Effect of trauma dose on spinal cord edema

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The spinal cord of anesthetized cats was subjected to impact trauma of different intensities to determine how changes in trauma magnitude affect the formation and distribution of edema. All animals underwent a laminectomy to expose the cord segments corresponding to the T5-7 vertebrae. Fourteen cats were injected with fluorescein-labeled albumin, and then subjected to 260, 360, 500, or 700 gm-cm injury to the spinal cord. They were sacrificed at 8 hours after trauma. Twelve cats were injected with fluorescein-labeled dextrans of 20,000, 40,000, 70,000, or 150,000 molecular weight (MW) prior to 500 gm-cm injury, and sacrificed 8 hours after trauma. Serial cord sections from both groups were studied by fluorescence microscopy. In nine cats, sections of cord were removed 8 hours after trauma of 260, 360, or 500 gm-cm impact, and 1-cm sections were assayed for dry weight. Extravasated tracers were present in areas of hemorrhage at the site of impact in all animals. Extension of tracers and increases in tissue water rostrally and caudally from the site of impact were observed consistently with time only in animals receiving 500 or 700 gm-cm trauma. The distance of migration was similar for all tracers. The longitudinal distribution of increased tissue water was consistent with the distribution of fluorescent markers. The findings indicate that the longitudinal extension of posttraumatic edema is directly related to the amount of initial trauma.

KEY WORDS • spinal cord • spinal cord edema • spinal cord injury • paraplegia

POSTTRAUMATIC edema has been implicated clinically as a complicating factor in spinal cord injury. Experimentally, it has been demonstrated that an impact injury to the spinal cord will result in changes in vascular permeability and in spinal cord water content. However, it remains unknown how edema may affect the integrity of spinal cord pathways. An initial step in answering this question requires that the distribution of edema in the contused spinal cord be accurately defined.

The occurrence rather than the distribution of posttraumatic spinal cord edema has been studied previously by measuring differences in tissue water content, and by histological and fluorescent tracer techniques. These studies have often not agreed on the presence or the time course of edema development. This is likely due to the different experimental models, trauma doses, and methods for measuring edema used.

In the current investigation, animals were subjected to impact trauma of different intensities with the aim of determining how changes in the magnitude of trauma might affect the formation and distribution of edema within the spinal cord in the first 8 hours following injury. Edema was examined by either of two methods. The distribution of fluorescent tracers, which were injected prior to trauma, was studied microscopically. In other animals, the dry weight of traumatized and control cord samples was measured.

Materials and Methods

General Procedure

Adult male or female cats, weighing between 2.0 and 5.0 kg, were anesthetized with sodium pentobarbital (40 mg/kg intraperitoneally), paralyzed with Flaxedil, and artificially ventilated following a tracheostomy. The femoral artery was cannulated for measurement of arterial blood pressure. The femoral vein was cannulated for administration of drugs, fluids, and fluorescein-labeled compounds. A laminectomy was performed, leaving the dura mater intact and exposing the spinal cord segments corresponding
Effect of trauma dose on spinal cord edema to the T5–7 vertebrae. An impact injury was inflicted at T-6 by dropping a weight down a vented tube on an impounder resting on the exposed dura. The weight was 20 gm, and was dropped from heights of 13, 18, 25, or 35 cm. These height and weight combinations produced what is conventionally termed a 260, 360, 500, or 700 gm-cm injury. Previous work in our laboratory has established that 260 gm-cm injury produced transient paraplegia, 360 gm-cm injury produced some permanent deficits, and 500 and 700 gm-cm injuries produced total, permanent paraplegia. Endtidal CO2 and rectal temperature were monitored and kept within normal limits throughout the experiment.

**Fluorescein-Labeled Albumin Series**

In this series of experiments, 14 cats were injected with 10 cc of fluorescein-labeled albumin (0.5% fluorescein-isothiocyanate in 8% albumin in saline) 10 minutes prior to 260, 360, 500, or 700 gm-cm injury. Cats were sacrificed by exsanguination 8 hours after trauma. A section of thoracic cord, 6 to 10 cm in length, was removed and fixed by immersion in 10% formalin. After fixation, the cord was sectioned serially at 100 μ, and the pattern of fluorescent spread evaluated by fluorescence microscopy.

**Dry Weight Series**

In this series of experiments, nine cats were prepared as described above, and an impact injury of 260, 360, or 500 gm-cm was inflicted at T-6. Eight hours after trauma, the cats were sacrificed by barbiturate overdose. A 6- to 10-cm segment of thoracic cord was excised, the dura removed, and the sectioned into 1-cm pieces. The pieces were weighed and dried in a 70°C oven. The dried samples were weighed and the dry weight calculated.

**Labeled Dextran Series**

In this series of experiments, 12 cats were prepared surgically as described above, and injected with 200 gm in 10 cc saline of fluorescein-labeled dextrans of 20,000, 40,000, 70,000, or 150,000 molecular weight (MW) 10 minutes prior to receiving a 500 gm-cm impact contusion. Cats injected with the lowest molecular weight dextran also underwent bilateral renal artery ligation before injection. Eight hours after trauma, the cats were sacrificed as described above for fluorescence microscopy analysis of the marker distribution.

**Results**

**Fluorescein-Labeled Albumin Series**

Extravasated fluorescein-labeled albumin (FLA) was present at the site of impact in all animals. The FLA was associated with petechial hemorrhages in the gray and white matter. In addition, there was evidence of centrifugal spread of FLA from the gray to the white matter. This centrifugal spread was more pronounced at 500 and 700 gm-cm trauma intensities. At the 500 and 700 gm-cm trauma doses, FLA also extended rostral and caudal to the site of injury along the central portions of the dorsal, lateral, and ventral white matter as previously described (see below and Fig. 3). The distance of spread was usually the greatest in the lateral white matter. In the 260 and 360 gm-cm experiments, there was minimal extension of FLA outside the segment of injury.

The average maximal distance of FLA spread is shown in relation to trauma dose in Fig. 1. For the 260 and 360 gm-cm injuries, mean spread was 5.0 ± 1.9 (SD) mm and 5.8 ± 1.6 mm, respectively. These values are not significantly different. However, for the 500 gm-cm injuries the mean extension of FLA was 14.0 ± 3.3 mm from the center of impact. For the 700 gm-cm injuries, the mean rostral and caudal extension was 11.2 ± 3.3 mm. The values for 700 and 500 gm-cm injuries were statistically different at the p = 0.01 level for each other and from the 360 and 260 values, as determined by an analysis of variance. The finding that FLA extension is less following 700 gm-cm...
than after 500 gm-cm injury is surprising, and may be artifactual. Alternatively, it is possible that with devastating injuries the cord vasculature may be so compromised that normal mechanisms of FLA extension are partially disrupted.

**Dry Weight Series**

In these series of experiments, there was a decreased dry weight in the 1-cm segment that included the center of the impact. The values for this segment were 30.6 ± 1.5%, 30.2 ± 2.3%, and 28.6 ± 0.6% for 260, 360, and 500 gm-cm trauma, respectively. An analysis of variance demonstrated no significant difference between these values.

In the segments 1 cm proximal and 1 cm distal to the "at trauma" segment, the mean values for weight were within the control range for 260 and 360 gm-cm trauma: 34.06 ± 1.5% and 33.45 ± 1.05%, respectively. For the 500 gm-cm group, the dry weight was 32.1 ± 0.6%. This latter value was statistically different from the former two at the p = 0.5 level, by an analysis of variance. At the segments 2 cm proximal and distal to the "at trauma" segments, all means were within the control range. The values were 34.8 ± 1.2%, 34 ± 0.5%, and 34.3 ± 1.08%, respectively, for the 260, 360, and 500 gm-cm groups.

The results of this series are summarized in Fig. 2. It can be seen that the "at trauma" values are significantly different from control values (2 cm proximal and distal) for all trauma doses. However, in the segments 1 cm proximal and distal, only the 500 gm-cm group was statistically different from control.

The results of this dry weight series are consistent with results of the FLA study, which demonstrated that extension of labeled albumin outside the zone of impact occurred with 500 gm-cm injury but not with 260 or 360 gm-cm injury.
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*Labeled Dextran Series*

In the series of experiments in which animals were injected with fluorescein-labeled dextrans varying in molecular weight from 20,000 to 150,000, the pattern of spread was indistinguishable from that reported with FLA. In addition, the distance of migration was similar for all markers tested. The mean extension from trauma center was 13.5 ± 1.04 mm for the 20,000 MW dextran, 14.3 ± 3.4 mm for the 40,000 MW dextran, 13.6 ± 3.4 mm for the 70,000 MW dextran, and 15.0 ± 1.8 mm for the 150,000 MW dextran. The mean distance of spread for five cats injected with FLA and sacrificed at 8 hours after trauma was 14.0 ± 3.3 mm.

**Discussion**

As might be expected, the findings of the present study demonstrate the relationship of the magnitude of trauma to the formation and spread of edema. Trauma sufficient to produce a permanent paraplegia resulted in not only tissue damage in the area of impact, but an extension of labeled albumin and dextrans and an increase in tissue water rostral and caudal to the site of injury. In contrast, the lowest trauma dose, 260 gm-cm, which produces only transient paraplegia, was not followed by increased water or extravascular fluorescence outside the region of trauma at the time studied in these experiments. A similar relation-ship has been observed by Griffiths and Miller. These investigators noted Evans blue-labeled albumin had spread a distance of one segment from the point of impact 6 hours after trauma of 500 gm-cm intensity, although trauma of 200 gm-cm intensity resulted in less spread.

When posttraumatic spinal cord edema has been studied by measuring changes in tissue water content alone, the results have been less clear. Yashon, et al., found an increase in percentage water as early as 5 minutes after trauma, which persisted for as long as 15 days in monkeys which had been subjected to trauma of 300 gm-cm. Using a specific-gravity gradient column method and a tissue punch technique, with edema expressed as percent increase in tissue volume, Osterholm found increases ranging from 127% in the anterior gray matter to 24% in the lateral white matter at the site of impact 1 hour after injury. In contrast to these workers, Lewin, et al., did not find a significant increase in tissue water content until 2 days had elapsed after trauma of 150 gm-cm in the cat. In this latter study, by the 3rd and the 6th day after trauma all tissue blocks measured were involved with edema. By the 9th day, evidence of edema regression was apparent.

It is likely that the changes in tissue water content observed at the site of impact shortly after trauma are influenced by the hemorrhage and necrosis that follow the trauma in that location and, therefore, do not reflect true edema. Whether vessels rostral and caudal to the injury site become permeable to water and smaller molecules at later times after trauma, as suggested by the work of Lewin, et al., is unsettled. Nemeček, et al., experimented with trauma sufficient to produce a permanent paralysis in the rabbit,

![Fig. 3](image-url)

**Fig. 3.** Fluorescence photomicrographs of spinal cord at 8 hours after 500 gm-cm injury in cats pretreated with fluorescein-labeled dextrans of the following molecular weights: 20,000 (A); 40,000 (B); 70,000 (C); and 150,000 (D). Sections are taken from regions 2 mm rostral or caudal to the impact zone.
and noted a disparity between the longitudinal spread of histological changes, of fluorescence, and of increased tissue water beginning 3 hours after trauma. They also found an increased water content further rostrally and caudally thereafter. Although a correspondence was found in our study between sections showing extravascular fluorescence and an increased water content up to 8 hours after trauma of the same magnitude, this time interval may be inadequate to investigate fully the changes that may occur in vascular permeability with this experimental model.

The extension of edema longitudinally in the white matter after trauma of greater magnitude is likely to be associated with the development of tissue pressure gradients between the area adjacent to the injury site and areas more rostral and caudal. The occurrence of such gradients after impact trauma to the spinal cord has been demonstrated by Shapiro, et al.9 The delay of 1 to 2 hours after trauma for peak tissue pressures to occur adjacent to the site of impact and for significant pressure gradients to develop between this area and more remote areas noted by these workers corresponds with the delay of 1 to 2 hours in the spread of fluorescein-labeled albumin observed in our study. The delay in spread during the same period in which pressure gradients are developing would seem to reflect the time required to overcome the resistance to spread that may be conferred by the white matter. The finding that fluorescein-labeled dextrans of different molecular weight migrated the same distance indicated further longitudinal extension in the white matter may then occur by bulk flow requiring smaller pressures to sustain.7,8

The present study confirms that impact trauma to the spinal cord produces vascular damage at the site of injury which results in the extravasation of serum proteins and an increase in tissue water. For edema to extend rostrally and caudally from the site of impact, it appears that the trauma must be of sufficient magnitude to produce paraplegia.

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References


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