Intervertebral disk extrusion is one of the most common neurologic diseases in dogs, causing pain and neurologic deficits that range from mild ataxia to complete paralysis and loss of anal sphincter control. Treatment options depend on the severity of clinical signs and include cage confinement of mildly affected dogs and spinal decompressive surgery for more severely affected dogs. Although treatment success rates are high for dogs with mild to moderate IVDE, only as many as 60% of dogs with paraplegia and loss of deep pain sensation will recover. Dogs that recover from IVDE, whether by conservative or surgical treatment, are at risk for recurrence, with reported recurrence rates as high as 20% in some breeds.

Intervertebral disk extrusion can occur in all breeds of dogs but is most common in chondrodystrophic breeds, such as Dachshund, Pekingese, French Bulldog, Basset Hound, Welsh Corgi, Beagle, and American Cocker Spaniel. These breeds evolved through direct selection for the pathological trait of disproportionate dwarfism, which is a result of altered epiphyseal chondroblastic growth and maturation. In chondrodystrophic dogs, the intervertebral disks can undergo a degenerative process known as chondroid metaplasia, in which the native notochordal cells of the nucleus pulposus are replaced by newly formed chondrocyte-like cells. This results in loss of elasticity caused by hardening and often calcification of the nucleus pulposus, which predisposes the intervertebral disks to extrusion through the annulus fibrosus.

To reduce the prevalence of IVDE in dogs, both physical and genetic factors have been investigated for associations with the disease in the general canine population and in Dachshunds specifically.27-37 Findings regarding the relationship between thoracolumbar vertebral column length or body weight and the frequency and severity of IVDE are contradictory.28,36,38 Yet, smaller skeletal size has been associated with increased risk of thoracolumbar IVDE in different breeds.50

### Characteristics of and risk factors for intervertebral disk extrusions in Pekingese

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**OBJECTIVE**
To characterize and identify risk factors for intervertebral disk extrusion (IVDE) in Pekingese.

**DESIGN**
Retrospective case-control study.

**ANIMALS**
426 Pekingese (81 with confirmed IVDE and 345 without IVDE) admitted to a veterinary teaching hospital from 2005 through 2015.

**PROCEDURES**
Medical records were reviewed and data were extracted regarding age, sex, body weight, body condition score, coat color, chief reason for initial evaluation, body system involved, and diagnosis. Survey radiographs of the vertebral column were examined. Data were compared between the confirmed IVDE and non-IVDE groups.

**RESULTS**
Confirmed IVDE was uncommon in dogs < 2 years of age (2/81 [2%]). The extrusion was primarily located in the thoracolumbar (n = 57 [70%]) and cervical (22 [27%]) regions; the most common sites were T12-13 and C6-7. The number of radiographically visible calcified disks was significantly greater in the confirmed IVDE versus non-IVDE group, and the presence of calcified disks in the T10-L4 region was associated with increased odds of IVDE (OR, 21.2). Black coat color was significantly more prevalent in the confirmed IVDE versus non-IVDE group and was associated with increased odds of developing IVDE (OR, 1.6). Mean body weight and the proportion of spayed female dogs were significantly greater in the confirmed IVDE versus non-IVDE group.

**CONCLUSIONS AND CLINICAL RELEVANCE**
Several risk factors for confirmed IVDE in Pekingese were identified that could be useful for counseling clients about the disease or, with additional research, designing selective breeding programs to reduce the prevalence of IVDE in the breed. (J Am Vet Med Assoc 2018;252:846–851)
In Dachshunds, evidence of calcified disks on survey radiography is an established risk factor for IVDE\textsuperscript{30,34,39} as well as its recurrence.\textsuperscript{9,10} It has also been shown that the likelihood of developing radiographically visible disk calcifications is hereditary in Dachshunds.\textsuperscript{22,35} Because of the established association between intervertebral disk calcification and IVDE, radiographic screening has been used in the selective breeding of Dachshunds with the aim to reduce the prevalence of IVDE in the breed.\textsuperscript{26,27,39}

Pekingese, a common chondrodystrophic breed in many countries, are reportedly 10.3 times as likely to develop IVDE as other breeds, second only to Dachshunds (OR, 12.6).\textsuperscript{37} However, no studies have been conducted involving Pekingese specifically, and risk factors for IVDE in this breed have not been reported. The purpose of the study reported here was to characterize IVDE in Pekingese and identify risk factors for the disease.

## Materials and Methods

### Animals and data collection

Medical records of all dogs admitted to the Koret School of Veterinary Medicine Teaching Hospital from January 1, 2005, through December 31, 2015, were retrospectively reviewed to identify those pertaining to Pekingese. Pekingese could be included only once, and dogs with multiple visits or admissions were allocated to groups in accordance with their main reason for evaluation or diagnosis.

Data were extracted for each dog regarding age, sex, body weight, body condition score (9-point scale, with 1 representing extremely thin and 9 representing obese), coat color (black, white, gray, parti-colored, or brown, which included all shades of brown from cream to dark brown), chief complaint at initial evaluation, body system involved, and diagnosis. To qualify for inclusion in the confirmed IVDE group, dogs were required to have that diagnosis confirmed by advanced imaging (eg, myelography, CT following myelography, or MRI) and to have subsequently undergone spinal decompressive surgery. Medical records for these dogs were reviewed for findings of complete physical and neurologic examination, spinal radiography, and advanced imaging and for the description of the surgical procedure. The term cervical IVDE was applied to dogs with extrusion in the C2-T1 region, thoracolumbar IVDE for those with extrusion in the T10-L4 region, and caudal-lumbar IVDE for those with extrusion in the L4-L7 region. Dogs with only suspected IVDE for which no advanced imaging or decompressive surgery had been performed were excluded from the study. Dogs were included in the non-IVDE group if they had a confirmed diagnosis other than IVDE.

### Radiographic evaluation

Radiographic images of the vertebral column were obtained for dogs in both groups and reviewed by a radiologist. Only good-quality radiographs from T10 through L4 pertaining to dogs $\geq$ 2 years of age were used. To provide optimal viewing of the area of interest for the study, imaging software\textsuperscript{4} was used for magnification and contrast changes. All visible intervertebral disk calcifications from T10 through L4 were counted, including calcifications of disk material in the intervertebral disk space, intervertebral foramen, and adjacent vertebral canal. For dogs in the confirmed IVDE group, the disk at the extrusion site was classified as calcified or not calcified through examination of lateral radiographs obtained prior to surgical decompression.

### Statistical analysis

Quantitative data are reported as mean $\pm$ SD, median, and range. Qualitative data are reported as frequency (%). To compare quantitative data between 2 independent groups, the 2-sample $t$ test (for normally distributed data) and Mann-Whitney nonparametric test (for nonnormally distributed data) were used. The $\chi^{2}$ and Fisher exact tests were used to assess associations between 2 qualitative variables. Logistic regression was also performed to identify associations between several variables (coat color, sex, and number of CDVR) and IVDE. All tests applied were 2-tailed, and values of $P < 0.05$ were considered significant.

### Results

#### Animals

A total of 472 Pekingese were admitted to the teaching hospital during the 11-year study period. Forty-six (10%) of these dogs were excluded from the study because IVDE had been suspected but not confirmed.

The confirmed IVDE group included 81 dogs (46 [57%] sexually intact males, 13 [16%] castrated males, 11 [14%] sexually intact females, and 11 [14%] spayed females). Mean $\pm$ SD age was 5.0 $\pm$ 2.6 years (median, 4.5 years; range, 1.5 to 12.0 years). Only 2 of the 81 (2%) dogs were $<2$ years of age. Mean body weight of the 80 dogs for which this variable was recorded was 6.1 $\pm$ 1.2 kg (13.4 $\pm$ 2.6 lb; median, 6.0 kg [13.2 lb]; range, 3.5 to 9.0 kg [7.7 to 19.8 lb]). Body condition score was recorded for 80 dogs, with a median value of 5 (range, 3 to 7). Coat color was brown for 40 of the 78 (51%) dogs for which it was recorded, white for 20 (26%) dogs, black for 11 (14%) dogs, gray for 4 (5%) dogs, and parti-colored for 3 (4%) dogs. Concurrent diseases included brachycephalic syndrome (n = 2 [2%]) and mitral regurgitation (1 [1%]).

The non-IVDE group included 345 dogs (207 [60%] sexually intact males, 31 [9%] castrated males, 80 [23%] sexually intact females, and 27 [8%] spayed females). Age was recorded for 341 dogs, with a mean of 5.2 $\pm$ 4.1 years (median, 4.0 years; range, 0.1 to 15.4 years). Mean body weight of the 299 dogs for which this variable was recorded was 5.2 $\pm$ 1.8 kg (11.4 $\pm$ 4.0 lb; median, 5.2 kg [11.4 lb]; range, 0.1 to 12.8 kg [0.2 to 28.2 lb]). Mean body weight of the 206 dogs that were $\geq$ 2 years of age was 5.5 $\pm$ 1.7 kg (12.1 $\pm$ 3.7 lb; median, 5.5 kg [12.1 lb]; range, 2.5 to 12.8 kg [5.5 to 28.2 lb]).
The most common site for IVDE in the cervical region was C6-7 and in the thoracolumbar region was T12-L3. Three (4%) dogs died following spinal decompressive surgery. One dog that underwent caudal-lumbar hemilaminectomy was euthanized at the owner’s request 1 week after surgery because of lack of neurologic improvement. Another dog that underwent thoracolumbar hemilaminectomy died of severe respiratory distress during recovery from anesthesia, which was attributed to its brachycephalic condition. The third dog died a few hours following thoracolumbar hemilaminectomy after failing to regain a normal breathing pattern and development of hypoxia.

CDVR

Fifty-four of 81 (67%) dogs in the confirmed IVDE group and 47 of 345 (14%) dogs in the non-IVDE group received radiographic screening for calcifications. In the confirmed IVDE group, the calcification site was in the thoracolumbar region of most dogs (n = 40 [74%]) and in the cervical region of 12 (22%) dogs; the lowest prevalence of CDVR (2 [4%]) was in the caudal-lumbar region. Nine (17%) dogs with confirmed IVDE had no calcification from T10 through L4. Examination of the extrusion sites on radiographs revealed that the extruded disk was calcified in 48% (26/54) of dogs with confirmed IVDE.

The number of CDVR in the confirmed IVDE group was significantly (P < 0.001) greater than in the non-IVDE group (mean difference, 2.2 CDVR; 95% CI, 1.6 to 2.8 CDVR). This difference was more prominent in the thoracolumbar region than in the cervical region, but both differences were significant (P < 0.001). Dogs with ≥1 CDVR in the examined region were 21.2 times as likely to have IVDE as dogs with no CDVR (OR, 21.2; 95% CI, 7.6 to 58.8). Dogs with CDVR in the confirmed IVDE group were significantly younger than dogs with calcified disks in the non-IVDE group (mean ± SD age, 5.0 ± 2.5 years vs 6.2 ± 3.2 years; P = 0.049). Mean and median age and sex distribution did not differ significantly between groups.

To further investigate the association between age and CDVR, each group was further separated into 3 age subgroups. Age distributions in the confirmed IVDE and non-IVDE groups, respectively, were 59% (32/54) and 45% (21/47) for 2 to <5 years of age, 28% (15/54) and 34% (16/47) for 5 to <8 years of age, and 13% (7/54) and 21% (10/47) for ≥8 years of age. No significant differences between groups in these age distributions were identified.

### Table 1—Number of CDVR in the T10-L4 region in Pekingese with confirmed IVDE and without IVDE (non-IVDE).

<table>
<thead>
<tr>
<th>Dog group</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>Mean ± SD</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any IVDE (n = 54)</td>
<td>9</td>
<td>9</td>
<td>11</td>
<td>5</td>
<td>12</td>
<td>5</td>
<td>3</td>
<td>2.5 ± 1.8</td>
<td>2</td>
</tr>
<tr>
<td>Cervical IVDE (n = 12)</td>
<td>3</td>
<td>5</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>1.7 ± 1.7</td>
<td>1</td>
</tr>
<tr>
<td>Thoracolumbar IVDE (n = 40)</td>
<td>6</td>
<td>3</td>
<td>9</td>
<td>5</td>
<td>10</td>
<td>4</td>
<td>3</td>
<td>2.9 ± 1.8</td>
<td>3</td>
</tr>
<tr>
<td>Caudal-lumbar IVDE (n = 2)</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1.5 ± 0.7</td>
<td>NC</td>
</tr>
<tr>
<td>Non-IVDE (n = 47)</td>
<td>38</td>
<td>6</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0.4 ± 1.8</td>
<td>0</td>
</tr>
</tbody>
</table>

NC = Not calculated.
Discussion

The present retrospective study revealed some characteristics of Pekingese that were associated with IVDE. Radiographic detection of calcified disks in the T10-L4 region was a strong risk factor for IVDE in the evaluated dogs, increasing the likelihood of this disease 21-fold. Calcification of the nucleus pulposus is a feature of disk degeneration common in chondrodystrophic dogs.15,16 Disk calcification is considered a dynamic process, given that radiographic evidence may appear and disappear over time.29,34 The prevalence of disk calcification increases in dogs up to 2 to 2.5 years of age,16,29 followed by partial or complete resolution in dogs > 3 years of age.29,34 Because both the occurrence of IVDE and its radiographic evidence are age-related, radiographs of dogs < 2 years of age were excluded from CDVR assessment on the basis of reported data for other chondrodystrophic breeds.29 In addition, mean age was similar in the non-IVDE and confirmed IVDE groups (5.2 vs 5.0 years, respectively). We therefore concluded that age had no important role in the significant difference identified between groups in the number of CDVR or occurrence of IVDE.

In the present study, no CDVR were detected in 17% of dogs with confirmed IVDE, which is similar to the value reported for Dachshunds with IVDE (13%).27 In the Dachshund study,27 disk extrusions occurred almost equally at sites with or without radiographic evidence of calcification. These findings suggest that radiography alone cannot be used to exclude disk extrusion. Nevertheless, findings of several other studies22,30,39 suggest that in Dachshunds, screening of breeding candidates by radiography of the vertebral column may reduce the incidence of disk extrusion in the population. A hereditary basis of disk calcification has been demonstrated in Danish Dachshunds, in which a locus on chromosome 12 was identified as the site of the mutation responsible for the trait.35,39 Consequently, if this trait is hereditary in Pekingese as well, then a similar breeding selection approach should be considered.

The sites of disk extrusion in the Pekingese of the present study were primarily within the thoracolumbar region, with only 27% in the cervical region. In the thoracolumbar region, the most commonly affected location was T12-13 intervertebral disk. This finding, as well as the overall distribution of extrusions along the thoracolumbar region, was similar to most reported data for other breeds.5–10 However, in the cervical region, the most common location for IVDE was C6-7 and the number of CDVR decreased gradually toward the cranial-cervical disk spaces. This finding appears to be unique to our cohort of Pekingese. In most studies involving chondrodystrophic dogs with IVDE, C6-7 was the site with the lowest incidence of extrusion. This dissimilarity may be explained by differences among breeds in the anatomic conformation of the vertebrae or intervertebral disks. Pekingese generally have a shorter neck than Dachshunds, which might result in a different biomechanical load affecting the caudal-cervical disk spaces, predisposing Pekingese to extrusions there. French Bulldogs are reportedly prone to caudal-lumbar disk extrusion, unlike the general anatomic distribution of extrusions characteristic of Dachshunds.57 It would be reasonable to assume that more differences exist among breeds.

Black coat color (vs nonblack coat color) was a significant risk factor for disk extrusion in the present study, representing a 60% increase in the odds of confirmed IVDE. No significant association was found in other coat colors. However, color coat was recorded for only 90% of dogs. Other research31,41 has shown that the risk of disk calcification may be associated with different coat characteristics in Dachshunds. Because coat type (eg, wirehaired vs smooth coated and short vs long hair) is genetically controlled, this finding supports a genetic basis for disk extrusion.

Obesity has been identified to be associated with IVDE, with a median BCS of 5.5 (9-point scale) in affected dogs versus 5.0 in unaffected dogs and an OR of 1.62.28 In the present study, mean body weight was significantly higher in the IVDE group than the non-IVDE group. Because the non-IVDE group included a higher proportion of immature dogs, dogs < 2 years of age were then excluded from this analysis. Nevertheless, the difference between groups was still significant. This finding may have been attributable to a greater prevalence of obesity or skeletally larger dogs in the confirmed IVDE group. Because body condition was not documented for dogs in the non-IVDE group, nor were physical features such as body length and height, these possibilities could not be explored.

Inconsistencies exist in the literature regarding male predominance in dogs with IVDE. Whereas large-scale studies9,38 have revealed equal distributions between males and females, others have shown a distinct male predilection.25,37,42 No significant sex predisposition was identified in the present study.

Concurrent disease was recorded for only 3 of the 81 (3.7%) dogs with confirmed IVDE in the study reported here. However, we believe that in this specific breed, the actual prevalence of concurrent disease was probably higher than recorded. In the authors' experience, when dealing with acute IVDE in dogs, both the owners and physician focus on this major concern and can fail to report or diagnose more minor problems. A prospective study design may help overcome this bias.

Because of the retrospective nature of the study reported here, inconsistencies in radiographic parameters, such as collimation, contrast, and sharpness, were encountered by the radiologist during evaluation. This limitation was minimized through exclusion of all images that were difficult to evaluate. Nevertheless, more accurate results could have been obtained had specific and similar protocols been used. Another limitation was the age restriction on radiographic
analysis. In Pekingese, information regarding the age at which disk calcification is radiographically visible is lacking. However, reports concerning Dachshunds have indicated that radiographic screening of the vertebral column should be performed when dogs are between 1 and 2 years of age. Given that information, we presumed that disk calcification would be less visible on radiographs obtained when the Pekingese were < 2 years of age.

Findings of the study reported here highlighted the unique characteristics of Pekingese with IVDE as well as common features shared with other chondrodystrophic breeds. Additional studies are needed to determine conclusively whether selection of breeding dogs based on CDVR would have an impact on the prevalence of IVDE in Pekingese. Such studies should include prospective, standardized, serial radiographic evaluation of Pekingese, beginning at an early age, as well as follow-up evaluation to determine occurrence of IVDE during their lifetime. Because genetic factors associated with IVDE can differ among dog breeds, genetic analysis would be useful for determining the hereditary basis for disk calcifications and IVDE in Pekingese.

Footnotes
a. Synapse workstation software for Synapse picture archiving and communication system, Fujiﬁlm Medical Systems, Stamford, Conn.

References
34. Stigen O. Calcification of intervertebral discs in the Dachshund—


From this month’s AJVR

Pharmacokinetics and pharmacodynamics after oral administration of tapentadol hydrochloride in dogs

James Howard et al

**OBJECTIVE**
To evaluate pharmacokinetic and pharmacodynamic characteristics of 3 doses of tapentadol hydrochloride orally administered in dogs.

**ANIMALS**
6 healthy adult mixed-breed dogs.

**PROCEDURES**
In a prospective, randomized crossover study, dogs were assigned to receive each of 3 doses of tapentadol (10, 20, and 30 mg/kg, PO); there was a 1-week washout period between subsequent administrations. Plasma concentrations and physiologic variables were measured for 24 hours. Samples were analyzed by use of high-performance liquid chromatography–tandem mass spectrometry.

**RESULTS**
Tapentadol was rapidly absorbed after oral administration. Maximum plasma concentrations after 10, 20, and 30 mg/kg were 10.2, 19.7, and 31 ng/mL, respectively. Geometric mean plasma half-life of the terminal phase after tapentadol administration at 10, 20, and 30 mg/kg was 3.5 hours (range, 2.7 to 4.5 hours), 3.7 hours (range, 3.1 to 4.0 hours), and 3.7 hours (range, 2.8 to 6.5 hours), respectively. Tapentadol and its 3 quantified metabolites (tapentadol sulfate, tapentadol-O-glucuronide, and desmethyltapentadol) were detected in all dogs and constituted 0.16%, 2.8%, 97%, and 0.04% of the total area under the concentration-time curve (AUC), respectively. Plasma AUCs for tapentadol, tapentadol sulfate, and tapentadol-O-glucuronide increased in a dose-dependent manner. Desmethyltapentadol AUC did not increase in a linear manner at the 30-mg/kg dose. Sedation scores and heart and respiratory rates were not significantly affected by dose or time after administration.

**CONCLUSIONS AND CLINICAL RELEVANCE**
Oral administration of tapentadol was tolerated well, and the drug was rapidly absorbed. Adverse events were not apparent in any dogs at any doses in this study. (*Am J Vet Res* 2018;79:367–375)