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TITLE: Acute Herniation of Nondegenerate Nucleus Pulposus: Acute Noncompressive Nucleus Pulposus Extrusion and Compressive Hydrated Nucleus Pulposus Extrusion

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1 **Acute herniation of non-degenerate nucleus pulposus: acute non-compressive**
2 **nucleus pulposus extrusion and compressive hydrated nucleus pulposus extrusion**

3

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15 **Keywords:** High-velocity low-volume disc extrusion, traumatic disc extrusion, ANNPE,
16 HNPE, spinal cord contusion

17

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21

22 SYNOPSIS

23 Acute herniation of non-degenerate nucleus pulposus material is an important and relative
24 common cause of acute spinal cord dysfunction in dogs. Although there is some discussion
25 about the most appropriate terminology, two types of herniation of non-degenerate or
26 hydrated nucleus pulposus have been recognized; acute non-compressive nucleus pulposus
27 extrusion (ANNPE) and acute compressive hydrated nucleus pulposus extrusion (HNPE).
28 Spinal cord contusion plays an important role in the pathophysiology of both conditions.
29 Sustained spinal cord compression is not present in ANNPE, while varying degrees of
30 compression are present in HNPE. Both conditions typically affect older dogs and affected
31 animals can present with a characteristic clinical presentation. Magnetic resonance imaging
32 (MRI) is the diagnostic modality of choice and specific MRI findings have been described
33 to obtain a reliable clinical diagnosis. Although affected animals often present with severe
34 neurological signs, good outcomes can be achieved if appropriate treatment is initiated.

35

36 Key Points

- 37 • Acute non-compressive nucleus pulposus extrusion is characterized by a sudden
38 extrusion of non-degenerate nucleus pulposus without remaining spinal cord
39 compression
- 40 • Hydrated nucleus pulposus extrusion is characterized by a sudden extrusion of
41 hydrated nucleus pulposus, which results in varying degrees of spinal cord
42 compression
- 43 • Dogs with acute non-compressive nucleus pulposus extrusion, and to a lesser extent
44 dogs with hydrated nucleus pulposus extrusion, can present with characteristic
45 clinical signs
- 46 • Magnetic resonance imaging (MRI) is the diagnostic modality of choice for both
47 conditions. Specific MRI findings have been described for both conditions
- 48 • While there is consensus about the best treatment for acute non-compressive
49 nucleus pulposus extrusion, the ideal treatment for hydrated nucleus pulposus
50 extrusion is unknown

51

52 INTRODUCTION

53 Acute intervertebral disc herniation is the most common spinal emergency in dogs and can
54 be defined as a localized displacement of intervertebral disc material beyond its normal
55 anatomical boundaries.¹ “Hansen type I” intervertebral disc disease or “intervertebral disc
56 extrusion” is the most common and best characterized spinal cord condition in dogs.²⁻⁴ In
57 this condition, acute extrusion of dehydrated and calcified nucleus pulposus through a fully
58 ruptured annulus fibrosus is preceded by advanced chondroid degeneration of the
59 intervertebral disc (IVD) and the nucleus pulposus in particular.² Acute spinal cord injury
60 (SCI) in dogs with “Hansen type I” intervertebral disc disease is caused by a combination
61 of spinal cord contusion and varying degrees of sustained spinal cord compression.⁴⁻⁶
62 However, following continuous developments and increased availability of magnetic
63 resonance imaging (MRI) in veterinary medicine, it is increasingly recognized that acute
64 extrusions can also occur of non- or minimally degenerate nucleus pulposus. Although
65 there is some discussion concerning the most appropriate terminology, two types of acute
66 herniation of non-degenerate nucleus pulposus are currently recognized; acute non-
67 compressive nucleus pulposus extrusion (ANNPE) and hydrated nucleus pulposus
68 extrusion (HNPE). Differentiation and diagnosis is based on well-reported clinical
69 characteristics and diagnostic imaging findings.^{7,8} Several reports have now explored the
70 typical clinical presentation, diagnostic findings and management of ANNPE and HNPE,
71 revealing some stark contrasts with traditional “Hansen Type I” IVD extrusions and
72 emphasizing the need for an accurate diagnosis in such cases.⁷⁻¹⁴ Although both ANNPE
73 and HNPE refer to an acute extrusion of non-degenerate nucleus pulposus and subsequent

74 acute SCI, there are also important differences that might influence clinical decision-
75 making regarding management and prognosis.

76

77 **INTERVERTEBRAL DISC ANATOMY**

78 Although a detailed description of canine IVD anatomy is beyond the scope of this
79 manuscript, an understanding of the basic anatomical concepts is desirable to understand
80 the clinical characteristics and treatment recommendations for dogs with ANNPE and
81 HNPE. All vertebral bodies, with the exception of the first and second vertebrae and the
82 fused sacral vertebrae, are interconnected by an IVD.¹⁵ The IVD is composed of a centrally
83 located nucleus pulposus, an outer annulus fibrosus, the transitional zone and adjacent
84 vertebral endplates.⁵ The healthy and non-degenerate nucleus pulposus is a mucoid,
85 translucent, gelatinous structure (**Figure 1**). It is well hydrated and is mainly composed of
86 water.¹⁶ The nucleus pulposus is surrounded by the annulus fibrosus, which consists of a
87 network of concentrically organized collagen layers forming fibrous lamellae. The annulus
88 fibrosus is thicker ventrally than dorsally, which results in an eccentric localization of the
89 nucleus pulposus in the IVD.¹⁵ The thinner dorsal annulus fibrosus in combination with the
90 eccentric location of the nucleus pulposus are believed to predispose the nucleus pulposus
91 to extrude in a dorsal direction towards the vertebral canal and spinal cord.¹⁵ The most
92 central part of the annulus fibrosus is more cartilaginous and forms the interconnection
93 between the nucleus pulposus and annulus fibrosus. This well-demarcated region is called
94 the transitional zone.^{2,5} The dorsal and ventral borders of the IVD are formed by
95 respectively the dorsal and ventral longitudinal ligament, while the cranial and caudal
96 borders are formed by the cartilaginous vertebral endplates.¹⁵ These vertebral endplates

97 have an important role in supplying the IVD with nutrients. Small molecules can reach the
98 different components of the IVD through diffusion and osmosis from the capillary buds
99 through the vertebral endplates.¹⁷ The nucleus pulposus is a remnant of the embryological
100 notochord and the predominant cell type of the non-degenerate nucleus pulposus is
101 therefore the notochordal cell. The transitional zone contains chondrocyte like cells, the
102 outer layer of the annulus fibrosus contains fibrocyte-like cells and the more central layers
103 of the annulus contain a mixed population of fibrocytes and chondrocyte-like cells.¹⁸
104 Intervertebral disc degeneration is a complex and multifactorial process and is associated
105 with changes in the composition of these cells and their associated extracellular matrix.
106 Early IVD degeneration is characterized by histological changes in the nucleus pulposus,
107 which can be summarized as a gradual replacement of notochordal cells by chondrocyte-
108 like cells.^{5,18} Clinically irrelevant degenerative changes of the IVD however also occur
109 during the physiologic process of aging¹⁹ and changes seen in early pathological IVD
110 degeneration can be indistinguishable from age-related changes.⁵

111

112 **ACUTE NON-COMPRESSIVE NUCLEUS PULPOSUS EXTRUSION**

113 There have been several terms used historically to describe this condition, with the current
114 consensus of ANNPE used as it describes the key features of a sudden extrusion of non-
115 degenerate nucleus pulposus, causing spinal cord contusion without significant
116 compression.^{7,13} Previous terms used have included traumatic disc extrusion, high-velocity
117 low-volume disc extrusion, traumatic disc prolapse and Hansen Type III intervertebral disc
118 disease.^{2,20-22} ANNPEs have been diagnosed in dogs and less frequently in cats^{23,24}, and
119 typically present with a very characteristic peracute onset of clinical signs during exercise

120 or following trauma.^{7,13,24} Clinical signs are distributed according to the neuroanatomical
121 location and extent of the lesion, and typically stabilize within 24 hours before improving
122 or remaining static depending on the SCI severity.^{7,13}

123

124 **Pathophysiology**

125 Understanding the pathogenesis of ANNPE requires an appreciation of the normal canine
126 IVD anatomy outlined above. The strong osmotic gradient within the normal, non-
127 degenerate nucleus pulposus acts to draw water into the nucleus pulposus and therefore
128 create a naturally high intradiscal pressure.⁵ The combination of this healthy hydrated
129 nucleus pulposus surrounded by a dense and fibrous annulus fibrosus, allows mobility as
130 well as great stability.⁵ The normal IVD is therefore able to withstand marked variations
131 of physiological loading and biomechanical stress without suffering structural
132 compromise. However, in circumstances whereby the vertebral segment and IVD are
133 subjected to supraphysiological forces, such as during intense exercise or trauma, structural
134 integrity may fail.²² In such a scenario, a small tear may occur in the complex lamellar
135 structure of the annulus fibrosus, leading to a sudden extrusion of non-degenerate nucleus
136 pulposus material dorsally into the vertebral canal (an ANNPE). It has been suggested that
137 the annular lamellae in dogs are more vulnerable to such tears with increasing age.²⁵ In
138 ANNPE the nuclear material is hypothesized to extrude with great force, causing a focal
139 contusive injury to the adjacent spinal cord.⁷ As the extradural material is non-degenerate
140 and therefore highly hydrated, it typically rapidly dissipates or is resorbed, leaving minimal
141 to no spinal cord compression.^{7,22}

142 This hypothesis is supported by post-mortem findings in affected dogs of small tears in the
143 dorsal annulus, as well as non-degenerate nucleus pulposus material extradurally in the
144 vertebral canal.²⁶ The adjacent region of spinal cord may demonstrate evidence of focal
145 contusive injury, haemorrhage and necrosis.²⁶

146

147 **Clinical presentation and differential diagnosis**

148 Dogs with ANNPE often have a characteristic clinical presentation and present with a
149 peracute onset of often severe neurological deficits, clinical signs are lateralized in up to
150 90% of affected cases¹³ and are non-progressive after the initial 24 hours.^{7,10,13} Although
151 dogs often vocalize at onset of clinical signs and a moderate degree of spinal hyperesthesia
152 can be noted on initial clinical examination, this condition is typically not associated with
153 severe or sustained spinal pain.^{7,13} A study has indicated that these specific clinical
154 characteristics are indeed significantly associated with a diagnosis of ANNPE and that they
155 can be used to raise a high clinical index of suspicion for this particular disorder.¹ Clinical
156 signs are associated with intense exercise, such as running, in approximately 60% of cases
157 and external trauma in up to 40% of affected animals.⁷ Although any breed can be affected,
158 older large breed dogs, and especially Border collies, seem vulnerable for this condition.¹³
159 This clinical presentation is very similar and almost indistinguishable from dogs with
160 ischemic myelopathy or fibrocartilagenous embolic myelopathy.²² Ischemic myelopathy
161 should therefore be considered the most important differential diagnosis for ANNPE.
162 Although both conditions can be differentiated by MRI ^{27,28}, a recent study identified
163 differences in clinical presentation between dogs with ANNPE and ischemic myelopathy.¹³
164 Dogs with ANNPE were significantly older (mean age of 7.0 years for dogs with ANNPE),

165 were more likely to have a history of vocalization at onset of clinical signs (in 62% of dogs
166 with ANNPE), had more often spinal hyperesthesia (48% of dogs with ANNPE) during
167 initial examination and had more often a lesion affecting the C1-C5 spinal cord segments
168 compared to dogs with ischemic myelopathy.¹³ Dogs with ischemic myelopathy more
169 likely had a lesion affecting the L4-S3 spinal cord segments compared to dogs with
170 ANNPE.¹³ Compared to the general hospital population, Border collies were
171 overrepresented for ANNPE, while English Staffordshire Bull terriers were
172 overrepresented for ischemic myelopathy.¹³ As outlined above, onset of clinical signs is
173 associated with external trauma in up to 40% of dogs with ANNPE.⁷ This is also reflected
174 in earlier reports referring to this condition as “traumatic disc extrusion”.²¹ This highlights
175 that ANNPE should be considered in animals suffering from spinal cord dysfunction
176 immediately after external trauma and that ANNPE should be considered an important
177 differential diagnosis for vertebral fracture and luxation.

178 Although “Hansen type I” intervertebral disc disease is the most common canine spinal
179 emergency, affected animals often present with a different clinical presentation compared
180 to dogs with ANNPE.¹ Dogs with “Hansen type I” intervertebral disc disease most
181 commonly present with an acute instead of peracute onset of clinical signs, clinical signs
182 are often progressive beyond the first 24 hours after their onset, affected animals more
183 commonly display spinal hyperesthesia and clinical signs are not often obviously
184 lateralized.³

185

186 **Diagnosis**

187 It is often possible to reach a high clinical index of suspicion for ANNPE prior to diagnostic
188 tests being performed due to the highly characteristic clinical presentation.¹ When making
189 a presumptive diagnosis based on clinical presentation, it should be emphasized to the
190 owner that any deterioration or failure to improve as expected should lead to a re-
191 evaluation of the diagnosis. A definitive diagnosis of ANNPE can only be achieved through
192 visualization and histological examination of extruded non-degenerate nucleus pulposus
193 material in the vertebral canal.²⁶ However, as this can only be confirmed on post-mortem
194 examination, in clinical cases a presumptive antemortem diagnosis is based on combining
195 the typical clinical presentation with supportive diagnostic imaging findings.^{7,27,28} The
196 potential uses and limitations of individual diagnostic tests are outlined below.

197

198 *Radiography and myelography*

199 The main use for survey radiographs is to rule out vertebral fractures and subluxations in
200 cases with a history of external trauma immediately preceding the onset of clinical signs.
201 However, the sensitivity for detecting vertebral fractures and subluxations using survey
202 radiographs is only 72% and 77.5%, respectively.²⁹ In ANNPE it can be possible to identify
203 a narrowed IVD space on survey radiographs. This radiographic finding is however not
204 specific for animals with ANNPE.

205 Although myelography has now largely been superseded by advanced cross-sectional
206 imaging modalities, it can be used to exclude compressive spinal conditions such as Hansen
207 Type I IVD extrusion.³⁰ In ANNPE myelography may reveal a small, focal extradural
208 lesion overlying an IVD, with an adjacent intramedullary pattern due to focal spinal cord

209 swelling.⁹ However, it will not allow accurate differentiation between ANNPE and other
210 causes of an intramedullary lesion such as ischemic myelopathy.

211

212 Computed Tomography

213 As with myelography, computed tomography (CT) can be used to exclude selected
214 compressive conditions such as “Hansen Type I” IVD extrusion^{30,31}, as well as being the
215 diagnostic imaging modality of choice for excluding vertebral fractures and subluxations.²⁹
216 However, CT will also not allow differentiation between other intramedullary spinal cord
217 lesions. The use of CT or myelography does however allow the exclusion of differential
218 diagnoses which require urgent surgical intervention. It can therefore guide an appropriate
219 management plan if no MRI is available.

220

221 Magnetic resonance imaging

222 MRI is the diagnostic imaging modality of choice for diagnosing ANNPE (**Figure 2**).^{7,27}

223 The following criteria can be used to make a presumptive diagnosis of ANNPE using MRI

224 7:

- 225 • Focal intramedullary spinal cord T2-weighted hyperintensity (typically
226 isointense on T1-weighted sequences)
- 227 • Lesion located overlying an IVD space, often lateralized
- 228 • Reduction in volume of the T2-weighted hyperintense nucleus pulposus
- 229 • Mild narrowing of the affected IVD space
- 230 • Small volume of extradural material or signal intensity change dorsal to the
231 affected IVD, with minimal to no spinal cord compression

232 The intramedullary lesion, representing an area of spinal cord edema secondary to
233 contusive injury, is typically well demarcated and may affect grey matter preferentially.
234 Although mild post-contrast enhancement of the lesion on T1-weighted sequences has been
235 reported²¹, usually this is not present.⁷ In dogs with this typical clinical presentation, a
236 common differential diagnosis for such a focal intramedullary spinal cord T2-weighted
237 hyperintensity is ischemic myelopathy.^{7,27} A recent study has shown moderate
238 interobserver and moderate to good intraobserver agreement for differentiating between
239 ANNPE and ischemic myelopathy using the criteria outlined above.²⁷ The findings of this
240 study also suggested that a smaller, focal intramedullary lesion length is more often
241 associated with a diagnosis of ANNPE compared to longer lesions in ischemic myelopathy,
242 as well as lesions diagnosed as ANNPE being more often lateralized.²⁷

243

244 **Treatment**

245 There are currently no neuroprotective treatments available with proven efficacy in directly
246 treating the contusive primary spinal cord injury. Treatment of ANNPE therefore involves
247 supportive medical management, consisting of restricted activity, supportive nursing care
248 and physical rehabilitation.⁷ As 48% to 57% of dogs with ANNPE present with evidence
249 of spinal hyperesthesia^{7,13}, appropriate analgesia may be indicated for the first few days.
250 Restricted activity with short lead walks has been recommended in the management of
251 ANNPE for a period of 4-6 weeks, to minimise the risk of further extrusion of nuclear
252 material.^{7,22} Nursing care requirements essential to prevent complications and aid recovery
253 vary between cases depending on the severity of neurological dysfunction, and may
254 involve:

- 255 • Manual bladder expression or urinary catheter maintenance in cases of urinary
256 incontinence
- 257 • Monitoring for and management of respiratory dysfunction in severe cervical
258 myelopathies. This includes regular turning of recumbent patients every 4 hours
259 to avoid lung atelectasis or accumulations of secretions
- 260 • Prevention of dermatological consequences of prolonged recumbency such as
261 urine scald, pressure sores and decubital ulcers
- 262 • Nutritional support to maintain body condition and support physical
263 rehabilitation

264 Physical rehabilitation is increasingly recognized as important in supporting the recovery
265 of patients with spinal cord injuries in both human and veterinary medicine.^{32,33} The aims
266 and requirements of physical therapy will be dictated by the severity of neurological
267 dysfunction, but typically aim to maintain joint range of motion, minimize muscle atrophy
268 and prevent patient discomfort during the recovery period.³⁴

269

270 **Outcome**

271 Overall recovery rates are variable with successful outcomes ranging from 66.7% to
272 100%.^{7,9,13,21} It is however difficult to compare findings between studies due partly to
273 differences in definitions of “successful outcome”, inclusion criteria, and management
274 protocols, as well as the limited number of animals with the most severe injuries.^{7,9,13,21}

275 **Table 1** shows a summary of outcome data in studies including at least 10 dogs. Factors
276 reported to be associated with a poor prognosis include severity of neurological
277 dysfunction and the extent of intramedullary lesions on MRI.⁷ Severity of neurological

278 dysfunction has been shown to be associated with an unsuccessful outcome, with 0 out of
279 8 cases with paraplegia and absent nociception and only 7 out of 13 tetra/paraplegic dogs
280 with intact nociception having successful outcomes in one study.⁷ In the same study all 21
281 dogs with less severe neurological grades had successful outcomes.⁷ Although long-term
282 outcome has only been reported for a limited number of cases with paraplegia and loss of
283 nociception, only 2 of a total of 14 reported dogs were reported to have a successful
284 outcome (**Table 1**).^{7,13,21}

285 Using MRI, outcome has been shown to be associated with the length of the intramedullary
286 T2-weighted hyperintensity on sagittal images and lesion cross-sectional area as a
287 percentage of total spinal cord area on transverse images.⁷ The maximal cross-sectional
288 lesion area has been suggested to represent the best predictor of outcome in dogs with
289 ANNPE, with a cut-off value of >90% to predict unsuccessful outcome with a sensitivity
290 of 86% and specificity of 96%.⁷ Several studies have found urinary or fecal incontinence
291 to be a possible long-term complaint following ANNPE, with 10 out of 42⁷, 7 out of 46⁹
292 and 7 out of 26¹³ dogs experiencing long-term reduced urinary or fecal continence (**Table**
293 **1**). The ability to manage the consequences of urinary or fecal incontinence may therefore
294 be an important factor in determining long-term outcome, as well as an important
295 consideration in the care of affected animals.^{7,13}

296 Overall recovery times following ANNPE are variable and are likely influenced by the
297 severity of spinal cord injury.⁷ Reported recovery times in dogs diagnosed with ANNPE
298 include median durations of hospitalization from 3 (range 0 – 58)¹³ to 4.5 (range 0 – 29)⁷
299 days, with time to independent ambulation varying from a median of 2¹³ (range 0 – 84) to
300 16.5⁷ days (range 2 – 93). It may take several months before maximum improvement is

301 reached, with a median time to maximum clinical improvement of 2 months (range 0 – 48)
302 reported in one study.¹³

303

304 **Acute non-compressive nucleus pulposus extrusion in cats**

305 Although ANNPE has also been reported in cats, the current literature is limited to case
306 reports and small case-series.^{20,23,24} Affected cats also present with a peracute onset of
307 non-progressive and variably painful clinical signs.^{23,24} In contrast to dogs, cats most often
308 present with symmetrical instead of lateralized clinical signs and up to three quarters of
309 affected cats present after external trauma, such as a road-traffic accident or a fall from a
310 height.²⁴ This highlights that also in cats ANNPE should be considered an important
311 differential diagnosis for vertebral fracture and luxation. The cervical spinal cord segments
312 are not often affected in cats.²⁴ Although prognosis for neurological improvement is good,
313 it seems unlikely for affected cats to experience a full neurological recovery. A recent case
314 series indicated that all cats for which long-term outcome was available had regained an
315 ambulatory status, but none of them had become neurologically normal.²⁴

316

317 **HYDRATED NUCLEUS PULPOSUS EXTRUSION**

318 More recently, another type of minimally to non-degenerate nucleus pulposus extrusion
319 has been reported in dogs.^{8,35} In contrast to animals with ANNPE, an amount of well-
320 hydrated, gelatinous, extradural material can be identified in the vertebral canal, which is
321 associated with varying degrees of spinal cord compression.⁸ Although there is some
322 controversy about the most appropriate terminology^{8,14,36}, acute compressive hydrated
323 nucleus pulposus extrusion (HNPE) is currently considered most appropriate.³⁶ Because of

324 similarities between MRI findings in dogs and discal cysts in humans, this condition was
325 initially referred to as “canine intraspinal discal cysts”.³⁵ Human discal cysts are extradural
326 lesions that communicate with the IVD. Affected people present most often with a chronic
327 progressive history of a painful lumbar radiculopathy. Surgery in people confirms an
328 obvious cyst wall, consisting of dense fibrous connective tissue and the serous or
329 serosanguinous content of these cysts lack IVD material.³⁷ Dogs however present with an
330 acute onset of clinical signs, surgery has not been able to demonstrate an obvious capsule
331 or cyst wall delineating the extradural material and cytological or histopathological
332 evaluation of the liquid extradural material has consistently revealed findings compatible
333 with minimally degenerate nucleus pulposus.^{8,11,12,14,35} It has therefore been suggested that
334 these lesions should not be referred to as ‘canine intraspinal discal cysts’ and that acute
335 compressive HNPE might appear more appropriate.³⁶ Because cytological and histological
336 examination of collected extradural material consistently reveals a degree of partial nucleus
337 pulposus degeneration, it has more recently been suggested to refer to this condition as
338 ‘partially degenerated disc extrusions’.¹⁴ As outlined above, it can however be impossible
339 to distinguish changes seen in early pathological IVD degeneration from age-related
340 changes.⁵ Although the pathophysiology of HNPE is currently unknown, there are possible
341 similarities with ANNPE with extrusion of hydrated nucleus pulposus through a single
342 fissure in the dorsal annulus fibrosus secondary to sudden changes in IVD pressure and
343 biomechanics.¹²

344

345 **Clinical presentation and differential diagnosis**

346 HNPE has a predilection for the cervical region and clinical signs are therefore reflected
347 by acute cervical spinal cord dysfunction. Clinical signs are often severe and symmetrical
348 (i.e. not lateralized) with non-ambulatory tetraparesis and tetraplegia being the most
349 common clinical presentations. Cervical spinal hyperesthesia is only noted in a minority of
350 cases.^{8,11,12,38,39} Although so far only one case has been reported with possible HNPE
351 affecting the thoracolumbar vertebral column³⁵, the authors of this manuscript have seen
352 several dogs with clinical and imaging findings compatible with thoracolumbar HNPE
353 **(Figure 3)**. Cervical HNPE can affect small and large chondrodystrophic and non-
354 chondrodystrophic dogs.^{8,11,38,39} Affected animals are generally older with a median age
355 around 9 years.^{8,39} Onset of clinical signs is spontaneous and only rarely associated with
356 intense physical exercise.^{8,12,39}

357 Differential diagnoses for cervical compressive HNPE include other causes of acute
358 cervical myelopathies such as cervical ANNPE, ischemic myelopathy and compressive
359 “Hansen type I” intervertebral disc extrusion. In contrast to dogs with ANNPE or ischemic
360 myelopathy, onset of clinical signs is only rarely associated with intense physical exercise
361 and neurological deficits are typically symmetrical.^{8,11,12} Dogs with cervical HNPE have
362 more severe neurological deficits and less severe cervical hyperesthesia compared to dogs
363 with other compressive cervical myelopathies, such as acute ‘Hansen type I’ cervical
364 intervertebral disc extrusions.³⁸

365

366 **Diagnosis**

367 Magnetic resonance imaging is the diagnostic modality of choice to diagnose HNPE and
368 several studies have reported consistent, almost pathognomonic, MRI findings.^{8,11,12,14}

369 MRI abnormalities in dogs with cervical HNPE include (**Figure 4**):

- 370 • Ventral, midline, extradural compressive material homogenous hyperintense on
371 T2-weighted sequences and isointense in all sequences to normal, non-degenerate,
372 nucleus pulposus lying immediately dorsal to the affected IVD
- 373 • The compressive material can have a characteristic bilobed or “seagull
374 appearance”, which can possibly be explained by the location of the compressive
375 material ventral to the apparent intact dorsal longitudinal ligament¹²
- 376 • The affected intervertebral disc space is narrowed, has a reduced volume of
377 nucleus pulposus and an ill-defined dorsal annulus fibrosus⁸
- 378 • The overlying spinal cord can demonstrate focal intraparenchymal hyperintensity
379 suggestive for spinal cord contusion and the extruded material can demonstrate
380 variable degrees of contrast enhancement^{8,12,14}

381 A recent study has evaluated the usefulness of CT to evaluate cervical HNPE. Although
382 unenhanced CT was not useful in detecting a lesion, IV contrast enhanced CT revealed a
383 lesion in all, but one case. The observed lesion was a well-demarcated hypodense lesion
384 dorsal from the IVD space showing rim enhancement.³⁹ Contrast enhanced CT had a
385 sensitivity of 91% and specificity of 100% to differentiate between HNPE and “Hansen
386 type I” IVD extrusion.³⁹

387 Extruded material removed during surgery can have a white, water-like, opaque and liquid
388 to gelatinous appearance.^{8,12,14} Cytology and histology of compressive material reveals

389 findings compatible with nucleus pulposus with evidence of early degeneration (**Figure**
390 **5**).^{11,12,14,39}

391

392 **Treatment and outcome**

393 Outcome seems dependent on severity of clinical signs with unsuccessful cases
394 demonstrating tetraplegia with respiratory compromise at initial presentation.^{8,39} Despite
395 these often severe neurological deficits, good outcomes, characterized by rapid and
396 complete neurological recoveries, have been reported after both medical and surgical
397 treatment.^{8,11,12,35,39,40} Medical management can consist of restricted exercise in
398 combination with appropriate nursing care, physiotherapy, hydrotherapy and appropriate
399 anti-inflammatory drugs and analgesia. Surgical treatment typically consists of
400 decompressive surgery by a ventral slot procedure. The ideal type of treatment is currently
401 uncertain.^{36,39} Although it is unclear which dogs would benefit from surgical therapy
402 instead of medical management, the combination of severe neurological signs and obvious
403 spinal compression on MRI have been considered indications for surgical treatment.^{8,12,1}
404 The acute onset of severe clinical signs and reported rapid improvements after initiation of
405 medical treatment could suggest that spinal cord contusion plays a major role in the
406 pathophysiology of HNPE, questioning the value of surgical decompression in this
407 condition.¹¹ Furthermore, several reports have indicated spontaneous regression of
408 extradural compressive material in animals that underwent medical management.^{11,40}
409 Further research is therefore necessary to compare the clinical presentation and outcome
410 of dogs treated medically or surgically for cervical acute compressive HNPE. A recent
411 study has compared the clinical presentation and outcome of 18 dogs treated medically and

412 16 dogs treated surgically for cervical HNPE. Although more dogs in the surgical group
413 demonstrated cervical hyperesthesia, no other significant differences were seen for
414 signalment, clinical presentation or imaging findings. All dogs for which long-term
415 outcome was available had experienced an excellent neurological recovery and no
416 significant differences in short –and long-term outcome variables were seen between dogs
417 treated surgically or medically for cervical HNPE.⁴¹

418

419 **SUMMARY**

420 ANNPE and acute compressive cervical HNPE are increasingly recognized as common
421 spinal emergencies in dogs. A reliable presumptive clinical diagnosis can be obtained by
422 combining typical clinical characteristics and well-described MRI findings. Although the
423 pathophysiology of both conditions is not yet fully elucidated, good outcomes can be
424 obtained if appropriate treatment is initiated. Further research is needed to evaluate the best
425 type of treatment in dogs with acute compressive cervical HNPE.

426

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431

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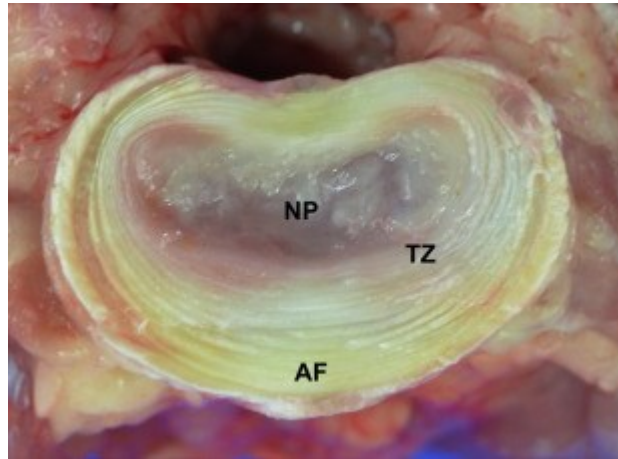
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544 extrusion in dogs. Submitted

546 **FIGURE LEGENDS**

547 **Figure 1.** Transverse section through a normally hydrated L1-L2 intervertebral disc
548 illustrating the centrally located nucleus pulposus (NP), annulus fibrosus (AF) and
549 transitional zone (TZ). Note the eccentric location of the NP and wider ventral AF.



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552 **Figure 2.** (A) Mid-sagittal T2-weighted magnetic resonance image (MRI) of the cervical
553 vertebral column of a dog with a C2-C3 ANNPE. There is a focal, intramedullary hyperintensity
554 of the spinal cord immediately dorsal to the C2-C3 intervertebral disc (IVD) space (arrow). The
555 C2-C3 IVD nucleus pulposus has a markedly reduced volume and signal intensity (asterisk). (B)
556 Transverse T2-weighted image at the level of C2-C3 IVD space. There is a focal, lateralized
557 intramedullary hyperintensity of the spinal cord predominantly affecting the grey matter (arrow).
558 There is also a small volume of markedly hyperintense extradural material ventrolateral to the
559 spinal cord (open arrowhead), causing minimal compression. (C) Transverse T1-weighted MRI at
560 the same level as (B). The intramedullary lesion is isointense to spinal cord grey matter, and the
561 extradural material is hypointense to adjacent epidural fat.

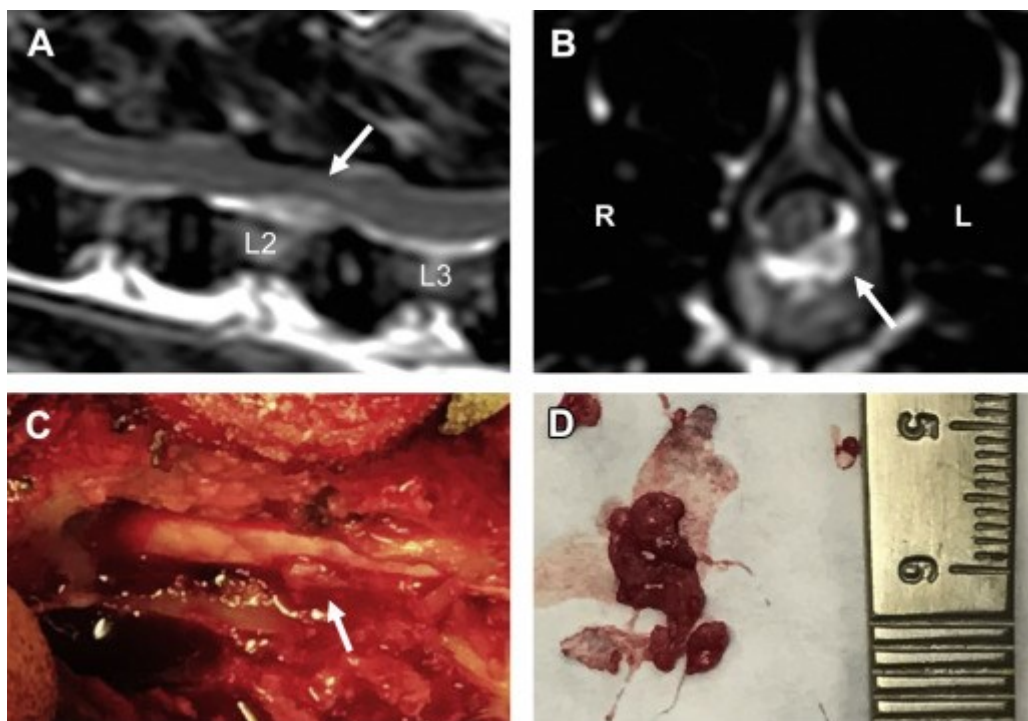


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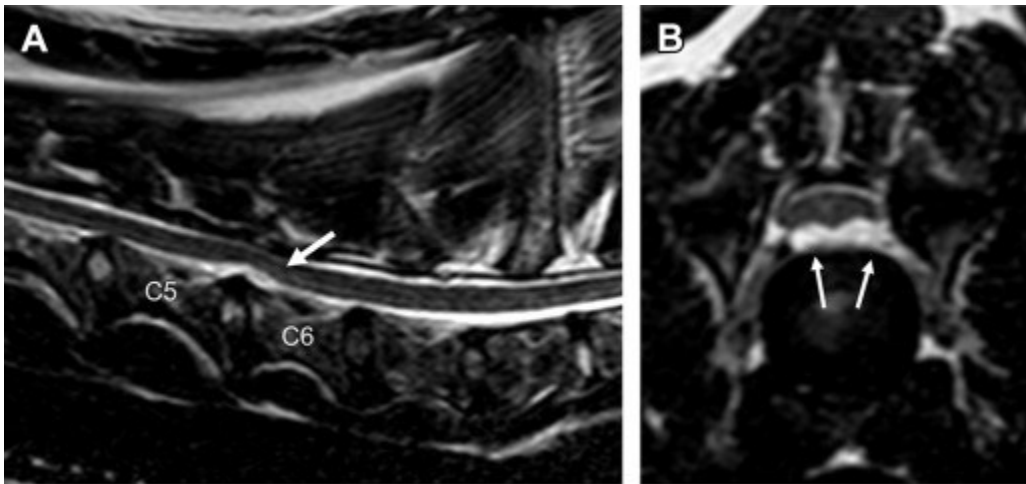
565 **Figure 3.** (A) Mid-sagittal T2-weighted magnetic resonance image (MRI) of a dog with an
566 L2-L3 compressive hydrated nucleus pulposus extrusion (HNPE). Note the hyperintense
567 nature of the extruded material (arrow) and decreased volume of hydrated nucleus pulposus
568 in the L2-L3 intervertebral disc (IVD). (B) Transverse T2-weighted image at the level of
569 the L2-L3 IVD space. There is left lateralized ventral extradural compression of
570 hyperintense material (arrow). (C) Intraoperative image of the same dog illustrating focal
571 spinal cord compression (arrow). (D) The gelatinous nature of the compressive nature can
572 be appreciated after surgical removal



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575 **Figure 4.** (A) T2-weighted sagittal magnetic resonance image (MRI) of a dog with a C5-
576 C6 acute compressive hydrated nucleus pulposus extrusion (HNPE). A ventral extradural
577 compression overlying the C5-C6 intervertebral disc (IVD) is visible (arrow). The
578 compressive material has the same intensity as normally hydrated nucleus pulposus. The
579 intervertebral disc space is mildly narrowed and contains a reduced volume of normally
580 hydrated nucleus pulposus. (B) T2-weighted transverse MR image at the C5-C6 IVD space.
581 The extruded material has the typical bilobed or 'seagull' appearance (arrows).

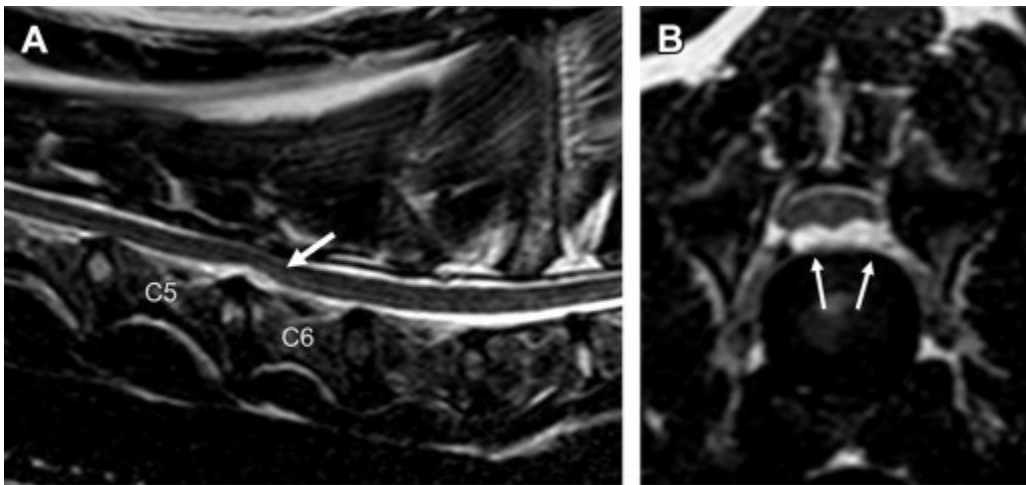


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585 **Figure 5.** (A) Intraoperative image of the same dog as in Figure 4. The transparent water-
586 like extruded material is visible (arrow) after completion of the ventral slot. (B) Impression
587 smear cytology of the extruded material reveals basophilic cells with characteristics of
588 notochordal cell and chondrocytes, consistent with extruded nucleus pulposus with signs
589 of early degeneration.



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593 **Table 1.** Long-term follow-up of studies including more than 10 dogs diagnosed with acute
 594 non-compressive nucleus pulposus extrusion

Reference	Number of dogs	Dogs reported to demonstrate functional recovery (%)	Dogs with long-term continence data available	Dogs with long-term reduced continence	Comment
Chang et al, 2007	11	10 (90.0)	0	n/a	10 out of 11 dogs recovered partially or completely, including 2 of 3 with loss of nociception
De Risio et al, 2009	42	28 (66.7)	42	10 (23.8)	Success defined as able to perform daily activities and complete urinary and fecal continence. Unsuccessful outcome in all 8 cases with loss of nociception
McKee et al, 2010	46	46 (100)	46	7 (15.2)	Outcome reported as ability to urinate. Two dogs with loss of nociception euthanized shortly after diagnosis and not included in follow-up
Fenn et al, 2016	37	30 (81.1)	26	7 (26.9)	Success defined as able to perform daily activities and complete urinary and fecal continence. Unsuccessful outcome in all 3 cases with loss of nociception

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