half of the spinal cord, while in the remaining seven animals the screw was more centrally placed. The degree of sagittal compression, as estimated on the MR image, averaged 29% (range 10% to 50%). An average of 20% (range 13% to 33%) of the spinal canal area was compromised by the screw (Fig. 5). Four animals with laterally placed screws showed evidence of root compression. One animal in the sham-operated group showed evidence of epidural scarring with significant compression of the spinal cord on the MR image.

Only the axial MR images showed significant signal and structural changes in the cord; the sagittal images demonstrated only compressive changes. The previously described "snake eyes" appearance, indicating varying degrees of myelomalacia of the central gray matter, was easily seen as high signal intensity in the central gray matter on T1-weighted images (Fig. 6 left).
These “snake eyes” were seen in 14 animals, including three animals undergoing sham operations. The region of high signal intensity was frequently adjacent to or encompassing a small area of low signal intensity. This was most commonly and best seen at the level of compression, but was occasionally present above or below the level of compression. Three animals had a solitary large low-intensity lesion, representing gross cavitation at the late stage of myelomalacia (Fig. 6 right).

Of the MR images obtained in 10 animals before sacrifice, “snake-eye” lesions were seen on the axial images in eight. On four the lesions were similar to those seen on the first image, and on four the lesions showed improvement. No evidence of snake-eye lesions appeared on either study in two animals.

**Microangiography**

Two investigators independently reviewed the microangiograms. Neurologically and pathologically normal animals that underwent sham operations were considered controls. Five angiograms were uninterpretable because of underperfusion. The remaining 13 microangiograms were evaluated for perfusion of the anterior spinal artery and the radicular and medullary arteries. The anterior spinal artery was perfused in all 13 cases, and the radicular arteries showed bilateral perfusion on nine microangiograms (Fig. 7 left). In three microangiograms radicular filling was decreased on one side at the level of compression, and in one it was decreased bilaterally. In eight of 13 microangiograms, an enlarged and increased number of medullary vessels existed within the gray matter (Fig. 7 right). Medullary vasculature appeared normal in the remaining subjects. Asymmetry appeared in all but one microangiogram showing abnormal vasculature.

**Histopathology**

It is interesting to note that the pathological changes found were overwhelmingly in the gray matter. There was moderate to profound neuronal loss in 13 animals (Figs. 8 and 9); this was most clearly manifest as a loss of large motor neurons. Neuronal loss was asymmetrical in 12 animals and was obvious on the same side as the area of greatest compression. Cell loss was also seen contralaterally, but to a lesser degree, and it occurred predominantly at the level of compression. In six animals the loss clearly extended to the level below that of the compression. In one case there was loss above the level of compression.

Evidence of necrosis involving the gray matter, frequently the intermediate gray area and the anterior

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**Fig. 5. Left:** Sagittal magnetic resonance (MR) image (TR 2000 msec, TE 30 msec) in Dog 17 showing the degree of compression by an anteriorly placed screw. **Right:** Axial MR image (TR 800 msec, TE 20 msec) in Dog 9 showing a cross section of the area compromised by the anteriorly placed screw.

**Fig. 6. Left:** Axial magnetic resonance (MR) image (TR 800 msec, TE 20 msec) in Dog 15 showing high signal intensity “snake-eye” lesions (arrow) within the spinal cord. **Right:** Axial MR image (TR 800 msec, TE 20 msec) in Dog 13 showing a single large low signal intensity area (arrow) that proved to be gross cavitation.

**Fig. 7. Left:** Microangiogram of the whole spinal cord in Dog 7 demonstrating normal perfusion of the anterior spinal artery and radicular arteries. **Right:** Microangiogram, axial view, in Dog 8 showing both central and peripheral intramedullary circulation. The vasculature is increased asymmetrically in the gray matter compared with the control.
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horn, was present in eight animals (Figs. 8 and 9). In one animal necrosis extended below the level of compression. In four animals frank macrocavitation of the spinal cord, located mainly in the gray matter, occurred at the level of compression (Fig. 8). Four other animals had microcavitation of less than 2 mm in diameter in the intermediate gray matter.

Demyelination and clear evidence of significant axonal degeneration of long ascending or descending tracts were absent except in cases of large cavitation. There was little evidence of glial scar formation. In nine cases proliferation of vessels was seen within the substance of the cord at the damaged level (Fig. 10). Based on their histology, these vessels appeared to be small arterioles. These vascular structures had thick, hyalinized walls surrounded by halos of inflammatory cells. Such vascular changes were not seen in segments above or below the damaged segments.

Discussion

Evaluation of This Model

There are various salient features of this experimental model and its results. 1) Up to 30% of the cross-sectional area of the cervical canal was compromised. 2) The model included elements of both anterior and posterior compression. 3) Compression of the spinal cord did not result in acute persistent neurological deficits. All the animals returned to a normal neurological status after surgery. 4) All dogs had a normal level of activity with free neck motion. 5) Neurological deficits developed in a delayed fashion; the earliest abnormalities emerged 4 months after the initial compressive procedure. 6) The neurological deficits were progressive in nature, becoming worse in a gradual or sometimes stepwise fashion, much like the human condition. 7) All of these neurological changes were produced with

FIG. 8. Photomicrograph demonstrating cell loss in the anterior horn, tissue necrosis, and focal cavitation within the anterior horn in Dog 17. A fixation artifact produced the fracture seen extending into the dorsal horn. Luxol fast blue-cresyl violet, × 56.

Fig. 9. Montage of photomicrographs from Dog 10 showing the ventral horns ipsilateral (Ip) and contralateral (Co) to compression. Actual necrosis was restricted to a rather small lesion (L) in the gray matter on the side ipsilateral to the compression. A comparison of the two sides reveals a profound loss of large motor neurons and diminution of myelinated fibers in the gray matter, but little frank damage to the cord. Weil, × 15.
compression alone and did not require a secondary insult to the spinal cord such as hypotension or vascular ligation. In addition, no evidence of radicular or spinal artery occlusion appeared on microangiography. 8) Universal pathological changes affected the gray matter, particularly neuronal death with eventual edema/necrosis and cavitation in the intermediate gray zone and anterior horn. 9) Pathological changes occurred predominantly under the area of compression. 10) Unilateral pathological changes were associated with the asymmetry of compression. 11) Spinal cord blood flow values indicating a state of hyperemia occurred imme-
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diately after compression, and an eventual drop in blood flow took place after prolonged compression.

Although superior in some respects to previous animal models, this model also fails to reproduce perfectly the conditions of human cervical spondylotic myelopathy, for several reasons. Because the dog is a quadruped, the anatomy and biomechanics of its cervical spine differ from those of the upright human. In addition, the major motor tract in the dog is the rubrospinal tract rather than the lateral corticospinal tract, as it is in humans.\textsuperscript{36} The anteriorly placed screw produced an extradural mass effect behind the vertebral body rather than at the intervertebral disc space. The screw produced a rigid mass effect in the animals while, in humans, repeated bulging of the disc may occur with changes in position. Likewise, the posteriorly placed washer created only static posterior compression and did not mimic the dynamic infolding of the human ligamentum flavum on extension.

Postoperative MR images demonstrated variability in the degree of compression ranging from 10\% to 50\% of the sagittal diameter of the cervical canal. More accurate and consistent placement of the compressive devices would likely produce even more reliable results than those obtained with this study, and would allow the sham-operated animals to serve as a true control.

**Pathophysiology of Chronic Spondylotic Myelopathy**

The results of this model, supported by a wealth of experimental and clinical information available in the literature, prompt us to propose the following pathophysiological theory of chronic compressive myelopathy.

In the normal cervical spine, there exists a physiological reserve space that accommodates changes in the cervical cord during each extension and flexion of the neck (Fig. 11A and B). Prominent in changes during extension are a decrease of the transverse area of the canal by 11\% to 16\% and an increase of the transverse area of the cord by 9\% to 17\%.\textsuperscript{81} In human cervical spondylisis, as in this model, this reserve space is partially or completely obliterated by osteophytes, herniated disc material, or redundant ligamentum flavum (Fig. 11C). Hence, as postulated previously by Waltz,\textsuperscript{82} with every extension, there is a sudden intermittent pinching of the cord between the anterior osteophyte and the posterior infolding ligament (Fig. 11D). This pinching action produces forces concentrated within the central area of the cord, compromising the microcirculation at that level. Such intermittent compromise results in ischemia or hypoxia primarily within the watershed area, which is the intermediate zone of the gray matter. The intermittent tissue hypoxia initially insults the more vulnerable large motor neurons of the anterior horn and intermediate gray matter. With repetitive compression and resulting intermittent ischemia, edema and necrosis ensue within this central area of the spinal cord, eventually replaced by nonligotic cavitation. In addition, a reactive hypervascularity with thickening of the walls of the intermediolary arteries and capillaries occurs in response to chronic vascular insufficiency.

To support this theory, we explain below the accumulated clinical and experimental findings as they relate to the pathogenesis of chronic spondylotic myelopathy.

**Canal Compromise**

The role of canal compromise was recognized as early as 1838 by Key,\textsuperscript{49} who described a "projection of the intervertebral substance, or rather, the posterior ligament of the spine, which was thickened and presented a firm ridge which has lessened the diameter of the canal by nearly a third." Since that time, the effect of spondylotic bars and an infolding ligamentum flavum, which act to consume the reserve space by reducing the overall canal diameter and cross-sectional area, has been recognized as an important factor in chronic spondylotic myelopathy. The presence and severity of myelopathy have been repeatedly correlated with the sagittal diameter of the canal,\textsuperscript{80,87} cord deformity, and
cross-sectional area as demonstrated by CT myelography,26,27,68,71 and the presence of congenital spinal canal stenosis in which the reduced reserve space is totally consumed by mild spondylotic changes.22,35,48,58,83 Using pathological specimens, Fujiwara, et al.,71 were able to show a distinct correlation between the reduced cross-sectional area of the cervical spinal cord and microscopic pathological changes and clinical severity.

Infolding of the ligamentum flavum is also thought to contribute to myelopathy.72,79,80 Breig and El-Nadi,15 however, maintained that the dura, not the ligamentum flavum, buckles forward; Northfield82 has suggested that inward rotation of the lamina contributes to the posterior myelographic defect. A number of authors have noted compromise due to simultaneous anterior spondylotic bars and posterior infolding ligamentum flavum.12,22,55,75,83

The deformities of the cord and the indentations found in all of our animals agree with clinical findings reported for pathological examinations67 and CT scans,10,83 as well as MR images.4 This also agrees with the observation that, when compression is surgically removed and the subarachnoid space and cord resume their normal configuration, the subjects show clinical improvement. If the compression is not dealt with sufficiently, little or no clinical improvement takes place.26,44 In cases of severe compression, however, the injury is irreversible and improvement is limited.26,44

Effects of Movement on the Cervical Cord

Movement of the cervical spine has been studied and reported to be an important factor producing chronic spondylotic myelopathy. In 1956, O'Connell92 suggested that, in cases in which spondylotic protrusions were not severe, repeated cord trauma was a more important mechanism than compression. He postulated that this was brought about by the cord rubbing against the bony ridge when the neck flexes, while being held firmly against the ridge by the nerve roots. Reid71 concurred and added that, during neck flexion, the cord was also stretched. Other authors have pointed out that cord mobility was affected by "root-sleeve fibrosis" and adhesion of the dura to the posterior longitudinal ligament.1,81

In autopsy material, Breig and El-Nadi15 confirmed that the cord is longer during flexion and suggested that the transverse pial vessels were shut off as a result of tension. Adams and Logue4 reached a similar conclusion. They later noted increased movement of the cervical spine in patients with myelopathy and radiculopathy and that few patients with a high range of movement respond to treatment.1,3 This was supported by Barnes and Saunders,4 who found that the condition of patients with greater cervical mobility was more likely to deteriorate after conservative treatment. Otherwise, simple immobilization of the cervical spine by a cervical collar has been reported to improve myelopathy5,17 or arrest the disease.16

Myelopathy occurs earlier and with a higher frequency in patients who have movement disorders associated with cervical stenosis.57,80 González-Feria and Peraita-Peraita30 and, more recently, Cusick, et al.,18 have demonstrated that reducing excessive mobility may be important for a successful surgical outcome in this condition.

The Vascular Role

The Watershed Zone. The arterial supply to the spinal cord is divided into two groups, centrifugal and centripetal. The centrifugal system originates from the central sulcus artery, which leaves the anterior spinal artery at a right angle, passes dorsally through the anterior medial fissure, and courses to the right or left, entering the central gray matter to supply the anterior two-thirds of the cord. The centripetal system consists of penetrating branches from the entire pial plexus, which supply between one-half and one-third of the outer rim of the anterior and lateral white column and all of the posterior horn and the posterior white column. These are end arteries for both systems, entirely lacking anastomoses except at the capillary level. The zone in which centrifugal and centripetal end arteries overlap defines a last field for watershed. Turnbull, et al.,80 assigned to this watershed zone the inner one-fourth of the white matter and outer edge of the gray matter, excluding the posterior half of the posterior horn.

A capillary border zone exists between the anterior and posterior circulation located at the peripheral margins of the anterior horns and somewhere toward the midpoint of the posterior horns. The outline of this border zone in the gray matter corresponds precisely to the limits of the infarcted lesions seen in the transverse sections of the lumbar and sacral cord in DeGirolami and Zivin's experiment.19 By comparison, in humans, dogs, and cats, this border zone is less discrete and the territory of distribution of the anterior circulation is more extensive.

Evidence has been presented clearly showing that the long tracts of the white matter are spared during a relatively short period of ischemic insult, while the gray matter of the cord is destroyed.19,39,79 Animal studies have demonstrated different sensitivities of spinal cord structures to ischemic insults, including vascular occlusion, hypotension, and deprivation of oxygen. The common effect of anoxic insult is damage to gray matter, the motor neurons being more vulnerable than the interneurons.29

Pathology of Cervical Myelopathy in Humans. Cervical cord pathology associated with spondylosis has been described in more than 70 cases,8,21,55,61,63,67,83 and it has been repeatedly demonstrated that histological changes are greatest at the site of maximum compression. Changes in the gray matter range from consistent motor-neuron loss and ischemic changes in surviving neurons to necrosis and cavitation.5,55,63,75,78,83 Involvement of the white matter also varies in degree but is frequently minimal.1 When changes occur in the white matter, they are generally seen either in the ventral inner portion of the dorsal column, sparing the medial fiber of the dorsal root entry zone or in the lateral columns bordering the gray matter, with the anterior columns being only slightly damaged.

Astrogial and microglial participation is inconsis-
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tent, and nongliotic necrosis is frequently described. The anterior spinal artery has been notably free of both primary and secondary changes.\(^{10,20,41,42}\) Widespread proliferation of small thickened and hyalinized inter-
medullary blood vessels is frequently reported.\(^{10,20,27,55,61,62}\) These human pathological findings are almost identical to the pathological findings in this study and are also similar to the pathological findings in experimental models using vascular occlusion.\(^{13,15,44}\)

**Macrocirculation in the Spinal Cord.** Circulatory disturbances as a cause of chronic spondylotic myelopathy were proposed by Brain\(^{11}\) as early as 1948. Although Mair and Druckman\(^{22}\) stated that the ante-
rior spinal artery and its branches must be compressed by the herniated disc, thrombosis of the spinal artery related to adjacent spondylotic changes is seldom reported.\(^{40,41}\) Furthermore, atherosclerosis is not com-
monly associated with chronic spondylotic myelopath-
y and patients with atherosclerosis in the vertebral artery do not usually have signs of myelopathy. Nu-
rick\(^{40}\) found that generalized vascular disease did not adversely influence the severity or prognosis of myelo-
pathy.

In 1964, Taylor\(^{27}\) suggested that compression of the radicular artery at the intervertebral foramina led to ischemic cord damage; however, no explanation was offered for the absence of radiculopathy in these pa-
tients. The effect of root-sleeve fibrosis has been pro-
posed to impaire the blood flow through the radicular artery.\(^{10,14,15,25,26}\) Extension of the cervical spine further reduces by one-fourth the transverse area of the inter-
vertebral foramen, a reduction thought to be critical in an already narrowed opening.\(^{42}\) Narrowing of the cer-

cival intervertebral foramina, however, has been ob-
served on radiological studies in 75% of patients over 50 years of age.\(^{66}\) Thus, as an isolated finding, foraminal narrowing may not be associated with either myelopa-
y or radiculopathy. It is therefore natural to believe that the pathological feature of ischaemia in the absence of major vascular involvement indicates that the ischaemia is at the level of impaired microcirculation.

**Conclusions**

In this animal model, we produced delayed-onset cervical cord myelopathy, simulating human spondyl-
otic myelopathy, through artificial subclinical compre-
sion of the cervical cord. The model allows repeated neurological evaluations, SSEP recordings, and SCBF measurements, as well as diagnostic imaging (CT scans, myelograms, and MR images), postmortem microan-
gostrans, and histological evaluations. Correlations between the physical findings, physiological measures, noninvasive imaging, and histology can be studied and comparisons can be made between various treatment modalities.

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