

## A Retrospective Study of 40 Dogs With Polyarthrititis

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**Objective**—To characterize the epidemiologic, clinical, laboratory, and radiographic findings from dogs with polyarthrititis (PA).

**Study Design**—Retrospective clinical study.

**Sample Population**—Forty dogs.

**Methods**—Medical records of 40 dogs with a diagnosis of PA were reviewed. Retrieved data included breed, age at admission, sex, weight, clinical signs, and the results of synovial fluid analysis, complete blood count, serum chemistry profile, urinalysis, serologic screening tests for infectious diseases, and radiographic examination of affected joints.

**Results**—The incidence of PA was 0.37%. Twenty-nine breeds were represented; 16 dogs were male, and 24 were female. Mean body weight was  $20.1 \pm 15$  kg. The mean age at admission was  $5.6 \pm 4$  years. Eighty percent of dogs with PA had difficulty or reluctance walking, 35% were lame, 33% had spontaneous vocalization without any obvious reason, 20% had exercise intolerance, 18% were febrile, and 7.5% had an inability to rise or move. Joint pain was identified in 40% of dogs. Synovial fluid color varied from colorless (36%) to yellow-tinged (36%) or hemorrhagic (28%). Synovial fluid mean cell count varied from 10 cells ( $400\times$ ) to 50 cells ( $1,000\times$ ). Leukocytosis occurred in 59% of the dogs and was more frequently identified in dogs with very severe synovial inflammation. Thirty-one percent of affected dogs were anemic. Serum biochemical profiles were considered abnormal in 13% of the dogs. Joint radiography did not identify erosive arthritis.

**Conclusions**—PA is a common cause of locomotor abnormalities in dogs; however, true lameness and articular pain are not common clinical findings in dogs with PA.

**Clinical Relevance**—PA should be considered in the differential diagnosis for all dogs with difficulty walking.

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**L**OCOMOTOR problems are common in the dog. Although the cause of lameness or reluctance to walk is often identified, in some dogs, the origin of the signs remains unclear. Polyarthrititis (PA) should be considered as a potential diagnosis in these instances.

Reports of PA are sparse and often involve isolated cases.<sup>1-9</sup> PA is an inflammatory arthropathy involving more than one joint<sup>10</sup> and is considered an uncommon condition in dogs. Reported clinical signs are variable and include reluctance to walk, spontaneous vocalization, stiffness, lameness, and inability to stand or walk. Sometimes systemic signs such as pyrexia, inappetence, anorexia, and weight loss may be the only signs.<sup>1-13</sup> Depending on their origin, polyarthritides can be classified as infectious, crystal induced, or immune mediated.<sup>11,12</sup> Infectious arthritides may be viral, bacterial, mycoplasmal, protozoal, or fungal.<sup>12</sup> Crystal-induced arthritides are caused by the deposition of sodium urate crystals (gout) or calcium pyrophosphate dihydrate crystals (pseudogout) into the joints.<sup>7,12</sup> Immune-mediated arthritides are the result of the deposition and phagocytosis of immune complexes and release of damaging lysosomal enzymes within the synovial membrane (type III hypersensitiv-

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ity).<sup>11,12</sup> They include autoimmune arthritides (systemic lupus erythematosus, rheumatoid arthritis), arthritides associated with infections remote from the joints (reactive arthritides), with gastrointestinal or hepatic disease, or with neoplasia, drug-induced arthritides, and idiopathic arthritides.<sup>12</sup>

Idiopathic PA is the most common form of PA.<sup>11</sup> Young adults of large breeds are, reportedly, more affected.<sup>11,12</sup> The incidence of PA is probably underestimated because of the lack of clinical awareness and understanding. Diagnosis of PA is based on a significant increase of synovial fluid cell count in different joints. Synovial fluid cell count of inflammatory joints can be reliably determined or estimated by direct smears, hemocytometer, or Coulter counter.<sup>14-19</sup> Because a large case series of PA in dogs has not been reported, the purpose of our study was to retrospectively characterize the epidemiologic, clinical, laboratory, and radiographic findings of dogs diagnosed with PA.

## MATERIALS AND METHODS

The medical records of 40 dogs diagnosed and treated for PA between July 1998 and July 2000 were reviewed. Inclusion criteria were based on history and clinical signs and included documentation by the owner or referring veterinarian of spontaneous vocalization, pyrexia or systemic signs of unknown origin, exercise intolerance, chronic lameness, or difficulty walking without obvious signs of orthopedic or neurologic abnormalities. Spontaneous vocalization was defined as a dog that moaned at home or in the receiving room without obvious cause. Walking difficulty was defined as discomfort walking without obvious lameness of any limb. Retrieved data included breed, age at admission, sex, weight, clinical signs (especially articular pain) and the results of synovial fluid analysis, complete blood count, serum chemistry profile, urinalysis, serologic screening tests for infectious diseases, and radiographic examination of affected joints.

Synovial fluid was obtained by arthrocentesis of at least 3 joints (generally, both carpi and one stifle, unless another joint was painful on manipulation) in each dog. Arthrocentesis was performed in most patients without premedication or anesthesia. Joints were clipped and prepared aseptically, and synovial fluid was collected in a 2-mL syringe through a 23-gauge needle. Synovial fluid examination was systematically performed by 2 of the authors (D.J., L.C.). Color observed at sample collection was characterized as colorless, hemorrhagic, or yellowish. Viscosity was evaluated by

slowly expressing the fluid from the needle and was considered normal if the synovial fluid formed a long strand (>2.5 cm) before separating from the needle.<sup>19</sup>

Direct cytologic examination of May-Grunwald-Giemsa stained smears of the synovial fluid was performed immediately after sample collection, and the number of cells per field at 400× or 1,000× magnification (used if the cell number was too high at 400×) was recorded. Ten fields were examined in the body of each smear, and the mean cell count was recorded. The mean percentage (based on 10 fields) of polymorphonuclear (PMN) and mononuclear cells (lymphocytes and large mononuclear cells with phagocytic potential) was calculated. The synovial fluid was considered normal if no more than 2 cells/field at 400× magnification were noted and its differential included less than 12% PMN cells.<sup>16,17,19,20</sup> The mean cell count of the 3 sampled joints was calculated and was used to characterize the degree of synovial inflammation for each dog. Synovial fluid inflammation was graded as moderate (10 to 20 cells/field at 400×), severe (20 to 50 cells), or very severe (>50 cells). Microbial culture of synovial fluid was not performed.

Our normal range for white blood cell (WBC) count is 6 to  $13 \times 10^9/L$  (Laboratoire Vébiotel, Arcueil, France), so leukocytosis was defined in 4 categories: mild leukocytosis (13,000 to 20,000 WBC/ $\mu L$ ), moderate (20,000 to 30,000/ $\mu L$ ), severe (30,000 to 40,000/ $\mu L$ ), and very severe (>40,000/ $\mu L$ ). Anemia was defined as a hemoglobin concentration less than 12 g/L. Serum chemistry profile included measurement of blood urea nitrogen (BUN), creatinine, total protein, albumin, alanine aminotransferase (ALT), and alkaline phosphate concentrations. Antinuclear antibody (ANA) and rheumatoid factor (RF) titers were performed. The indirect ANA immunofluorescence test was considered negative if no antibodies were detected at dilutions of more than 1/40 (Laboratoire Vébiotel, Arcueil, France). Rheumatoid factor was detected using a latex test (Canine Rheumatoid Factor Test Kit; Synbiotics Europe, Lyon, France). Urinary strips were used to screen for proteinuria. If positive (protein >0.3 g/L), urine protein/creatinine ratios were calculated; ratios less than 1 were considered normal. Dogs from endemic zones for leishmaniasis, ehrlichiosis, or borreliosis were tested serologically.

Radiography (dorsoventral and lateral projections) of the most affected joint (based on synovial cytology results) was performed in each dog to rule out erosive arthritis.

### Statistical Analysis

The breed incidence in our study population was compared with our overall hospital population by using Fisher's exact test to determine whether a breed was at risk for PA. Statistical significance was set at  $P < .05$ .

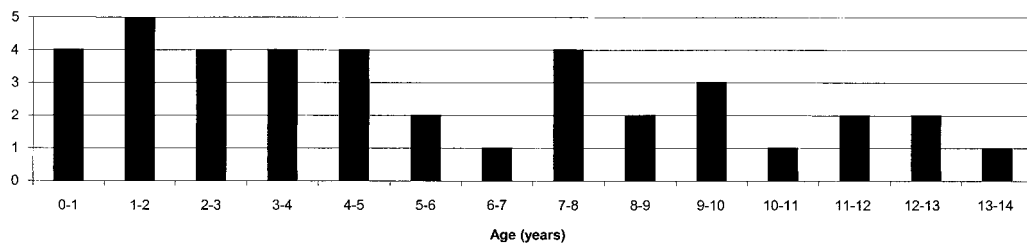


Fig 1. Age distribution of 40 dogs with polyarthritis.

## RESULTS

Arthrocentesis was performed in 131 dogs; 40 (31%) were diagnosed with PA. The incidence of PA in our hospital was 0.37% (40 of 10,811 dogs).

Twenty-nine breeds of dogs were represented, with the cocker spaniel most commonly affected (4 dogs) and seemingly at risk for PA (Fisher's exact test,  $P = .0085$ ). Sixteen dogs were male (14 intact, 2 neutered), and 24 were female (19 intact, 5 neutered). Female dogs were more frequently affected than male dogs. The mean age at admission was  $5.6 \pm 4$  years (range, 8 months to 13 years; Fig 1); young and middle-aged dogs were overrepresented (70% were  $<8$  years of age). The mean body weight was  $20.1 \pm 15$  kg (range, 2.5 to 80 kg; Fig 2); small- and medium-breed dogs were overrepresented.

There were clinical signs that related to PA: 32 dogs (80%) were reluctant to walk or had difficulties or stiffness when walking; 14 (35%) had lameness; 13 (33%) had spontaneous vocalization; 8 (20%) had exercise intolerance; 7 (18%) were febrile; and 3 (7.5%) were unable to rise or walk. Ten dogs (25%) had only subtle signs of lameness or difficulties walking. Articular pain (both carpal and stifle joints) was detected in 16 dogs by joint manipulation (flexion, extension, collateral ligaments tests). There was pain in the tarsus in 5 of these dogs, and there was pain in the elbow in 2 dogs. Hyperthermia, anorexia, prostration, exercise intolerance, or weight loss were the only clinical signs in 4 dogs (10%).

Synovial fluid color was recorded in 12 dogs (36

joints) and varied from colorless (13 joints) to yellow-tinged or cloudy (13 joints) or hemorrhagic (10 joints). In 6 dogs, the synovial fluid color varied between joints in the same individual. Viscosity was considered normal in 19 joints and decreased in 17 joints. Synovial fluid cell count ranged from 10 cells ( $400\times$ ) to 50 cells ( $1,000\times$ ). Synovial inflammation was classified as moderate in 17 dogs (42.5%), severe in 12 (30%), and very severe in 11 (27.5%). PMNs were the predominant cell type in 24 dogs, whereas mononuclear cells were the predominant cell type in 11 dogs. A mixed pleocytosis (50% PMNs, 50% mononuclear cells) characterized the distribution in 5 dogs, with neutrophils being the predominant cell type. Thus, neutrophils were the predominant cell type in 29 dogs (72.5%). In dogs with predominantly mononuclear inflammation, the degree of synovial fluid inflammation was classified as moderate. In 33 dogs, synovial fluid cell count showed  $>12\%$  of PMN cells (82.5%). When tarsal and elbow joints were affected, inflammatory changes observed cytologically were identical to those observed in the carpal or stifle joints.

Leukocytosis occurred in 17 of 29 dogs (59%) and anemia occurred in 8 (31%). The intensity of leukocytosis was not dependent on the degree of synovial fluid inflammation; however, leukocytosis was more frequent in dogs with severe or very severe synovial inflammation (Table 1). The results of serum biochemical profiles were considered normal in 33 of 38 dogs (87%). Abnormal serum chemistry results included elevated alkaline phosphatase ( $n = 3$ ) and ALT ( $n =$

Fig 2. Weight distribution of 40 dogs with polyarthritis.

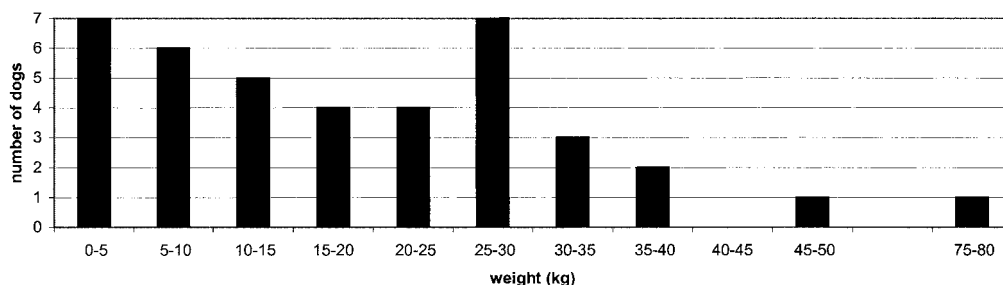


Table 1. Relationship Between Degree of Synovial Inflammation and the Intensity of Peripheral Leukocytosis in 29 Dogs With Polyarthritis

Synovial Fluid Inflammation		Intensity of Peripheral Leukocytosis				
Intensity (Cells/Field; 400×)	*No. of Dogs	Normal (6-13,000 cells/ $\mu$ L)	Mild (13-20,000 cells/ $\mu$ L)	Moderate (20-30,000 cells/ $\mu$ L)	Marked (30-40,000 cells/ $\mu$ L)	Very Marked (>40,000 cells/ $\mu$ L)
Moderate (10-20)	11	7	3	0	1	0
Severe (20-50)	10	3	4	2	1	0
Very severe (>50)	8	2	4	1	0	1

\* Number of dogs in which peripheral leucocytosis was measured.

1) concentrations, hypoalbuminemia (n = 2), hypoproteinemia (n = 1), hyperproteinemia (n = 1), hyperuremia (n = 1), and hypercreatininemia (n = 1). Proteinuria (protein-creatinine ratio >1) occurred in 4 (10%) dogs. Results of antinuclear antibody testing and rheumatoid factor titers were normal or negative in 34 of 38 dogs (89%) and 33 of 36 dogs (92%), respectively. Serologic testing was performed for borreliosis (21 dogs), ehrlichiosis (9 dogs), and leishmaniasis (7 dogs). Two dogs had elevated titers for *Borrelia* spp, 1 for *Ehrlichia* spp, and 2 for *Leishmania* spp. Their clinical signs did not differ from the other dogs. Examination of joint radiographs did not show erosive arthritis in any of the dogs.

## DISCUSSION

The aim of our study was to characterize the epidemiologic, clinical, laboratory, and radiographic findings of dogs diagnosed with PA. We suspected PA to be underdiagnosed and its epidemiology and clinical presentation to be incompletely described. The incidence of PA is unknown. In our referral clinic, the incidence of PA was 0.37%. In the 2-year study period, 31% of dogs in which arthrocentesis was performed for evaluation of an articular problem were diagnosed with PA. It appears that PA is not an uncommon condition.

Epidemiologic data from a large case series of dogs with PA has previously not been reported.<sup>1-12</sup> Young adult large-breed dogs are considered to be most commonly affected with PA.<sup>11-12</sup> Rheumatoid arthritis affects predominantly middle-aged dogs of small and medium breeds,<sup>11-12</sup> and German Shepherd dogs are the breed most commonly affected with systemic lupus erythematosus (SLE).<sup>21</sup> By contrast, our dogs with PA were predominantly young to middle-aged dogs of small and medium breeds. Cocker spaniels (medium-breed dogs) were seemingly at greater risk

for PA. A sex predisposition has not been reported in dogs with PA except for SLE (68% males).<sup>11,12,21</sup> In our study, females were more frequently affected (female to male ratio = 1.5).

Published clinical signs more commonly described for dogs with PA are lameness, articular pain, and hyperthermia. Subtle or nonspecific signs such as lethargy or weight loss are rarely reported.<sup>1-12</sup> In our study, the most frequent owner complaint was difficulty in walking, and in 25% of our dogs, it was the only clinical sign. Articular pain was absent in most dogs, and true lameness occurred in only one third of the dogs. Hyperthermia only occurred in 7 dogs (18%). Thus, in our affected population, the clinical presentation of PA often does not include lameness, articular pain, or hyperthermia. Indeed, the clinical signs that we detected were subtler than previously described and often limited to slight difficulty in walking. Such subtle signs could be encountered in a number of other diseases. Based on these signs, differential diagnosis should include osteoarthritis, muscle disorders, spinal disorders such as low-grade intervertebral disk disease, or medullary disorders such as meningitis, and PA. Systemic signs were the only clinical signs in 10% of our dogs, so PA should be included in the differential diagnosis list when a dog is admitted with systemic signs of unknown origin.

The carpus, stifle, and hock are reported to be the most commonly affected joints in immune-mediated PA,<sup>11,12</sup> whereas large proximal joints (hip, shoulder) are more commonly affected in infectious PA.<sup>11</sup> In our study, the carpus and stifle were the most commonly aspirated joints and were always affected. Based on our experience, if noninfectious PA is suspected, we recommend arthrocentesis of the carpi, stifles, or hocks.

Synovial fluid color, turbidity, and viscosity can be

easily assessed at the time of collection or when the sample is expelled onto a glass slide.<sup>19</sup> Reportedly, synovial fluid from inflammatory joints shows variable discoloration and decreased viscosity.<sup>11,12,17,19</sup> Discoloration may be because of pleocytosis; decrease in viscosity is caused by a deficiency of polymerized hyaluronic acid or a dilution from excess serum.<sup>11</sup> Synovial fluid was noted to be either colorless, yellow-tinged, hemorrhagic, aqueous, or viscous in our dogs; thus, normal synovial fluid color or viscosity cannot rule out PA.

A total white cell count and a differential cell count are essential in synovial fluid analysis.<sup>18</sup> Three techniques are available for counting white cells in synovial fluid: hemocytometer, electronic Coulter counter, and direct smears.<sup>18</sup> The laboratory test selected for analysis depends on the volume of synovial fluid obtained.<sup>14,16,17,19</sup> The size of the animal, the joint affected, and presence or absence of joint effusion determine the volume obtained and can vary from a few drops to more than 1 mL.<sup>19</sup> Direct smear examination is feasible even when a very small volume is collected, and it is accepted that a reliable estimate of synovial white cell count can be obtained by microscopic examination of a direct smear.<sup>14-17,19</sup> Synovial inflammation can be classified by cell count,<sup>17-19</sup> and it has been reported that the accuracy of the diagnoses of 4 clinicians for inflammatory joint disease using direct smears was 88%.<sup>18</sup> In this same report, the sensitivity and specificity of diagnosis were, respectively, 84% and 92%.<sup>18</sup> Therefore, we considered use of direct smears to be an accurate, sensitive, and specific method to confirm a diagnosis of PA. This would not hold true for degenerative arthropathies where diagnostic accuracy based on direct smears is only 30% (sensitivity, 25%; specificity, 40%).<sup>18</sup> The main practical advantage of using direct smears are the small volume of synovial fluid needed and the immediate availability of results. Other tests such as total nucleated cell counts (by hemocytometer or electronic Coulter counter), mucin clot test, and total protein content of the synovial fluid are valuable but not necessary to reliably diagnose PA.<sup>19</sup> Collection of a larger volume of fluid, which is not always possible, is needed to perform these tests.

The body of a normal synovial fluid smear contains about 2 cells/field at 400× magnification.<sup>16,19</sup> Our mean cell counts were always much higher than normal. In normal synovial fluid, neutrophils, when present, are in small number; usually representing less

than 12% (frequently <5%) of nucleated cells,<sup>16,17,19</sup> and large mononuclear cells and lymphocytes account for the remainder of the nucleated cells. Neutrophils are commonly the predominant cell type in PA,<sup>11,12</sup> and our results confirm this observation. Reportedly, when dogs with PA receive corticosteroids drugs, nucleated cell count decreases and the mononuclear-PMN ratio tends to increase.<sup>11</sup> Dogs with difficulty walking are often administered corticosteroid drugs before referral. Thus, the synovial fluid samples with predominantly mononuclear cells may correspond to dogs that were administered corticosteroids before our evaluation; however, we were unable to verify this from our records. Even if mononuclear cells were the predominant type, pleocytosis as seen in our results (>10 cells at 400×) corresponds to an abnormal inflammatory response and not to degenerative arthropathy, where total nucleated cell count is usually normal to slightly increased and mononuclear cells are the predominant cell type with PMNs low in number or absent.<sup>17,19,20</sup>

When septic arthritis is suspected, joint fluid should be cultured for microorganisms; however, failure to isolate microorganisms is common.<sup>17,19</sup> Infectious arthritides in dogs are uncommon, usually of bacterial origin, and monoarticular and result from external contamination of the joint.<sup>12,19,20</sup> Infectious PA is rare and may occur after hematogenous spread of organisms. It has been described with omphalophlebitis in neonates and bacterial endocarditis in mature animals.<sup>12,19,20</sup> Clinical signs characteristic of such diseases (eg, fever combined with cardiac murmur) should be apparent on physical examination.<sup>19</sup> In a septic joint, synovial fluid often contains numerous toxic neutrophils with pyknotic nuclei and ruptured or degranulated neutrophils, but microorganisms are infrequently observed.<sup>19,20</sup> Presence of PMNs in synovial fluid does not confirm sepsis.<sup>11,12,19</sup> In our study, none of the dogs was suspected of having septic PA based on these criteria. Synovial fluid cultures were not performed. Rapid positive clinical response to immunosuppressive drugs added support to our suspicion that there were no cases of septic PA included in our study.

CBC results often indicate mild to marked leukocytosis in the acute phases of PA, although the leukogram may be normal.<sup>11</sup> Leukopenia is a rare finding except in SLE (20% to 28% of affected dogs are leukopenic).<sup>11,21</sup> Confirming previous reports, our study showed that leukocytosis is a common abnor-

mality, but not an absolute finding in PA.<sup>11</sup> We showed that leukocytosis is more frequent when the degree of synovial fluid inflammation is severe; however, it is difficult to know whether this leukocytosis is directly related to the PA or to the presence of another inflammatory focus.

Anemia is reported infrequently in most nonerosive arthritides, with the exception of SLE (20% to 35%).<sup>11</sup> Anemia was more frequently encountered in our study than previously described, although SLE was not confirmed in any of the dogs. This anemia was probably secondary to chronic inflammation. Generally, results of serum biochemical profiles are normal; variably decreased albumin and absolute or relative increased serum globulin concentrations may be found, and mild, nonspecific increases in liver enzyme concentrations have also been reported.<sup>11</sup> Results of blood tests that reflect multisystemic involvement suggest canine SLE or an infectious process.<sup>11</sup> Our results were similar, and seemingly routine biochemical profiles rarely give specific indications of the underlying cause of PA.

Diagnosis of canine SLE or rheumatoid arthritis requires that a number of criteria should be satisfied according to the American Rheumatoid Association (ARA) and the French-language literature.<sup>10,11,21-23</sup> In our dogs with positive ANA titer and positive RF test, a definitive diagnosis of canine SLE or rheumatoid arthritis was not made because in each case too few of the ARA or French criteria were satisfied. Any chronic disease of infectious or noninfectious origin, associated with persistent antigen exposure and immune complex production, could potentially result in low positive titers of ANA or RF.<sup>10-12,21</sup>

Cases of PA associated with ehrlichiosis, borreliosis, or leishmaniasis have been reported.<sup>1,4,9</sup> In our study, 5 dogs (12.5%) had positive serologic tests for these diseases. These dogs did not have specific signs, and their clinical signs did not differ from the other dogs. Cases of PA associated with ehrlichiosis, borreliosis, or leishmaniasis are infrequent, but these diseases need to be considered, especially when dogs come from an endemic zone.

Joint radiographs can be used to distinguish erosive from nonerosive PA. The most significant and characteristic radiographic feature of erosive arthritis is the presence of erosions involving the articular surface or loss of trabecular bone density in the epiphyses.<sup>11</sup> The destructive lesions are progressive and occur in the subchondral or juxta-articular bone and are observed

as poorly demarcated or discrete radiolucent foci of various sizes.<sup>11</sup> Based on these criteria, erosive PA was not identified in any of our dogs, suggesting that nonerosive PA occurs more frequently than erosive PA.

Clearly investigations other than laboratory tests and joint radiographs are necessary to further delineate the causes of PA. Inflammatory or infectious sites remote from the joints, chronic hepatic or gastrointestinal disease, neoplasia, vaccine, or drug-induced reactions must all be investigated as potential causes whenever feasible.<sup>12</sup>

Based on our clinical experience, we conclude that PA is a common cause of locomotor problems in dogs without obvious trauma or neurologic deficits, particularly small and medium breeds less than 8 years of age. Clinical signs are often more subtle in PA than what has been previously described. PA should be considered in the differential diagnosis for any dog with difficulty walking, not just those dogs that have articular pain, articular effusion, and hyperthermia. In our experience, cytologic examination of a direct synovial fluid smear is a quick and accurate method to confirm PA.

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