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# Correlations between severity of clinical signs and histopathological changes in 60 dogs with spinal cord injury associated with acute thoracolumbar intervertebral disc disease

D. Henke [a,*], M. Vandevelde [a], M.G. Doherr [b], M. Stöckli [c], F. Forterre [c]

[a] Department of Clinical Veterinary Medicine, Division of Clinical Neurology, Vetsuisse Faculty, University of Bern, Bern 3001, Switzerland
[b] Veterinary Public Health Institute, Vetsuisse Faculty, University of Bern, Bern 3012, Switzerland
[c] Department of Clinical Veterinary Medicine, Division of Clinical Surgery, Vetsuisse Faculty, University of Bern, Bern 3001, Switzerland

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ABSTRACT

The outcome of spinal surgery in dogs with absent voluntary motor function and nociception following intervertebral disc (IVD) herniation is highly variable, which likely attests to differences in the severity of spinal cord damage. This retrospective study evaluated the extent to which neurological signs correlated with histologically detected spinal cord damage in 60 dogs that were euthanased because of thoracolumbar IVD herniation. Clinical neurological grades correlated significantly with the extent of white matter damage ($P < 0.001$). However, loss of nociception also occurred in 6/31 (19%) dogs with relatively mild histological changes. The duration of clinical signs, Schiff-Sherrington posture, loss of reflexes and pain on spinal palpation were not significantly associated with the severity of spinal cord damage. Although clinical-pathological correlation was generally good, some clinical signs frequently thought to indicate severe cord injury did not always correlate with the degree of cord damage, suggesting functional rather than structural impairment in some cases.



## Introduction

While diagnostic imaging and cerebrospinal fluid (CSF) analysis has become increasingly important for determining prognosis and treatment decisions in dogs with intervertebral disc (IVD) extrusion (Olby et al., 1999; Ito et al., 2005; Penning et al., 2006; Levine et al., 2009, 2010; Srugo et al., 2011), clinical assessment of spinal cord function remains essential. In particular, the presence or absence of nociception is considered to be the most important behavioural response used to determine prognosis in dogs with IVD disease (Gambardella, 1980; Scott, 1997; Scott and McKee, 1999). However, the outcome of surgical treatment in dogs with absent nociception varies widely in the veterinary literature. (Duval et al., 1996; Necas, 1999; Scott and McKee, 1999; Olby et al., 2003; Laitinen and Puerto, 2005; Ruddle et al., 2006). This might be due to differences in the severity of structural cord damage in dogs with a similar clinical presentation (Olby et al., 2004). Previous studies investigating the histopathological findings in naturally occurring spinal cord injuries have not evaluated the extent to which neurological signs reflect structural damage in dogs with IVD disease (Griffiths, 1972, 1978; Smith and Jeffery, 2006).

In the present study, the degree of spinal cord damage found on histopathological examination in 60 dogs with thoracolumbar IVD extrusion was compared to the severity of neurological deficits as assessed shortly prior to euthanasia. Clinical signs commonly considered to be associated with severe spinal cord injury and their rate of onset were specifically evaluated, including loss of spinal reflexes, loss of nociception and Schiff-Sherrington posture.

## Materials and methods

### *Study design*

Data were retrospectively evaluated from dogs that were euthanased with thoracolumbar or lumbar Hansen type I IVD extrusion and from which histopathological examination of the spinal cord was performed at the Neuropathology Laboratory of the Vetsuisse Faculty at the University of Bern (January 1985 to April 2011). Cases were included if well-documented records of the initial history, neurological findings, diagnosis and course of disease were available, the last neurological examination was performed within 12 h of euthanasia, a complete histopathological examination of the spinal cord had been performed and the material was available for re-evaluation.

### *Clinical data*

Data collected from the medical records included breed, age and sex, the duration of clinical signs, final neurological grade, the presence or absence of nociception, segmental spinal reflexes, pain on spinal palpation and Schiff-Sherrington

* Corresponding author. Tel.: +41 3163 12609.
*E-mail address:* diana.henke@vetsuisse.unibe.ch (D. Henke).

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**Table 1**
Grading of the spinal cord white matter lesions in the epicentre of the entire cross section.

| Grade | White matter changes |
|---|---|
| 0 | No pathological abnormalities |
| 1 | Small, focal, scattered areas of axonal and myelin sheet swelling; morphologically unremarkable tissue in >75% of the spinal cord cross-sectional area |
| 2 | Significant diffuse damage with normal gross architecture; morphologically unremarkable tissue in 50–75% of the spinal cord cross-sectional area |
| 3 | Significant diffuse damage with normal gross architecture; morphologically unremarkable tissue in 25–50% of the spinal cord cross-sectional area |
| 4 | Significant diffuse damage and loss of gross architecture in large areas; morphologically unremarkable tissue in 10–25% of the spinal cord cross-sectional area |
| 5 | Complete dissolution of the spinal cord over the entire cross-sectional area with loss of gross architecture; morphologically unremarkable tissue in <10% of the spinal cord cross-sectional area |

posture. The duration of clinical signs prior to presentation was defined as peracute (<8 h), acute (8–24 h), or chronic (>24 h). Survival time was recorded and, for dogs that underwent surgery, the duration of signs prior to surgery was recorded.

The severity of neurological signs at the last neurological examination was graded as grade I (spinal hyperaesthesia only), grade II (ambulatory paraparesis and/or ataxia and/or proprioceptive deficits), grade III (non-ambulatory paraparesis), grade IV (paraplegia with nociception present), or grade V (paraplegia with loss of nociception; Penning et al., 2006). In cases of grade disparity between the left and right limbs, the more severe grade was assigned. The site of IVD extrusion and therapeutic measures (immediate euthanasia, surgical or conservative treatment) were recorded.

### Histopathology

#### General assessment

Samples of spinal cord were removed shortly after euthanasia following a standard protocol, which included sampling at the site of IVD herniation (identified by the presence of disc material and/or haemorrhage adherent to the dura and mechanical deformation), on either side of the disc extrusion, any additional segments of cord exhibiting macroscopic changes and samples of macroscopically intact cord from the cervical, cranial thoracic, caudal thoracic and lumbar segments, including the intumescences. Segments were fixed in 10% neutral buffered formalin and then cross-sections were dehydrated in a graded ethanol series and embedded in paraffin wax. Sections (5 μm thickness) were stained with haematoxylin and eosin and, in selected cases, Alcian blue. Specimens were evaluated for the presence and location of disc material and the presence and degree of lesions in the white and grey matter. Particular attention was also paid to injury within the lumbar intumescence.

#### Semi-quantitative assessment

A scoring system of experimental traumatic lesions was modified and used to grade lesions (Horiuchi et al., 2009). The white matter at the epicentre (defined as the area with the most severe changes) was graded from 0 to 5, with grade 1 representing mild axonal changes and grade 5 representing complete destruction of the spinal cord parenchyma (Table 1, Fig. 1). Grades were based on the relative amounts of morphologically unremarkable white matter remaining over the entire circumference of the section. In addition, the dorsal, lateral and ventral columns of the white matter were evaluated separately in a similar manner to assess the symmetrical or asymmetrical distribution of any lesions. The grey matter at the epicentre was graded as grade 0 (no changes observed), grade 1 (75–100% of the grey matter intact), or grade 2 (<75% of the grey matter intact). All slides were examined and graded independently by two experienced observers (DH, MV) who were masked to the identity of the cases. If there was a discordance of $\geqslant 1$ grade between the observers, slides were re-examined and consensus was reached.

### Statistical analyses

Neurological grade was compared to histopathological grade in white and grey matter using the Kruskal–Wallis one-way analysis of variance (ANOVA) on ranks with Bonferroni correction for multiple comparisons. The same tests were used to determine if the histopathological grade was associated with pain on spinal palpation. An association between the distribution of lesions in the white matter (ventral, dorsal and lateral columns) and neurological grade was evaluated using Spearman rank correlation coefficients. The absence of nociception in relation to white and grey matter grades was expressed using cross-tabulations and proportions (%).

The duration of clinical signs was compared to the neurological grade and to the pathological grade at the epicentre using a Kruskal–Wallis one-way ANOVA on ranks and $\chi^2$ statistic with Bonferroni adjustment. In order to compare these data to published data, the correlation between duration of clinical signs and severity of white and grey matter changes in dogs with neurological grade 5 was evaluated separately.

Histopathological grades of 0 and 1 were classed together for statistical analysis. The threshold value for statistical significance was set to $P = 0.05$. All statistical analyses were performed using the software package NCSS 2007.[1]

[1] See: www.ncss.com.

## Results

### Animals

Of 124 dogs euthanased for IVD extrusion that underwent neuropathological evaluation, 60 dogs met the inclusion criteria. The range of ages was 3–11 years (median 6.7 years). Thirty-five dogs were male, 23 female and, in two dogs, sex was unrecorded. Dogs were of a variety of different breeds (Fig. 2).

### Clinical data

The severity of neurological signs was assessed as grade 2 in six dogs, grade 3 in six dogs, grade 4 in 17 dogs, and grade 5 in 31 dogs. The location of IVD herniation was thoracolumbar (Th9–L3) in 46 dogs, and lumbar (L4–L5) in 14 dogs. A Schiff-Sherrington posture was present in two dogs with thoracolumbar IVD herniation and two dogs with lumbar IVD herniation. Pain on spinal palpation was detected in 26/58 (44.8%) dogs. The presence or absence of spinal pain was not noted in the records of two dogs.

Information regarding the duration of clinical signs before presentation was available in 58 dogs; this was classed as peracute in 16/58 (27.6%), acute in 22/58 (37.9%) and chronic in 20/58 (34.5%). The median duration of clinical signs before presentation was 7.0 days (range 1–90 days). In dogs that underwent surgery, the median duration of clinical signs before surgery was 2.7 days (range 1–21 days). The overall median survival time was 10.6 days (range 1–90 days).

Thirty-one of 60 dogs (51.7%) were euthanased on the day of presentation following neurological examination or diagnostic imaging, due to poor prognosis or at the request of the owners. These dogs had a median neurological grade of 4 (range 2–5). One of 60 (1.6%) dogs died spontaneously, but the cause of death in this dog was not determined. Twenty-five of 60 (41.7%) dogs were treated surgically (median neurological grade of 5; range 2–5) and 3/60 (5%) were treated conservatively (median neurological grade of 3; range 2–4). Of the dogs treated surgically, two died during surgery or during the immediate postoperative period and two developed pancreatitis and severe disseminated intravascular coagulation and died within 2 weeks after surgery. All other dogs treated surgically or conservatively were euthanased because of lack of improvement or deterioration of clinical signs.

### White and grey matter changes at the epicentre of the spinal cord lesion

Changes in the white matter were graded as grade 0 in 1/60 (1.6%), grade 1 in 14/60 (23.3%), grade 2 in 9/60 (15%), grade 3 in 12/60 (20%), grade 4 in 8/60 (13.3%) and grade 5 in 16/60 (26.6%) dogs. Changes in the grey matter were graded as grade 0 in 5/60 (8.3%), grade 1 in 26/60 (43.3%) and grade 2 in 29/60 (48.3%) dogs. Discordance between the two observers was not greater than 1 grade in any case.

Lesions were distributed symmetrically in 53/60 (88.3%) dogs and asymmetrically in 7/60 (11.7%) dogs. White matter changes