Morphological Changes Caused by Pressure on the Spinal Cord

Fiona Wright and A.C. Palmer

The morphological changes of the spinal cord associated with inco-ordination in the horse were studied by Fraser and Palmer. Lesions were basically of 2 types: malacic and non-malacic, the former being associated with severe pressure on the cord. In the latter there was no apparent pressure on the cord and animals showing this type of lesion were defined as ‘true wobblers’. However, Rooney concluded from his investigation into the morphology of the cervical vertebrae in the horse that the lesions of true equine inco-ordination or ‘wobbles’ were associated with malformations of the intervertebral articulations, which could give rise to pressure on the cord.

The non-malacic lesions found by Fraser and Palmer were characterised by degeneration of white matter (including axons and myelin), hyalinisation of small vessels, especially veins and capillaries, and venous congestion in the white matter; the grey matter was affected to a lesser degree by the vascular change, and nerve cell degeneration was infrequently seen. They concluded that this non-malacic change might be attributed to venous obstruction, which would lead in turn to hyalinisation and myelin degeneration.

In the literature there are instances where venous obstruction has been implicated as an important factor in the pathogenesis of pressure lesions in the spinal cord: prolapsed inter-vertebral disc (P.I.D.) in dog, P.I.D. in man, and metastatic neoplasms in man. In the basset hound congestion, hyalinisation, and myelin degeneration were seen to accompany pressure on the cervical cord caused by congenital malformation of the vertebral canal. Myelin degeneration and hyalinisation have also been found associated with pressure on the cervical cord in cervical spondylosis in man (Fig. 1).
### Table I. Summary of clinical and histological findings in the series of animals with pressure lesions of the spinal cord

<table>
<thead>
<tr>
<th>Case no. and species</th>
<th>Site</th>
<th>Source of pressure</th>
<th>Duration of Clinical signs</th>
<th>White matter degeneration</th>
<th>Hyalinisation in white matter</th>
<th>Grey matter degeneration</th>
<th>Hyalinisation in grey matter</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPS 7 Lamb T8-9</td>
<td>Fracture: slight dislocation</td>
<td>2 months</td>
<td>+</td>
<td>+</td>
<td>M, +</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>CPS 34 Dog L1-2</td>
<td>P.I.D.</td>
<td>2 days</td>
<td>M, +</td>
<td>+</td>
<td>+C</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>CPS 60 Ram L4</td>
<td>Compression fracture</td>
<td>? 3 weeks</td>
<td>+</td>
<td>+</td>
<td>+C</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>CPS 68 Dog T13-L4</td>
<td>Compression fracture</td>
<td>1 week</td>
<td>+</td>
<td>+</td>
<td>+C</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>58/13 Dog T13-L1</td>
<td>P.I.D.</td>
<td>2-3 weeks</td>
<td>+</td>
<td>-</td>
<td>+C</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>58/23 Dog L1-2</td>
<td>P.I.D.</td>
<td>?</td>
<td>+</td>
<td>+</td>
<td>+C</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>59/107 Dog L1-2</td>
<td>P.I.D.</td>
<td>9 months</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>60/14 Dog C2-3</td>
<td>Fracture dislocation</td>
<td>2 months</td>
<td>+</td>
<td>+</td>
<td>Ast.</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>60/30 Dog L1-2</td>
<td>P.I.D.</td>
<td>12 days</td>
<td>TM</td>
<td>-</td>
<td>TM</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>60/31 Dog T8</td>
<td>Wedge-shaped vertebra</td>
<td>? chronic</td>
<td>+</td>
<td>+</td>
<td>+C</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>60/71 Dog ?L1-2</td>
<td>P.I.D.</td>
<td>? 9 weeks</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>60/74 Dog T10-11</td>
<td>Fracture</td>
<td>10 months</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>60/135 Dog ?L1-2</td>
<td>P.I.D.</td>
<td>8 months</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>61/3 Cat L1</td>
<td>Osteogenesis imperfecta</td>
<td>8 weeks</td>
<td>M, +</td>
<td>+</td>
<td>M</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>61/51 Lamb C7</td>
<td>Fracture</td>
<td>5 days</td>
<td>-</td>
<td>+</td>
<td>+C, H</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>61/97 Dog L2</td>
<td>P.I.D.</td>
<td>? days</td>
<td>TM</td>
<td>-</td>
<td>TM</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>61/122 Ram C3-4</td>
<td>Abscess</td>
<td>17 months</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>62/101 Piglet mid-T</td>
<td>Vertebral deformation</td>
<td>?</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>63/86 Dog C5-6</td>
<td>P.I.D.</td>
<td>6 weeks</td>
<td>M, +</td>
<td>+</td>
<td>+C, H</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>63/92 Dog T13-L4</td>
<td>P.I.D.</td>
<td>?</td>
<td>TM</td>
<td>-</td>
<td>TM</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>63/97 Dog T12-18</td>
<td>P.I.D.</td>
<td>3 weeks</td>
<td>TM</td>
<td>+</td>
<td>TM</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>63/110 Dog C2-3</td>
<td>Deformity (basset)</td>
<td>2 months</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>64/112 Dog C2-3</td>
<td>Deformity (basset)</td>
<td>? 7 months</td>
<td>M, +, Ast.</td>
<td>+</td>
<td>M, Ast.</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>65/57 Dog C2-3</td>
<td>P.I.D.</td>
<td>12 days</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>65/156 Dog C2-3</td>
<td>Deformity (basset)</td>
<td>4 months</td>
<td>+</td>
<td>+</td>
<td>+C</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>66/16 Dog C2-2</td>
<td>Deformity (basset)</td>
<td>1 month</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>67/83 Lamb C1-2</td>
<td>Fusion C1 to occiput</td>
<td>2 months</td>
<td>+</td>
<td>+</td>
<td>+C</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>
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Table I (Continued)

<table>
<thead>
<tr>
<th>Case no. and species</th>
<th>Site</th>
<th>Source of pressure</th>
<th>Duration of Clinical signs</th>
<th>White matter degeneration</th>
<th>Hyalinisation in white matter</th>
<th>Grey matter degeneration</th>
<th>Hyalinisation in grey matter</th>
</tr>
</thead>
<tbody>
<tr>
<td>67/109 Dog C_2-3</td>
<td>P.I.D.</td>
<td>1 month</td>
<td>+</td>
<td>+</td>
<td>M</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>67/151 Dog C_6-7</td>
<td>P.I.D.</td>
<td>1 month</td>
<td>+</td>
<td>+</td>
<td>+C</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>59/57 Dog L_7</td>
<td>Astrocytoma</td>
<td>4 months</td>
<td>+</td>
<td>-</td>
<td>+C</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>59/83 Dog C_3-4</td>
<td>Astrocytoma</td>
<td>? 12 days</td>
<td>+</td>
<td>+</td>
<td>+C</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>59/100 Dog C_1</td>
<td>Schwannoma</td>
<td>2 months</td>
<td>+</td>
<td>+</td>
<td>M</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>60/110 Dog C_3-4</td>
<td>Meningioma</td>
<td>3 months</td>
<td>M+</td>
<td>+</td>
<td>+C</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>61/42 Dog C_5-6</td>
<td>Meningioma</td>
<td>3 months</td>
<td>+</td>
<td>+</td>
<td>+C</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>62/92 Dog T_2-3</td>
<td>Osteosarcoma</td>
<td>6 weeks</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>63/120 Cow C_2-5</td>
<td>Neurofibroma</td>
<td>?</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

P.I.D. = Prolapsed intervertebral disc.

Deformity (basset) = congenital malformation of vertebrae in the basset (Wallace and Palmer).^2^9

White Matter: Grey Matter:
+ = demyelination +C = chromatolysis
M = partial malacia M = partial malacia
TM = total malacia TM = total malacia
Ast. = Astrocytosis Ast. = Astrocytosis
H = haemorrhage

Although the reason for the relatively selective degeneration of the white matter rather than the grey in the non-malacic lesions is not clear, it would appear that it may be associated with (a) pressure and (b) venous obstruction. Before embarking on an investigation of the pathogenesis of such lesions it was considered pertinent to extend our investigations to an additional series of animals of various species, and with various types of pressure lesions, available to us for histological examination. It is the purpose of this paper to describe our findings.

Materials and Methods

Material was obtained from all animals seen by one of us (A.C.P.) since 1954 in which pressure lesions of the cord were found at autopsy. These animals are listed in Table I. In most instances tissue was fixed in formol saline and embedded in paraffin wax. The majority of sections were cut in a transverse plane through the site of maximum damage. Haematoxylin and eosin (H. & E.) and haematoxylin and Van Gieson (H.V.G.) methods of staining were used as routine. The presence of hyalinisation was assessed on sections stained by H.V.G.
Results

All the animals examined were suffering from some condition resulting in local pressure on the spinal cord, the most common being prolapsed intervertebral disc in the dog. Histological examination of sections at the level of the source of pressure revealed a range of degenerative changes. White matter damage consisted largely of various degrees of degeneration of myelin and axons (Fig. 2). This process will henceforward be referred to as 'demyelination', according to the

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*Fig. 1.* Cervical cord from a case of spondylosis in man showing hyalinisation of vessels. H. & V.G. ×180.

*Fig. 2.* Case 60/74. Section of thoracic cord from a dog with a fractured vertebra. The white matter has a spongy appearance (evidence of axonal degeneration), and there is hyalinisation of vessels. Mallory's trichrome ×19.

*Fig. 3.* Case CPS 34. Lumbar cord from a dog with a prolapsed inter-vertebral disc. There is partial malacia of the white matter. H. & E., celloidin, ×14.
Fig. 4. Case 60/30. Section of cord and disc material from a dog with a prolapsed intervertebral disc. There is total malacia of both white and grey matter. H. & E. ×11.

definition by King and Meehan as it would appear to be primarily myelinoclastic in nature. Malacia occurred infrequently, and only in 4 cases was the white matter totally malacic. In sections showing partial malacia of the white matter demyelination was seen in areas not affected by the malacia. In the grey matter degenerative changes included various degrees of chromatolysis, glial reaction, and malacia. Partial malacia and chromatolysis occurred together in only one case. As in the white matter, total malacia was infrequent. Because it was not possible to gauge with any accuracy the degree of pressure acting on the cord, a quantitative assessment of the degree of degenerative change was not attempted.

The results are presented in Table I. In the 36 cases examined white matter degenerative changes are as follows: 23 with demyelination; 5 with partial malacia (in which demyelination is also observed)

Fig. 5. Case 67/109. Longitudinal section of the cervical cord of a dog with a prolapsed intervertebral disc showing malacia of the grey matter. H. & E. ×12.

Fig. 6. Case 60/31. Cervical cord from a dog with a wedge-shaped vertebral body showing hyalinisation of vessels and degeneration of white matter. There are swollen axons, distended medullated tubes, myelophages and oedema. H. & E. ×180.
(Fig. 3); 4 with total malacia; and 4 not affected. The grey matter degenerative changes are: 14 with chromatolysis; 1 with astrocytosis (which may have already gone through a chromatolytic phase); 6 with partial malacia (Fig. 5), (one of which also showed astrocytosis, and one chromatolysis); 4 with total malacia, and 11 not affected. Partial malacia appears to affect either white or grey matter, but rarely both together. Total malacia on the other hand always affects both white and grey matter (Fig. 4). The 4 cases of total malacia (all dogs) had a relatively short duration of clinical signs of pressure on the cord (12 days – 3 weeks). The duration of clinical signs in cases of partial malacia was 2 days – 3 months (plus 1 case of 27 months), and in cases showing no malacia it was 5 days – 10 months (plus 1 case of 17 months).

Hyalinisation of small vessels of the cord, especially veins and capillaries (Fig. 6) was found in both malacic and non-malacic lesions. The hyaline material in all cases was situated outside the vessel wall. It was found that hyalinisation could be distinguished from vascular hyperplasia by the presence in the latter of increased numbers of endothelial nuclei. In non-malacic lesions hyalinisation occurred in both white and grey matter, but was more common in white matter: 23 cases showed vessels affected in the white matter as opposed to 12 in the grey.

Hyalinisation was occasionally found to occur some distance along the cord from the site of the primary lesion.

The occurrence of demyelination is closely correlated with hyalinisation of vessels in the white matter. By comparison chromatolysis and hyalinisation of vessels in the grey matter rarely occur together. Furthermore the majority of cases with chromatolysis show a concomitant demyelination and hyalinisation of vessels in the white matter. This may indicate that chromatolytic changes are in fact secondary to changes in the white matter.

An attempt was made to assess the presence of congestion in the vessels of the parenchyma and pia arachnoid. Histologically this is indicated by accumulation of erythrocytes in distended vessels. However it was found difficult to make a clear cut distinction between normality and abnormality in this respect. Congestion may also be influenced by such factors as delay between death and fixation of the tissue, or by manipulation during removal of the cord from the vertebral column. We decided, therefore, that this was not a valid criterion to use in this series.
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Discussion

We could not estimate the degree of pressure acting on the cord in our cases, and hence it was not possible to say whether there were the same relationship between severe pressure and malacic lesions as in the horse. However the cases do seem to fall into 3 groups according to the histological changes of the cord at the site of pressure: (I) those in which there was total malacia involving both white and grey matter, (II) those in which there was partial malacia affecting white or grey matter, occasionally both, (III) those in which there was no malacia, but in which there was chromatolysis in the grey matter and/or demyelination in the white matter. In the latter group our results show that there is a tendency for white matter to be affected more often than grey. The chromatolytic changes in the grey matter may be the result of either damage to axons as they pass through affected white matter, or direct pressure injury to the ventral roots. The non-malacic lesions found in the present series are similar to those found by other authors in association with pressure on the cord, and also to those found in ‘wobblers’. It is possible that there is a common factor in their pathogenesis whatever the source of pressure on the cord.

We would like to suggest that the development of malacic or non-malacic lesions may depend upon both the degree of pressure and the rate of development of pressure. We consider that slight pressure on the cord would involve the veins, producing some obstruction of venous drainage and subsequent pathological changes primarily in the white matter. Brain suggested involvement of venous drainage in connection with disc protrusions in man purely on anatomical considerations. The veins of the cord surface are thin walled and are at a very low pressure, and hence would be affected before the arteries under the influence of an externally applied pressure. It seems likely that greater pressure would involve the arteries as well, and this would give rise to ischaemia and subsequent malacia.

A connection between failure of arterial supply and malacia was suggested by Saunders and Roberts in a case of epidural abscess in the cow. The small arteries supplying the dorsal half of the sacral cord were thrombosed, probably due to spread of inflammation from the abscess, and malacia was found in the dorsal and lateral white columns plus the dorsal tips of the sensory grey columns. The rate of development of pressure may also be an important factor. A slowly developing pressure allows time for some collateral drainage to be established.
Hence the resulting lesion would not be as severe as in the case of a rapidly developing pressure. In fact, 3 of the 4 cases showing total malacia in the present series had a relatively short duration of clinical signs (12 days – 3 weeks) indicating a rapid development of pressure; (duration of the 4th case was unknown). In comparison, the duration of clinical signs in cases showing partial malacia was 2 days to 3 months (plus 1 case of 27 months), and in cases showing no malacia it was 5 days – 10 months (plus 1 case of 17 months).

A case for the correlation between pressure, obstruction of venous drainage, and selective damage of the white matter can be made out from evidence in the literature. BARRON et al. described in their series of tumour cases in man changes affecting the white matter which took form of oedematous malacia. They claim that this was quite distinct from malacia produced by blockage of arterial circulation and moreover the grey matter was in most cases unaffected. This, together with the facts that (a) there seemed to be no correlation between the degree of distortion of the cord and the extent of histological damage, and (b) in many cases recovery followed laminectomy and decompression led them to believe that venous obstruction by the tumour might be the most important factor in the pathogenesis of the lesions.

In the dog, LINDBLAD et al. demonstrated blockage of the longitudinal venous sinuses in each of 19 dogs with prolapsed intervertebral discs, but found no evidence of interruption of arterial supply to the cord. BUNGE, BUNGE, and RIS in their study of lesions of the white matter produced in the cat by manipulation of the cerebrospinal fluid suggested that a possible cause of the demyelination found was oedema following venous collapse due to pressure on the surface of the cord.

Correlation between obstruction of venous drainage and selective damage to the white matter has also been shown by WOOLF. He carried out experimental obstruction of cerebral veins in the dog by injection of lard oil into the superior longitudinal sinus between 2 ligatures. He found that this resulted in changes in the white matter drained by the occluded vein. In animals surviving more than 3 months, there was an extensive loss of myelinated fibres, and those fibres which remained showed beading and swelling of the myelin sheath. The nerve cells though were unaffected.

However, MAIR and DRUCKMAN from an examination of 4 cases of disc protrusions in man found no evidence to suggest that the lesion of the compressed segment was the result of venous stasis.
Instead they found that the distribution of the lesion was identical to the field of the anterior spinal artery, and they therefore concluded that the lesion resulted from a reduction of blood supply from this artery. BREIG, TURNBULL, and HASSLER considered that the lesions of cervical spondylosis are caused by obstruction of the arterial supply to the cord. They believed venous drainage to be "too extensive to be deranged significantly by cervical spondylosis".

However, blockage of the arterial supply to the cord has been shown to result in selective degeneration of the grey matter. TARLOV stopped arterial supply to the cord in the dog by blocking the thoracic aorta, and found pathological changes (loss of nerve cells and chromatolysis) only in the grey matter.

TARLOV, though, believed that mechanical distortion of the cord rather than involvement of the blood vessels was the primary cause of the lesion and paralysis resulting from compression of the cord in the dog. He does not deny that the compressed cord may be ischaemic, but believes that for a small area of compression, oxygen will be supplied from surrounding non-ischaemic tissue by diffusion. His main argument for mechanical distortion is that compression produces changes predominantly in the white matter, whereas anoxia produces destruction of the grey matter. Other respects in which compression and anoxia differ are the time of onset of clinical signs, the time of onset of recovery, the capacity for recovery, and the order of disappearance of evoked spinal potentials.

There is therefore contradictory evidence as to the cause of different pressure lesions, but we believe that these may all fit into one pattern of progressive involvement of veins and arteries depending on the degree and rate of development of pressure.

Although it might appear that a small disc protrusion in itself would not produce significant pressure on the cord, there are additional functional considerations which may exacerbate the situation in that movement of the spine may bring a greater force to bear on the spinal cord than might be expected from a study of the situation post mortem. For example KAHN cited the restrictive effect of the ligamenta denticulata on the movement of the cord as an important factor in its compression by tumours. STOLTMANN and BLACKWOOD suggested that the bulging of the ligamenta flava into the cervical canal during extension of the neck was the main cause of the myelopathy of cervical spondylosis. During extension the spinal canal at the level of the cervical enlargement is completely filled by the spinal cord and
the infolded ligamenta flava. Hence a mass arising anteriorly will
tend to push the cord posteriorly and cause it to be compressed
against the ligamenta flava every time the neck is extended.

The hyalinisation of vessels found in pressure lesions may be a
secondary phenomenon associated with alteration of permeability of
the vessel wall resulting from increased venous pressure. CUMINGS7
showed a movement of soluble protein (mainly albumin) from the
vessels into the nervous tissue of brains affected by tumours. Hyalinisa-
tion would seem to be a common reaction of any vessel the perme-
ability of which is increased. In this respect hyalinisation found in
pressure lesions may be comparable to LENDRUM’s concept of ‘plas-
matic vasculosis’19 which he defines as ‘the extravasation of plasma,
with deposit in the vessel wall, or beyond, of one or more plasmatic
constituents’. This idea was based on his study of the arterioles of the
kidney in hypertensive diabetes. A similar phenomenon was also
found in the kidney and spleen of dogs with canine interstitial ne-
phritis1,2 and in the spleen of dogs with nephritis10. Hyalinisation is
also found associated with an increased vascular permeability, but not
with pressure, in the lesions of allergic encephalomyelitis. OLDSTONE
and DIXON16 have shown that the hyaline material in this case is fibrin,
and they suggest that this is precipitated from fibrinogen which
diffuses out of the vessels.

In the horse, FRASER and PALMER8 were unable to establish the
cause of spinal cord damage in a number of animals which they re-
garded as ‘true wobblers’. This failure may be ascribed to the method
by which the cords were removed from the vertebral canal, a method
which entailed cutting the vertebrae and thus destroying anatomical
relationships17. However, on the basis of the results presented in this
paper, it appears that the lesions in the wobbler are similar to non-
malacic lesions caused by pressure in other species, and it seems rea-
sonable to suppose that stenosis of the vertebral canal, albeit slight, is
the immediate cause of the wobbler syndrome in the horse. FRASER
and PALMER also suggested that venous obstruction might arise out-
side the vertebral canal, or the venous sinuses might be involved. In
view of the collateral nature of the cord circulation these two possi-
bilities are now regarded as being untenable.

On the basis of observations made on the cases presented in this
paper and a study of pressure lesions described by other authors we
conclude that there is no one cause of these lesions, but rather the
range from non-malacic to totally malacic represents a progressive in-
volvement of veins and arteries. A slight pressure will tend to affect the veins rather than the arteries and will result in changes mainly in the white matter, whereas greater pressure will also involve the arteries and will result in malacia. The rate of development of pressure may also influence the severity of the lesion because of the formation of collateral blood supply and/or drainage.

**Summary**

The morphological changes in the spinal cord caused by pressure are described in a series of domestic animals of various species. Three types of lesion are distinguished: totally malacic, partially malacic, and non-malacic. In the non-malacic lesion changes are predominantly in the white matter and consist of demyelination and hyalinisation of small vessels. The possibility that the immediate cause of such non-malacic lesions may be obstruction of venous drainage from the spinal cord is discussed.

**Zusammenfassung**


**Acknowledgements**

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**References**


Author's address: Mrs. Fiona WRIGHT, School of Veterinary Medicine, University of Cambridge, Madingley Road, Cambridge (U.K.).