INVITED REVIEW

Feline Degenerative Joint Disease

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Objective: To critically review and collate published information on feline degenerative joint disease (DJD) and identify areas in which information is lacking.

Study Design: Critical literature review.


Results: Although there are no prospective studies, the prevalence of radiographic DJD appears to be high and can be associated with clinical signs of decreased mobility. There appears to be a mismatch between radiographic and clinical examination findings (pain response). There is little information on the cause of DJD in different joints. There are no fully validated subjective or objective assessment systems for the measurement of chronic DJD-associated pain in the cat. Development of a feline model of chronic DJD-associated pain may speed the development and evaluation of candidate pain-alleviating compounds and treatments.

Conclusions: The high prevalence of feline DJD and lack of information about it, suggests further investigation is needed.

Clinical Relevance: Feline DJD occurs with high frequency, and yet there is little to guide the clinician on prevention or treatment.

INTRODUCTION

SURPRISINGLY LITTLE is known about feline degenerative joint disease (DJD) although there have been recent attempts to characterize feline joint disease based on radiographic changes and to evaluate associated clinical signs.1,2 Concurrently, there has been much speculation on feline DJD and likely, many erroneous presumptions based on DJD in other species especially in non-peer-reviewed literature. Thus, it seems timely to critically review what is known about feline DJD and to identify needed information to appropriately address this clinical entity. This review concentrates on the prevalence and causes of feline DJD, evaluates whether feline DJD is associated with pain, and reviews the evidence for efficacy of postulated treatments for this pain.

All mammals develop DJD, the progressive destruction of one or more components of joints—cartilage, subchondral bone, ligaments, and joint capsule. DJD affects synovial and cartilaginous joints but not fibrous joints (synarthroses). In synovial joints, degeneration is typically associated with variable synovial thickening, articular cartilage degeneration, subchondral bone sclerosis, periarticular osteophyte formation, and joint capsule thickening.3 For cartilaginous joints of the spinal column, degeneration generally results from degeneration of the intervertebral disk, with narrowing of the intervertebral space, sclerosis of the endplate, and formation of osteophytes (spondylosis deformans).4

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Submitted June 2008; Accepted February 2009

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0161-3499/09
doi:10.1111/j.1532-950X.2009.00597.x

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Primary DJD is an idiopathic phenomenon occurring without an apparent initiating factor whereas secondary DJD results from some predisposing condition, usually trauma. Primary osteoarthritis (OA), the most common form of primary DJD, is likely related to aging and typically occurs in older individuals. For feline synovial joints, there are several recognized and postulated primary and secondary causes of joint degeneration. DJD associated with Scottish Fold osteochondrodysplasia, mucopolysaccharidosis (MPS), and age-related cartilage degeneration has been described as primary DJD. Postulated secondary causes of DJD in cats are congenital, trauma, infectious and inflammatory, nutritional, and immune-mediated, although there is little evidence for many of these causes.

**Radiographic Prevalence of Feline DJD**

**Axial Skeleton.** In the first extensive radiographic evaluation of DJD of the feline axial skeleton, a single lateral radiograph of the entire vertebral column was taken of 150 cadavers of older cats before soft tissues were removed and the vertebral column inspected for osteophytes. Although osteophytes were observed in 68% of cats, only 85% were evident on lateral radiographs. New bone formation was termed “vertebral osteophytes” because little was known about the cause of the condition. Cervical vertebrae were seemingly equally affected with a sharp increase in prevalence of degenerative changes at the cervicothoracic junction. All thoracic vertebrae appeared commonly affected, with a peak incidence between the 7th and 8th vertebrae. Lumbar vertebrae were affected more than cervical, but less than thoracic, vertebrae. In the thoracic region, the cranial aspects of the vertebrae were more often affected whereas in the lumbar region, the caudal aspects of vertebrae were more often affected.

Hardie et al retrospectively reviewed radiographs of 100 cats >12 years old that had spinal radiography at a north American veterinary teaching hospital as part of a diagnostic workup for various conditions. Radiographs were included if any of the axial or appendicular skeletal joints were imaged. The vertebral column was divided into thoracic, lumbar, and lumbosacral regions, with the sternal articulations grouped together. Each visible articulation was scored for DJD according to Morgan. Lateral and ventral enthesiophytes, narrowing of intervertebral spaces, and apparent vertebral endplate sclerosis were recorded. Consistently viewed axial segments were the thoracic vertebral column (96 cats), sternum (92 cats), lumbar (30 cats), and lumbosacral vertebral column (18 cats). DJD was identified in 80 cats and in 26, only the vertebral column was involved with the most severely affected area being the lumbosacral junction.

In a similar study at a Scottish veterinary teaching hospital, radiographs of 218 cats (mean age, 6.5 years) were examined. Recorded axial skeleton (classified as cervical, thoracic, lumbar, lumbosacral, and sternal segments) abnormalities were enthesiophytes at ≥1 intervertebral joints, mineralization of any intervertebral disk, collapse of joint spaces, or osteophytosis of any of the articular facets. The authors considered “enthesiophytes” a more appropriate term than “vertebral osteophytes” because degeneration involved an enthesis. Of 1090 axial segments that could potentially have been radiographed in 218 cats, 513 axial segments had radiographs made of them. Axial skeletal DJD was evident in 45 (21%) cats, with only the sternal segment affected in 11 cats, spondylosis deformans in 17 cats, spondylosis deformans and spondylotic DJD in 16, and mineralized intervertebral disks in 1 cat. Spondylosis deformans was most commonly seen in the thoracic segment, at T7–8 and T9–10, findings very similar to Beadman et al. The most severe DJD was observed in the lumbar segment, in contrast to Hardie et al where the most severe lesions involved the lumbosacral joint.

Thoracic articular facet OA was reported in 6 (the subgroup that had obvious joint pain) of 25 cats that had complete skeletal radiography in a study evaluating clinical signs associated with appendicular joint OA. In another study evaluating measures of pain relief in cats with appendicular joint OA, of 12 of 13 cats (mean age, 14 years) had radiographic changes in the spinal column consisting of spondylosis deformans and/or radiographic signs consistent with intervertebral disk disease.

Skeletal joint pathology has been evaluated in nondomesticated felidae. Visual examinations of 386 big cat skeletons (e.g., leopard, mountain lion, African lion) in various north American collections revealed spondyloarthropathy in 3.6% of skeletons. Spondyloarthropathy was defined as evidence of facet joint or sacroiliac joint erosion or fusion, asymmetrical pattern of arthritis, reactive new bone formation, syndesmophytes (calcification within the annulus fibrosus), or peripheral joint fusion. In reviewing the report, seemingly axial degenerative changes were evident in 2.1%.

Although it appears that investigators are describing the same general findings for axial skeleton DJD, the nomenclature used varies. Most refer to spondylosis deformans (earlier referred to as vertebral osteoarthropathy) to describe new bone observed on ventral and lateral aspects of axial skeleton vertebrae; however, spondyloarthropathy has also been used. In humans, spondyloarthropathies are generally considered a group of related inflammatory joint diseases often associated with the MHC class I molecule HLA-B27: ankyllosing spondylitis, reactive arthritis, arthritis associated with inflammatory bowel disease, and psoriatic arthritis. In hu-
mans, the axial skeleton (particularly the sacroiliac joint) is often affected by these spondyloarthropathies; however, in its most accurate definition, it includes appendicular joint pathology as occurs in Reiter's syndrome. Until more is known about the histopathologic characteristics and cause(s) of the axial skeleton changes observed in felidae, spondylosis deformans, and facet joint DJD are the most appropriate descriptive terms. Given the possibility that true spondyloarthropathies might occur in felidae, it will be important for future studies to evaluate both appendicular and axial skeletal changes in detail, evaluating the microscopic changes associated with radiographic changes, and any association with concurrent diseases.

Summarily, published reports suggest that the most frequent site of axial skeleton DJD in cats is T7–10 with the most severe lesions occurring in the lumbar or lumbosacral region (Table 1). Clearly, the incidence of axial skeleton DJD is markedly different between studies. This may reflect differences in how DJD was classified, but more likely reflects age differences in study populations with Beadman et al observing axial skeleton DJD increasing in frequency with age.

**Appendicular Skeleton.** Langenbach et al prospectively evaluated the relationship between DJD and hip joint laxity in a nonrandomly selected group of 78 cats (mean age, 2.5 years; range, 6 months–9 years old); 22% were domestic shorthairs and 78% were purebreds from 8 different breeds. Orthogonal views were evaluated for DJD using radiographic criteria established for DJD in dogs. Hip dysplasia (HD) was found in 25 (32%) cats and DJD in 19%, with all cats with DJD having HD. Keller et al retrospectively evaluated cats, admitted to a north American veterinary teaching hospital, with ventrodorsal radiographic projections of the coxofemoral joints. Of 684 cats (mean age, 2.8 years), 6.6% (45 cats) had HD and 43 of these had concurrent coxofemoral joint DJD. Interestingly, the DJD was described as being different in appearance compared with DJD in dogs, with extensive remodeling and proliferative changes involving the craniodorsal acetabular margin and minimal remodeling of the femoral neck (Fig 1).

<table>
<thead>
<tr>
<th>Mean Cat Age (Years)</th>
<th>% of Cats with Axial Skeleton DJD</th>
<th>Most Commonly Affected Area</th>
<th>Most Severely Affected Area</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unknown (older)</td>
<td>58</td>
<td>Thoracic (T7–8)</td>
<td>—</td>
<td>Beadman et al</td>
</tr>
<tr>
<td>15</td>
<td>80</td>
<td>—</td>
<td>Lumbar</td>
<td>Hardie et al</td>
</tr>
<tr>
<td>6.5</td>
<td>21</td>
<td>Thoracic (T6–7, 9–10)</td>
<td>Lumbar</td>
<td>Clarke et al</td>
</tr>
<tr>
<td>11</td>
<td>—</td>
<td>Thoracic</td>
<td>Thoracic</td>
<td>Clarke &amp; Bennett</td>
</tr>
<tr>
<td>14</td>
<td>92</td>
<td>Thoracic</td>
<td>—</td>
<td>Lascelles et al</td>
</tr>
</tbody>
</table>

For some entries, data cannot be given because of the design or nature of the study (see text for full details). The definition of osteoarthritis and degenerative joint disease (DJD) varies between studies.

Hardie et al evaluated appendicular skeleton radiographs, scored according to Morgan, in 100 cats (mean age, 15 years; 68 domestic shorthairs, 17 domestic long hairs, 15 other) considering the primary joints of the limb individually and the joints of the feet as a single location. The most consistently examined joints were the elbow (71 cats), coxofemoral (18), and stifle (13) joints with the carpus, tarsus, and feet each examined in only 2 cats. DJD was observed in at least 1 appendicular joint in 64% of cats with the elbow, most severely affected. In non-
domesticated felidae, DJD was identified in 5.2% of the big cats with the elbow being most commonly affected, followed by the stifle and shoulder.

In a study evaluating feline shoulder and stifle synovial fluid, radiographs of all thoracic and pelvic limb joints (except the hip) were obtained. Of 52 cats evaluated, estimated age was distributed as <1-year-old (48%), 1–3 years (27%), 3–6 years (21%), and >6 years (4%). Sixteen cats (30%) had radiographic evidence of OA involving at least 1 joint, with the elbow being most frequently affected (21% of elbow joints examined) and although examined by a single radiologist, the criteria for diagnosing OA were not defined.

Clarke et al defined appendicular DJD as presence of periarticular and/or juxta-articular enthesiophytes, periarticular and intraarticular soft tissue mineralization, or OA where OA was defined as the radiographic presence of osteophytes, either with or without subchondral sclerosis, soft tissue mineralization, and enthesiophytes. Overall, 26% (605) of the total number (2616) of main appendicular joints (shoulder, elbow, carpus, hip, stifle, and hock) were available for radiographic evaluation. Of 218 cats (mean age, 6.5 years), 50 (23%; mean age, 10 years) had DJD of at least 1 appendicular joint (36 had OA, 6 enthesiopathy [affecting 13 different joints], and 8 had soft tissue mineralization [affecting elbows]). Normalized for the number of joints of each type examined, the most commonly affected joints were the hip (22%), elbow (16.4%), and stifle (8.2%); however, <7% of carpi and tarsi were visible on radiographs. In a similar study of 292 sets of feline radiographs (mean cat age not reported but mean age of clinic population, 8.2 years) evaluated for appendicular OA (defined as increased subchondral bone density or periarticular new bone), 63 (22%) had OA of at least 1 appendicular joint (mean age, 10.2 years). No obvious cause of OA was identified in 56 cats and lesions were bilaterally symmetrical in 41 (73%), with the elbow most commonly affected.

Clarke and Bennett, reported details of affected joints in 25 of 28 cats. These cats were those with obvious pain associated with manipulation of at least 1 joint with radiographic OA. In this group, the elbow, hip, and then hock were the most commonly affected joints. In another study evaluating measurement of chronic musculoskeletal pain in cats, 13 cats (mean age, 14 years) had every joint evaluated radiographically and a median of 4 appendicular joints in each cat had radiographic signs consistent with OA with the hip (16 joints) being most commonly affected, followed by elbow (11), and tarsus (11), then stifle (10), shoulder (5), and carpus (2).

Ossicles can be found consistently in the menisci of various mammalian species—rats, mice, hamsters—usually, in the cranial horn of the medial or lateral menisci and have been described as not being a cause of, or associated with, DJD. However in 3 cats with meniscal ossicles, it was suggested that the observed mineralization was a primary, naturally occurring vestigial structure in 1 cat, and, trauma associated in another, and both cats had DJD. When identified radiographically in 23 of 28 skeletally mature large nondomestic cats, they were considered a normal structure. Thus, it is unclear if meniscal ossicles in domestic cats (Figs 2 and 3) are indicative of DJD, and radiologic and histologic studies are required.

Summarily, the appendicular joints most commonly affected by DJD are the hip and elbow, followed by the stifle or possibly tarsus (Table 2); however, there are no reports where every joint in a randomly selected population of cats has been evaluated to ascertain the prevalence of DJD in cats. Further, similar to axial skeleton lesions, DJD is defined differently among studies. Hardie et al claimed that all joints with radiographic signs of DJD were osteoarthritic whereas Clarke et al attempted to distinguish between radiographic signs of DJD, like enthesiophytes and soft tissue mineralization (which, may not represent OA [Fig 4]) and OA. Seemingly, there are no studies in cats comparing the radiographic appearance of joints with histologic findings. Such comparison is needed to improve radiographic interpretation and to address the suggestion that feline DJD may be associated with less tendency for new bone formation compared with some species.

![Fig 2. Lateral projection of the stifle. Meniscal calcification (confirmed histologically) is evident with apparent associated degenerative joint disease.](image-url)
Causes of Feline DJD

Although Allan outlined common causes of OA in cats, there is little documented supporting evidence and most studies evaluating prevalence speculate on the cause of DJD. Clarke et al. indicated that 25% of OA cases resulted from trauma, with 50% of cases having no obvious cause suggesting that they may have been primary OA. Godfrey suggested only 13% of OA cases were secondary to a disease generally recognized as leading to OA, thus 87% were possibly primary OA, predicted on an absence of underlying disease typically considered to lead to secondary OA in other species. However, as Godfrey indicates, this approach has not been validated and it is unlikely that all cats were evaluated thoroughly enough during their lifetimes to rule out possible causes of DJD. Hardie et al. found little evidence in medical records to indicate likely cause of DJD and postulated that observed OA/DJD was likely secondary to undetermined factors (e.g., elbow dysplasia, chronic low-grade trauma, subtle malarticulation).

Of interest is the frequent bilateral occurrence of feline DJD, a characteristic of DJD caused by bilateral congenital malformations (e.g., joint dysplasia, osteochondrosis), systemic factors (e.g., endocrinopathy, metabolic disorders), neurogenic factors, chronic overuse, or possible primary OA. In a case report of arthroscopic debridement of bone fragments from an elbow joint with DJD and associated lameness, it was suggested, but not confirmed, that the cause may have been fragmented medial coronoid process. There are no reports of fragmented coronoid process in the cat.

The comparatively low incidence of appendicular joint DJD and OA in big (e.g., leopard, mountain lion, African lion) cats (5.2%) is interesting; however, because age was unknown the low incidence may reflect studying a younger population. Regardless, other studies seem to suggest that prevalence of DJD in young domestic cats is substantially higher. Of 386 big cat specimens, 283 were wild caught, and differences in lifestyle and diet between wild and domesticated cats may well account for the apparent differences. Interestingly, disease that Rothschild et al. classified as OA did not occur in wild caught big cats.

Two primary forms of OA are fairly well recognized in cats: Scottish Fold osteochondrodysplasia and MPS. The Scottish Fold is a purebred cat with generalized defective cartilage metabolism. The underlying...
ing osteochondrodysplasia affects both bone growth and formation of articular cartilage. Osseous deformities are most apparent in the distal appendicular skeleton, with affected joints having the appearance of an ankylosing polyarthritis with smoothly marginated periosteal bone around the carpal and tarsal bones.5,24,25 The best-studied feline form is MPS VI, which causes skeletal malformation that results in arthropathies.6 MPS VI is a lysosomal storage disease caused by a deficiency of the lysosomal enzyme N-acetylgalactosamine-4-sulfatase.30 Several case reports and small case series have been published26–32 and the radiographic signs described. In the appendicular skeleton, coxofemoral subluxation, generalized epiphyseal dysplasia, and DJD occur secondary to accumulation of abnormal levels of glycosaminoglycans in cartilage and connective tissue.

Although several authors have suggested that a large proportion of DJD in cats is primary,11,19 there is currently no supporting evidence. It is very possible that hitherto unrecognized factors, such as those that play a role in other species, may be responsible for DJD in cats. It is also possible that as yet unrecognized factors that do not play a significant role in DJD in other species, such as systemic inflammatory disease, may predispose to, or be the cause of, DJD in the cat.

Currently documented secondary causes of DJD in cats are nutritional, HD, and noninfectious polyarthropathies and infectious arthropathies. Hypervitaminosis A in cats occurs when diet consists mainly of liver,33–35 and results in progressive new bone formation on vertebræ resulting in ankylosing spondylarthropathy, and also around shoulder and elbow joints at ligament and tendon insertions.

HD was described in several cats in the 1970s.36–38 The dysplastic changes lead to secondary DJD, and the occurrence of degenerative changes in the coxofemoral joints associated with HD was confirmed by Hayes et al39 who suggested that the prevalence of HD was 1/180th of that in dogs at the same diagnostic facilities.39 Familial genetics was suggested as playing a role, because a potential predisposition was observed in pure bred cats, although there were insufficient cases to test this hypothesis. Medially luxating patellæ occurred concurrently with HD and was also suggested as a cause. A relationship between HD/laxity and coxofemoral joint DJD was also demonstrated in Langenbach’s study.15 In a nonrandomly selected, mainly pure-bred group of 78 cats, 15 of 25 cats with HD also had DJD, and the mean Norberg angle (NA) in cats with DJD was significantly lower than in cats without DJD (84 versus 95°), and the distraction index was significantly higher (0.6 versus 0.49). These findings were similar to those of Koeppel and Ebner40 who studied NA in relation to DJD in a random population of domestic shorthair cats.

In Keller’s retrospective evaluation of the incidence of HD in young cats, 43 of 45 cats with HD had degenerative changes, and all of these had a shallow acetabulum.17 It was noted that the shallow acetabulum is similar to the situation occasionally observed in humans; however, acetabular dysplasia does not appear to be a predictable risk factor for development of DJD in humans.41 No objective measure of acetabular depth was used; an acetabulum was considered shallow if <50% of the femoral head was covered.17 Whereas, this could be a primary structural defect, it is also possible that cats began with normal acetabular depth, but because of hip joint laxity and subsequent secondary changes, infilling occurred. Certainly, however, the radiographic appearance of coxofemoral joint DJD appears to be different in cats than dogs, with overall less bone formation on the femoral neck and head, and often-prominent new bone on the cranial effective acetabular rim.17 Histologic studies are needed to determine the role that congenital acetabular dysplasia plays in feline hip DJD. Although studies that have been performed suggest a relationship between HD and DJD, these studies have concentrated on cats with HD.

To further investigate the relationship between HD and coxofemoral joint DJD, prospective longitudinal studies are needed where a cohort of young cats are thoroughly evaluated for hip laxity and conformation, and then followed over time, with periodic evaluation for

**Fig 4.** Oblique projection of the elbow. There is soft tissue mineralization, confirmed by macroscopic inspection to be in the craniomedial joint capsule. It is unknown if such periarticular mineralization is associated with degenerative joint disease.
coxofemoral DJD. In a group of predominantly purebred cats, a weak association was found between medial patella luxation and HD,\textsuperscript{42} with a combination of HD and patella luxation being 3 times more likely than either condition alone. The weak association may reflect the small number of cats in the study. It was suggested that patella luxation was congenital because of the young age of presentation (2 years old) and the mainly bilateral (71%) nature of the condition. DJD was also observed in association with patella luxation; however, the relationship between patella luxation and development of DJD of the stifle is not clear.

Smith et al\textsuperscript{42} reported that only cats with grade 2 or 3 medial patella luxation had evidence of DJD in the affected stifle joint. In the only other published report of patella luxation in cats,\textsuperscript{43} 42 cats were evaluated; 27 cats (44 stifle joints) had radiographs that were scored according to published criteria for dogs.\textsuperscript{44} Out of a possible score of 27, 14 joints had a score of 0; 24 joints, a score of 1–9 (mild OA); 3 joints, a score of 10–18 (moderate OA); and 3 joints, a score of 19–27 (severe OA). The 3 cats with severe OA had grade 4 luxation. This data suggest that increasing severity of patella luxation in cats is more likely to lead to DJD in that joint. Again, as noted earlier, the sensitivity of radiographs for detection of DJD in cats is unknown, and there have been no reported morphologic evaluations of feline joints with, and without, patella luxation.

Although trauma is an often-quoted cause of DJD in cats,\textsuperscript{7,45} there is only sparse evidence to support this,\textsuperscript{1,11,19} and no studies evaluating the occurrence of DJD after joint trauma (e.g., fracture, dislocation).

Several forms of feline DJD with a suggested immune mediated basis have been described.\textsuperscript{46–49} Initially, 5 cases of polyarthritis\textsuperscript{48} were described, similar to an earlier case report\textsuperscript{47} and the term “chronic progressive polyarthritis” used to describe a deforming polyarthritis of predomi-
nantly the carpel and tarsal joints that was progressive over a period of weeks, and associated with pyrexia and lymphadenopathy. Later, when more cases were evaluated, it appeared that 2 forms existed—a more common form (17/20 cats), characterized by periosteal new bone formation and osteoporosis, and a less common form (3/20) characterized by a deforming, erosive arthritis.\textsuperscript{49} A larger series of suspected immune-based polyarthritis with detailed evaluation, suggested classification of feline immune-mediated polyarthritis as: feline rheumatoid arthritis, feline systemic lupus erythematosus, feline periosteal proliferative polyarthritis, and feline idiopathic polyarthritis.\textsuperscript{46} Erosive lesions were observed in feline rheumatoid arthritis, and new bone production in feline periosteal proliferative polyarthritis and to a lesser extent in feline idiopathic polyarthritis.\textsuperscript{46} Immune-mediated disease was considered the underlying cause in all of these cats.

Bacterial arthritis is occasionally seen as a cause of DJD. Polyarthritis has been associated with \textit{Mycoplasma fellei}.\textsuperscript{52} Recently, bilateral tarsal DJD associated with crypticoccosis was reported.\textsuperscript{53}

Anecdotally, it is often suggested that obesity causes DJD in cats. A causal relationship has not been proven, but the relationship between being overweight and lameness requiring veterinary care has been evaluated. Associations between starting body condition and specific diseases that developed, including lameness, was evaluated in 1457 cats studied over a 4.5-year period.\textsuperscript{54} Risk of developing lameness requiring veterinary attention was significantly increased for heavy (hazard ratio = 2.9) and obese (hazard ratio = 4.9) cats. It was suggested that excess bodyweight or a generalized lipid metabolic abnormality might lead to cartilage damage and OA; however, the cause of lameness and specifically if it was associated with DJD was not evaluated. In a retrospective radiographic study of the prevalence of DJD in cats, no significant association between bodyweight and radiographic signs of DJD was identified.\textsuperscript{11}

\textbf{Is Feline DJD Associated with Pain?}

Although 90% of the cats evaluated by Hardie et al\textsuperscript{9} had radiographic evidence of axial and/or appendicular skeleton DJD, only 4% had mention of arthritis or problems with mobility noted in the medical records. The records evaluated were referral hospital records and the cats were not referred for mobility problems. Godfrey\textsuperscript{19} reported that \(\frac{1}{3} (21/63)\) of cats with radiographic appendicular joint OA had clinical signs of mobility impairment, and were radiographed for that reason (lameness, stiff gait, difficulty jumping, hindlimb weakness, shuffling forelimb gait, and inactivity). In another study, 16.7% of the cats with radiographic signs of DJD were lame; however, it was suggested that lameness per se may not be the most obvious clinical sign associated with feline DJD.\textsuperscript{11}

In a feline cruciate transection model of OA, ground reaction forces and limb kinematics recovered to presurgical levels over 1 year, despite progression of radiographic OA.\textsuperscript{55} Indeed, static differences between the operated and control side disappeared after 3–4 months, and dynamic loading differences at the walk disappeared after 6 months. In a discussion of the model, it was indicated that after 5 years the joints have severe radiographic signs of OA without associated pain.\textsuperscript{56} In contrast, several studies have identified cats with radiographic DJD and mobility impairment\textsuperscript{1,2,57}; NSAID administration significantly improved mobility. Two of these studies were not blinded\textsuperscript{1,57} and used veterinarian and owner assessments that have not been validated;
however, an objective measure of activity was used in addition to owner assessments in the other study.\textsuperscript{2} Clearly, in some cats radiographically apparent DJD is likely associated with pain and results in impaired mobility.

Recent studies have emphasized that lameness is often not the presenting complaint—rather, owner-observed impaired mobility.\textsuperscript{1,2} If the impact of DJD on the quality of life of cats is to be evaluated, validated methods to assess pain and mobility impairment need to be developed. There appears to be a mismatch between radiographic and clinical examination findings. Clarke and Bennett\textsuperscript{1} reported data that suggest 34\% of joints assumed to be painful on manipulation during a clinical examination did not have any signs of radiographic OA. In another study, there was only moderate overlap between the variables, “radiographic DJD” and “pain on manipulation”; 55 joints had radiographic signs of OA (as defined radiographically in dogs), but only 18 (33\%) were painful on manipulation.\textsuperscript{2} Pain is difficult to evaluate in cats but further work is needed to confirm this. Of the 55 joints assessed as painful, 37 had no radiographic signs of OA. Six of these had other pathology (periarticular soft tissue mineralization or meniscal calcification), and it may be that such pathology can be associated with pain. Histologic studies evaluating this mismatch (painful joints with no obvious radiographic findings) are required to shed further light on whether or not this is a real phenomenon or simply because of misinterpretation of clinical examination findings.

In all reports of feline immune-mediated joint disease, cats are reportedly painful, stiff, and reluctant to be manipulated, suggesting that immune-mediated DJD can be associated with pain in the cat,\textsuperscript{46–49} but the degree of discomfort has not been evaluated further. Of 7 reported cases of feline lumbosacral disease, 5 cats had clinical signs of pain, hyperesthesia, or reduced activity associated with lumbosacral DJD.\textsuperscript{58,59}

\textit{Treatment Efficacy for Suspected DJD-Associated Chronic Pain}

Currently, there is only evidence for NSAIDs having a beneficial effect (pain alleviating and mobility enhancing) in painful feline nonimmune-mediated DJD.\textsuperscript{1,2,57,60} Treatment of an infectious cause of feline DJD has been associated with a resolution of pain,\textsuperscript{51,52} as has treatment of immune-mediated joint disease with immunosuppressive drugs.\textsuperscript{46–49} The level of evidence for a pain-alleviating effect of treatments varies from objective measures in clinical cases,\textsuperscript{2} to open-label studies with nonvalidated subjective assessments in clinical cases,\textsuperscript{1,57,60} to subjective reporting on clinical cases.\textsuperscript{46–49,51,52} Other treatments may be effective but have not been evaluated. Part of the reason for the lack of evidence-based information about treatment of feline DJD-associated pain is the lack of validated outcome measures, and partly because of a lack of understanding of how to diagnose the disease, and lack of understanding about its causes.

There is concern about use of NSAIDs in cats, especially on a chronic basis, although meloxicam has recently been approved in the European Union for long-term treatment of feline musculoskeletal pain. This concern is generally centered around the perception that NSAIDs are metabolized more slowly in cats than dogs. Most NSAIDs are cleared from the body through hepatic metabolism (often primarily glucuronidation) and then biliary and/or renal excretion of the resultant polar metabolites. Given the known propensity for reduced glucuronidation of drugs in cats compared with other species,\textsuperscript{61–67} differences in NSAID disposition between cats and other species might be expected. Aspirin, acetaminophen, and carprofen have relatively prolonged elimination half-lives in cats compared with dogs, most likely because of slower drug clearance via glucuronidation. In contrast, similar or even reduced drug elimination half-lives are observed in cats, compared with dogs, for drugs cleared by oxidative enzymes, including piroxicam and meloxicam. There are several exceptions, including flunixin and ketoprofen, both of which are known undergo glucuronidation in dogs\textsuperscript{68,69} and yet are not eliminated more slowly in cats. Presence of alternate metabolic and nonmetabolic pathways for drug elimination may compensate for slowed glucuronidation of NSAIDs in the cat.

Chronic painful disease demands repeated administration of analgesic drugs, and there is little current information on the pharmacokinetic (PK) and toxic effects of repeated administration of NSAIDs in cats. In cats administered flunixin 1 mg/kg orally every 24 hours for 7 days, no drug accumulation occurred.\textsuperscript{70} In fact, the maximal concentration and the \textit{AUC}_{0–24} were less on day 7 than on day 1, suggesting that the drug was eliminated more rapidly. Serum thromboxane concentrations were <75\% of baseline up to 7 hours after administering flunixin on day 1, but for only 2 hours on day 7. The alanine aminotransferase (ALT) increased from 11.4 to 21.3 IU/L, suggesting that liver toxicity may be a problem with chronic administration. The only other report evaluating repeated dosing of a NSAID in cats evaluated piroxicam, and compared the PK values when piroxicam (0.3 mg/kg orally every 24 hours) was administered for 10 days either alone or with cimetidine. Compared with day 1, piroxicam half-life was higher on day 10 (11 versus 14 hours) as was \textit{C}_{max}, and \textit{T}_{max} was shorter on day 10 in cats administered piroxicam alone. Administration of cimetidine with piroxicam did not make any clinically significant differences to measured PK variables. Four of 7 cats in
the piroxicam group and 2 of 7 cats in the piroxicam + cimetidine group had evidence of gastric erosions at 10 days. Efficacy of piroxicam or flunixin has not been evaluated for chronic musculoskeletal pain in the cat.

There have been no reports of total joint replacement in the cat, and only sporadic reports of joint arthrodesis, with 1 reporting arthrodesis for painful DJD. As noted earlier, arthroscopic removal of osteochondral fragments from an elbow with DJD, suspected caused by a fragmented coronoid process, resulted in subjective resolution of lameness. There are also a few reports of clinical signs of pain associated with lumbosacral DJD being abolished after surgical decompression.

An often posed question is “do cats with musculoskeletal pain need to be treated?” Their small size and the fact that they are not generally expected to perform activities or go for walks like dogs has led to suggestions that they are able to adapt their lifestyles well and “cope” with any discomfort. This question will be better answered once more has been done to evaluate actual and perceived changes in cats’ activity and quality of life of cat treated for chronic musculoskeletal pain.

What Outcome Measures are Available to Evaluate Painful Feline DJD?

Pain associated with joint disease can result in impaired or decreased limb use. Cats have been the subjects in experimental locomotion studies that have focused on the organization of muscle reflexes during locomotion, during posturing, equilibrium and body segment movement, and on joint mechanics. Systems most commonly used in dogs to measure kinetic variables (force plates) cannot be easily used in cats, although miniature triaxial force plates have been used in the standing cat, and force plates have been used to measure limb loading in standing cats as part of studies evaluating cruciate ligament deficient experimental cats. Recently, use of pressure sensing walkway devices have been described for assessment of acute limb pain in cats after onychectomy and also for defining normal kinetic variables in cats. The same system was not useful in assessing pain relief because of the multiple limbs involved in clinical cases with DJD (unpublished data); however, further work is needed.

Pain from knee and hip joints in humans can often result in decreased mobility and decreased distance moved. This decreased distance moved appears to be both total daily distance, and also distance moved in a single effort. Likewise, in dogs and cats, OA is also assumed to impair mobility and daily distance moved. Evaluation of a small accelerometer found that activity counts generated by the accelerometer correlated well with objectively measured activity in cats. The same device was subsequently used in client-owned cats in the home environment and appeared promising as an objective measure of total distance moved. Assuming that painful DJD results in decreased total distance moved in cats, then such measures may be a valid means of both assessing treatments for DJD-associated pain, and also for evaluating other assessment methods, such as owner-based assessments; however, there is much to learn about the data generated by accelerometers. Any movement—forced or spontaneous—will create “activity counts,” and disease and treatment may have different effects on activity at different times of the day. External influences in the home (e.g., visitors, new pets, other activity) may well significantly affect activity of cats being evaluated.

Subjective assessment of cats with musculoskeletal pain has been described but subsequent studies have highlighted the fact that clinical signs do not generally include lameness or gait disturbances. Instead, it appears that altered behavior in the home environment may be the best way to assess musculoskeletal pain—lack of socializing, lack of jumping, decreased height of jumping, reduced grooming, hiding, and grumpiness; however, little is known about what behaviors should be evaluated, and there are currently no validated owner-based subjective assessment systems for use in cats with chronic DJD-associated pain. Generation of a valid questionnaire is a time-consuming and expensive process, consisting of item generation, readability testing of the instrument, reliability testing of the instrument (test–retest) and finally testing the instrument for validity and sensitivity by comparing outcomes from the instrument to objectively measured variables. Indeed, such systems are only beginning to be developed for dogs despite the substantial knowledge base for DJD in dogs. Despite the difficulties involved, understanding which treatments may be effective in chronic musculoskeletal pain in cats will advance little until there are validated outcomes measures applicable to clinical cases.

Models of DJD Pain in Cats

Clearly, there is a need for a model of DJD-associated pain and mobility impairment in the cat. Any model should be histologically similar to the naturally occurring disease and have pain as a feature. These requirements have only fairly recently been identified as being important in DJD pain research in the basic sciences. Further, it would be ideal if the model of DJD used a clinically relevant joint. Currently, there is only 1 feline model of chronic joint OA. In this cruciate transection model, ground reaction forces and limb kinematics recovered to near presurgical patterns over the 1-year-period postoperatively, despite progression of radiographic OA. It has been suggested that despite substantial progression of
signs of OA over a 5-year period, the joints did not seem to be causing pain.\textsuperscript{56} Urate crystal induced synovitis has been studied as an acute model of feline joint pain.\textsuperscript{93,94} After injection of 20 mg sodium urate crystals into the stifle joint, signs of lameness occurred within ~1 hour, reaching a maximum after 2–4 hours, lasting for 6–8 hours, and limb use then returned to normal over the next several days. That sodium urate injection is associated with pain was demonstrated by a decreased lameness after administration of morphine\textsuperscript{93} or meloxicam.\textsuperscript{94} This model may well reflect changes seen in the synovium in naturally occurring disease, but this has not been evaluated.

\textit{Future Directions}

Of immediate interest would be information on how prevalent radiographic DJD is in a randomly selected cat population that is representative of the larger cat population, and whether radiographic DJD is obviously associated with any particular characteristics, e.g., age, breed, sex, indoor/outdoor status, etc. Likewise the relationship between radiographic appearance and morphologic features, particularly histologic characteristics, requires investigation to better understand the mismatch between radiographic and clinical examination findings. As this data is evaluated, hypotheses need to be formulated about possible causes of DJD in different joints, and careful observation and collection of general health status data, in addition to comparisons with other species, will help in guiding investigations. Determination of the causes or predisposing factors will help guide treatment, and in this respect, there is a very real need for validated subjective and objective assessment systems for the measurement of chronic DJD-associated pain in the cat. Development of a feline model of chronic DJD associated pain will help speed the development and evaluation of candidate pain-alleviating compounds and treatments.

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