Development of a model to induce transient synovitis and lameness in the hip joint of dogs

Elham A. Hassan BVSc., MVSc., PhD  
Nicolaas E. Lambrechts BVSc., MMEDVET  
George E. Moore DVM, PhD  
Hsin-Yi Weng BVM, MPH, PhD  
Hock Gan Heng DVM, MVS, MS  
Gert J. Breur DVM, PhD

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From the Department of Surgery, Anesthesiology and Radiology, Faculty of Veterinary Medicine, Cairo University, Cairo, Egypt; PO-12211 (Hassan); and the Departments of Veterinary Clinical Sciences (Lambrechts, Breur) and Comparative Pathobiology (Moore, Weng), College of Veterinary Medicine, Purdue University, West Lafayette, IN 47907. Dr. Lambrechts’ present address is Department of Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Fort Collins, CO 80523.

Address correspondence to Dr. Lambrechts (nic.lambrechts@colostate.edu).

OBJECTIVE  
To develop a model of hip joint synovitis on the basis of intra-articular injection of a sodium urate suspension in dogs and to characterize associated gait changes.

ANIMALS  
6 healthy adult dogs.

PROCEDURES  
Each dog was sedated, and synovitis was induced by injection of 1 mL of a sodium urate suspension (20 mg/mL) into the right hip joint under ultrasonographic guidance. Observational and instrumented gait analyses to determine temporospatial, kinetic, and kinematic variables were performed prior to and 4, 8, and 24 hours after sedation and synovitis induction.

RESULTS  
Injection of a sodium urate suspension into the hip joint of healthy dogs resulted in lameness of the ipsilateral pelvic limb as determined by observational and instrumented gait analyses. For all dogs, lameness was clinically detectable within 1.5 to 2 hours after injection, reached its maximum intensity at 4 hours after injection, and had subsided by 24 hours after injection.

CONCLUSIONS AND CLINICAL RELEVANCE  
Results indicated that injection of a sodium urate suspension into the hip joint of healthy dogs reliably induced synovitis and signs of pain and lameness in the ipsilateral pelvic limb that lasted 24 hours. This model can be used in conjunction with instrumented gait analysis to provide information on gait changes associated with hip joint disease and might be useful for evaluating the efficacy of analgesics or other interventions for the treatment of hip joint disease in dogs. (Am J Vet Res 2015;76:869–876)

Hip joint disease is the most commonly diagnosed joint disorder of dogs. Results of a study that involved almost 500,000 dogs examined at 16 veterinary teaching hospitals in the United States from 1980 through 1989 indicated that hip joint disease accounted for approximately 40% of all joint-related diseases diagnosed. Joint disease can result in loss of joint function and secondary degenerative changes and is associated with signs of pain.

Examination of hip joint function often includes evaluation of an individual’s gait by observational or instrumented gait analysis. Instrumented gait analysis is an objective method for analyzing gait and involves the use of sophisticated equipment to measure both motion (kinematic analysis) and force (kinetic analysis). Although both kinematic and kinetic analyses have been used to evaluate dogs with hip joint disorders, they have not, to our knowledge, been used simultaneously. A limitation in many of those studies is that gait alterations for dogs with hip joint disease of varying severity were determined before and after some type of intervention or treatment but not before the disease developed. Also, a reliable model for hip joint disease and arthritis in dogs has not been developed and described. Consequently, the effect of pain on hip joint function and pelvic limb gait has not been evaluated, and the unique characteristics of lameness associated with hip joint disease have yet to be determined with instrumented gait analysis. A standardized model for induction of hip joint disease in dogs will be a useful tool for evaluating associated signs of pain and the efficacy of medical and surgical treatments.

Intra-articular administration of sodium urate crystals induces acute reversible synovitis and signs of pain in dogs, analogous to gout in human patients. In dogs, intra-articular injection of sodium urate has been frequently used to induce synovitis of the stifle joint, generally to assess the efficacy of various analgesics. To our knowledge, this method has not been used to induce synovitis in the hip joint.

The primary goal of the study reported here was to evaluate intra-articular injection of a suspension of sodium urate crystals for the induction hip joint syno-
vitis in dogs. A secondary goal was to characterize the lameness and kinetic and kinematic gait changes associated with that model of hip joint synovitis. A reliable model for induction of hip joint synovitis in dogs will be a valuable tool for assessing the analgesic efficacy of both medical and surgical interventions for canine hip joint disease.

**Materials and Methods**

**Animals**

Six adult purpose-bred hound-type dogs (3 males and 3 females) with a median body weight of 25.7 kg (range, 21.5 to 29.9 kg) were used in the study. All dogs were considered healthy on the basis of results of a physical examination, CBC, and serum biochemical analysis and were routinely treated for intestinal and external parasites. Prior to study initiation, all dogs underwent complete orthopedic (including Barlow and Ortolani tests and 2-view pelvic radiographs to confirm physeal closure) and neurologic examinations. None of the dogs had evidence of orthopedic or neurologic disease. Each dog was acclimated to leash walking and the gait laboratory for 2 weeks prior to commencement of the study. All study procedures were approved by the Institutional Animal Care and Use Committee of Purdue University.

**Study design**

Each dog was sedated twice, 4 hours prior to baseline gait analysis and immediately before induction of synovitis in the right hip joint by injection of a sodium urate suspension with ultrasonographic guidance. Instrumented gait analysis followed by visual gait analysis and a physical examination were performed on each dog prior to and 4 hours after initial sedation to determine the effects of sedation on gait and at 4, 8, and 24 hours after induction of synovitis. Lameness was subjectively assessed at 1, 2, 3, 4, 8, and 24 hours after induction of synovitis on a scale of 0 to 5 as described. Each dog was acclimated to leash walking and the gait laboratory for 2 weeks prior to commencement of the study. All study procedures were approved by the Institutional Animal Care and Use Committee of Purdue University.

**Sedation protocol**

Each dog was sedated with dexmedetomidine (0.008 mg/kg, IV) twice, 4 hours prior to and immediately before induction of synovitis. Dogs were provided with supplemental oxygen via a face mask while sedated. Sedation was reversed with atipamezole (IV) in a volume equal to the volume of dexmedetomidine administered.

**Synovitis induction protocol**

A suspension of sodium urate was prepared by the addition of 500 mg of sodium urate to 25 mL of saline (0.9% NaCl) solution. The suspension was stirred with an automated stirrer overnight (approx 12 hours) and then vibrated for 60 minutes. The pH of the suspension was adjusted to within a range of 7.0 to 7.2 by the addition of hydrochloric acid or sodium hydroxide as necessary. The suspension was autoclaved for 10 minutes at 120°C, and the pH was rechecked and adjusted as necessary. The suspension was then divided into 1.5-mL aliquots and placed into sterile vials. The suspension was agitated by vortexing for 30 minutes before injection.

For each dog following the second sedation, 1 mL of the sodium urate suspension (20 mg/mL) was injected into the right hip joint with a 25-gauge spinal needle and ultrasonographic guidance through a lateral approach as described. The same radiologist injected the suspension into the hip joint of all dogs. Following injection of the sodium urate suspension, sedation was reversed and each dog was visually assessed for signs of pain every 30 minutes. Excessive signs of pain were defined as a change in behavior or vocalization. Rescue analgesia was provided to dogs with excessive signs of pain by administration of hydromorphone (0.05 mg/kg, IM) and carprofen (4.4 mg/kg, PO).

**Instrumented gait analysis**

Prior to each gait analysis session, each dog was weighed and 5 adhesive reflective markers were attached to the skin on the lateral aspect of each pelvic limb at the dorsalmost aspect of the iliac crest, greater trochanter, stifle joint, lateral tibial malleolus, and distal portion of the fifth metatarsal bone. Dogs were walked in a straight line at a comfortable velocity along a 10-m-long walkway with a centrally positioned PSW (2 × 0.5 m). The PSW was calibrated in accordance with the manufacturer’s specifications and recorded walking at a 60-Hz sampling frequency.

A digital video camera that was interfaced with the PSW was used to verify foot placement during each trial. A 2-D kinematic system with a video camera was positioned at a perpendicular angle above the PSW to capture video for determination of joint excursions and angles in the sagittal (x and y) plane as described. A trial was defined as a single pass over the walkway. A trial was considered valid if a dog walked in a straight line down the walkway without overt head movement or stopping, hesitating, or pacing and maintained a constant speed and completed at least 2 gait cycles (8 sequential paw strikes) across the PSW. For each instrumented gait analysis, at least 10 trials were recorded for each dog and the first 6 valid trials (3 each for the right and left pelvic limbs) were used for data analysis. The same handler walked all dogs during all trials.

**Statistical analysis**

Data obtained from the PSW were analyzed with designated software. For each of 6 valid trials, the digital video recording was reviewed to ascertain the sequence with which the 4 limbs struck the PSW and identify the corresponding frame numbers for each paw strike. These data were then used to determine
temporospatial and kinetic variables (PVF, %PVF, %WD, duration of the stance and swing phases, stride length, and stride velocity) for each limb. Custom-written codes for the 2-D kinematic system software were used to calculate joint angles and excursion and determine kinematic variables (peak flexion and extension and range of motion for the hip, stifle, and tarsal joints) for each limb for the same 6 valid trials. Symmetry indices (indicators of the difference between the limb of interest [right pelvic limb] and the contralateral limb) and intertrial variability (CV; an indication of variability between steps) were calculated for each variable and tabulated in spreadsheets.

Descriptive statistics were used to summarize temporospatial, kinetic, and kinematic variables and lameness scores over time. Lameness scores were compared over time with the Friedman test followed by a Dunn test with the Bonferroni adjustment for pairwise comparisons. Instrumented gait analysis data were analyzed with a mixed linear model that included time, side, and their interaction as fixed effects and dog as a random effect. All analyses were performed with commercially available statistical software, and values of \( P < 0.05 \) were considered significant.

Results

Baseline analyses

Prior to sedation, none of the dogs had a visual gait abnormality, and all dogs were assigned a lameness score of 0. All dogs were confirmed to be at a walk during the instrumented gait analysis on the basis of limb velocity (range, 0.93 to 1.14 m/s) and duty factor (ie, percentage of the stride when the limb is bearing weight). None of the instrumented gait variables differed significantly between the right and left pelvic limbs. The instrumented gait variables obtained prior to sedation did not differ significantly from those obtained 4 hours after sedation, which suggested that sedation had no effect on the variables assessed. Therefore, the baseline values obtained prior to sedation were used for all analyses.

<table>
<thead>
<tr>
<th>Lameness score ( * )</th>
<th>Baseline</th>
<th>1 h</th>
<th>2 h</th>
<th>3 h</th>
<th>4 h</th>
<th>8 h</th>
<th>24 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>6</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>1</td>
<td>4</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
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<td>1</td>
<td>2</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Median (range) 0.0 (0–0) 1.0 (0–1) 2.5 (1–5) 4.5 (3–5) ‡‡ 4.0 (3–5) ‡‡ 2.0 (1–5) 1.0 (0–1)

*Subjectively graded on the basis of visual assessment (0 = clinically normal, 1 = lameness barely detectable, 2 = mild lameness, 3 = moderate lameness, 4 = severe lameness with affected limb carried when trotting, and 5 = non-weight-bearing lameness with the affected limb continuously carried).

‡Value differs significantly \( P < 0.05 \) from that at baseline.

‡‡Value differs significantly \( P < 0.05 \) from that at 1 hour after synovitis induction.

Synovitis induction

Dispersion of the sodium urate suspension within the hip joint was ultrasonographically evident in all dogs. A small volume of the suspension was observed leaking along the needle outside of the joint cavity during injection in 2 dogs. This leaked volume was compensated by injecting an additional 0.2 to 0.3 mL of the suspension before the needle was removed from the joint. The initial injection of sodium urate did not induce a clinically evident response (ie, signs of pain and an increase in lameness score were not observed) in 2 dogs, and the synovitis induction protocol was repeated for those 2 dogs. None of the dogs required rescue analgesia following induction of synovitis.

The frequency distribution of lameness scores for the dogs before and after synovitis was induced were summarized (Table 1). Two hours after injection of the sodium urate suspension, 4 dogs developed muscle fasciculations in the area of the right hip joint and all 6 dogs had noticeably shifted their weight to the left pelvic limb. Lameness severity peaked for all dogs at 4 hours after induction of synovitis but had resolved by 24 hours after sodium urate injection.

Instrumented gait analysis

Temporospatial (limb velocity, stride length, and durations of gait cycle, stance phase, and swing phase), kinetic (PVF, %PVF, and %WD), and kinematic variables (peak extension and flexion and range of motion) for the right and left pelvic limbs and symmetry indices for those variables before and after synovitis was induced in the right hip joint were summarized (Table 2). The temporospatial and kinetic variables for the thoracic limbs were summarized in a supplementary table.

Temporospatial variables

Compared with the baseline values, limb velocity and stride length of the right pelvic limb were significantly decreased at 4 and 8 hours after synovitis induction but returned to values similar to baseline at 24 hours after synovitis induction. The durations of the gait cycle and swing phase for the right pelvic limb...
were unaffected by induction of synovitis in the hip joint; however, the duration of the stance phase was significantly decreased from baseline at 4 hours after synovitis induction. At 24 hours after synovitis induction, none of the temporospatial variables for the right or left pelvic limb differed significantly from baseline.

The mean limb velocity, stride length, and durations of the gait cycle and stance phase for the left pelvic limb at 4 and 8 hours after synovitis was induced in the right hip joint were significantly higher, compared with the corresponding variables for the right pelvic limb. The symmetry indices for all 5 temporospatial variables were significantly different from baseline at 4 hours after synovitis induction.

### Table 2

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pelvic limb</th>
<th>Baseline</th>
<th>4 h</th>
<th>8 h</th>
<th>24 h</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Limb velocity (m/s)</strong></td>
<td>Right</td>
<td>1.14 ± 0.12</td>
<td>0.45 ± 0.46*</td>
<td>0.52 ± 0.41*</td>
<td>0.99 ± 0.12</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>1.14 ± 0.14</td>
<td>1.01 ± 0.16†</td>
<td>0.92 ± 0.22‡</td>
<td>0.99 ± 0.12</td>
</tr>
<tr>
<td><strong>Stride length (m)</strong></td>
<td>Right</td>
<td>0.81 ± 0.07</td>
<td>0.38 ± 0.39*</td>
<td>0.46 ± 0.46*</td>
<td>0.76 ± 0.08</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>0.81 ± 0.07</td>
<td>0.65 ± 0.11†</td>
<td>0.64 ± 0.10†</td>
<td>0.76 ± 0.07</td>
</tr>
<tr>
<td><strong>Gait cycle duration (s)</strong></td>
<td>Right</td>
<td>0.72 ± 0.08</td>
<td>0.46 ± 0.44</td>
<td>0.59 ± 0.48</td>
<td>0.77 ± 0.08</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>0.72 ± 0.08</td>
<td>0.67 ± 0.19†</td>
<td>0.75 ± 0.23</td>
<td>0.77 ± 0.07</td>
</tr>
<tr>
<td><strong>Swing phase duration (s)</strong></td>
<td>Right</td>
<td>0.30 ± 0.03</td>
<td>0.23 ± 0.22</td>
<td>0.28 ± 0.15</td>
<td>0.33 ± 0.02</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>0.30 ± 0.03</td>
<td>0.24 ± 0.06</td>
<td>0.27 ± 0.02</td>
<td>0.30 ± 0.01</td>
</tr>
<tr>
<td><strong>PVF (N)</strong></td>
<td>Right</td>
<td>72.6 ± 21.6</td>
<td>26.5 ± 27.5*</td>
<td>32.4 ± 27.5*</td>
<td>56.9 ± 9.8</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>74.5 ± 19.6</td>
<td>87.3 ± 16.7†</td>
<td>87.5 ± 20.6</td>
<td>61.8 ± 5.9</td>
</tr>
<tr>
<td><strong>%PVF (%)</strong></td>
<td>Right</td>
<td>428.9 ± 9.9</td>
<td>125.3 ± 13.8</td>
<td>126.5 ± 8.9</td>
<td>127.4 ± 7.1</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>435.6 ± 6.5</td>
<td>139.9 ± 7.1†</td>
<td>136.5 ± 6.6†</td>
<td>149.4 ± 9.7†</td>
</tr>
<tr>
<td><strong>%WD (%)</strong></td>
<td>Right</td>
<td>67.5 ± 7.8</td>
<td>34.6 ± 6.6†</td>
<td>30.8 ± 8.2‡</td>
<td>24.5 ± 2.3</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>68.1 ± 7.8</td>
<td>141.7 ± 17.9*</td>
<td>142.8 ± 18.2*</td>
<td>15.11 ± 10.39</td>
</tr>
<tr>
<td><strong>Hip joint</strong></td>
<td>Right</td>
<td>142.9 ± 9.9</td>
<td>125.3 ± 13.8</td>
<td>126.5 ± 8.9</td>
<td>127.4 ± 7.1</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>135.6 ± 6.5</td>
<td>139.9 ± 7.1†</td>
<td>136.5 ± 6.6†</td>
<td>149.4 ± 9.7†</td>
</tr>
<tr>
<td><strong>Peak extension (°)</strong></td>
<td>Right</td>
<td>151.9 ± 8.4</td>
<td>127.1 ± 17.9*</td>
<td>127.9 ± 18.2*</td>
<td>141.9 ± 8.8</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>153.7 ± 7.1</td>
<td>151.3 ± 7.0</td>
<td>146.8 ± 7.5†</td>
<td>157.7 ± 9.6†</td>
</tr>
<tr>
<td><strong>Peak flexion (°)</strong></td>
<td>Right</td>
<td>107.9 ± 6.4</td>
<td>103.1 ± 13.8</td>
<td>103.8 ± 10.4</td>
<td>96.0 ± 3.9</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>98.1 ± 6.6†</td>
<td>108.6 ± 7.5</td>
<td>107.9 ± 8.6</td>
<td>115.7 ± 13.1†</td>
</tr>
<tr>
<td><strong>Range of motion (°)</strong></td>
<td>Right</td>
<td>35.2 ± 4.4</td>
<td>22.3 ± 8.6*</td>
<td>22.8 ± 10.1*</td>
<td>32.0 ± 3.9</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>37.5 ± 9.2</td>
<td>31.4 ± 5.9†</td>
<td>28.7 ± 4.9†</td>
<td>36.3 ± 6.6</td>
</tr>
<tr>
<td><strong>Stifle joint</strong></td>
<td>Right</td>
<td>151.9 ± 8.4</td>
<td>127.1 ± 17.9*</td>
<td>127.9 ± 18.2*</td>
<td>141.9 ± 8.8</td>
</tr>
<tr>
<td></td>
<td>Left</td>
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</tr>
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<td></td>
<td>Left</td>
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<td>31.4 ± 5.9†</td>
<td>28.7 ± 4.9†</td>
<td>36.3 ± 6.6</td>
</tr>
</tbody>
</table>

*Within a row, value differs significantly (P < 0.05) from that at baseline. †Value differs significantly (P < 0.05) from the corresponding value for the right pelvic limb.

See Table 1 for remainder of key.
variables were significantly increased from baseline at 4 and 8 hours after synovitis induction but had returned to baseline values at 24 hours after synovitis induction. For all 6 dogs, the mean CVs for the temporospatial variables ranged from 0.03 to 0.09 for the right pelvic limb and from 0.03 to 0.15 for the left pelvic limb. Within individual dogs, the mean CVs for the temporospatial variables ranged from 0.02 to 0.15 for the right pelvic limb and from 0.01 to 0.029 for the left pelvic limb.

**Kinetic variables**

The means for all 3 kinetic variables for the right pelvic limb were significantly decreased from baseline at 4 and 8 hours after synovitis induction but had returned to baseline values at 24 hours after synovitis induction (Table 2). For the left pelvic limb, %WD was significantly increased from baseline at 4 hours after synovitis induction. The means for all 3 kinetic variables for the right pelvic limb were significantly lower, compared with those for the left pelvic limb at 4 and 8 hours after synovitis induction. Similar to the temporospatial variables, the symmetry indices for all 3 kinetic variables were significantly increased from baseline at 4 and 8 hours after synovitis induction but had returned to baseline values at 24 hours after synovitis induction. For all 6 dogs, the mean CVs for the kinetic variables ranged from 0.05 to 0.07 for the right pelvic limb and from 0.04 to 0.10 for the left pelvic limb. Within individual dogs, the mean CVs for the kinetic variables ranged from 0.03 to 0.10 for the right pelvic limb and from 0.02 to 0.13 for the left pelvic limb, although the mean CVs for the kinetic variables could not be calculated for the right pelvic limb at 4 and 8 hours after synovitis induction for the dogs that were completely non-weight bearing on that limb.

**Kinematic variables**

Mean range of motion for the right hip joint was decreased significantly from baseline at 4 and 8 hours after induction of synovitis but did not differ significantly from baseline at 24 hours after synovitis induction. The mean peak extension and peak flexion for the right hip joint did not vary significantly from baseline at any time during the 24-hour observation period after sodium urate injection (Table 2). None of the kinematic variables for the left hip joint varied significantly from baseline at any time during the 24 hours after induction of synovitis in the right hip joint. Compared with the left hip joint, the mean peak flexion of the right hip joint was significantly greater at baseline but significantly less at 24 hours after sodium urate injection, the mean peak extension of the right hip joint was significantly less at 4, 8, and 24 hours after sodium urate injection, and the mean range of motion of the right hip joint was significantly less at 4 and 8 hours after sodium urate injection. The symmetry index for peak extension of the hip joint at 4 hours after synovitis induction was significantly greater than that at baseline.

Mean peak extension and range of motion for the right stifle joint were significantly decreased from baseline at 4 and 8 hours after sodium urate was injected into the right hip joint but returned to baseline values by 24 hours after sodium urate injection (Table 2). None of the kinematic variables for the left stifle joint differed significantly from baseline at any observation. Compared with the left stifle joint, the mean peak extension of the right stifle joint was significantly less at 4, 8, and 24 hours after sodium urate injection, the mean peak flexion of the right stifle joint was significantly less at 4 hours after sodium urate injection, and the mean range of motion for the right stifle joint was significantly less at 4 and 8 hours after sodium urate injection. The symmetry index for peak extension and range of motion for the stifle joint were significantly increased from baseline at 4 and 8 hours after sodium urate injection but did not differ significantly from baseline at 24 hours after sodium urate injection. The symmetry index for peak flexion of the stifle joint was significantly increased from baseline only at 4 hours after sodium urate injection.

The mean range of motion for the right tarsal joint was significantly decreased from baseline at 8 hours after sodium urate injection into the right hip joint (Table 2). None of the kinematic variables for the left tarsal joint differed significantly from baseline at any observation. Compared with the left tarsal joint, mean range of motion for the right tarsal joint was significantly less at 4 and 8 hours after sodium urate injection. The symmetry index for peak extension of the tarsal joint was significantly increased from baseline at 4 hours after sodium urate injection, and the symmetry index for the range of motion of the tarsal joint was significantly increased from baseline at 4 and 8 hours after sodium urate injection.

For all 6 dogs, the mean CVs for the kinematic variables of the 3 pelvic limb joints assessed ranged from 0.01 to 0.15 for the right pelvic limb and from 0.01 to 0.15 for the left pelvic limb. Within individual dogs, the mean CVs for the kinetic variables ranged from 0.00 to 0.32 for the right pelvic limb and from 0.00 to 0.15 for the left pelvic limb. Within individual dogs, the mean CVs for the kinetic variables for the pelvic limb joints ranged from 0.00 to 0.71 for the right pelvic limb and from 0.00 to 0.32 for the left pelvic limb.

**Discussion**

Although use of sodium urate to induce acute synovitis in the stifle joints of dogs has been well described,9–14 to our knowledge, the present study was the first to describe the use of sodium urate to induce acute and transient synovitis in the hip joints of dogs and the associated gait changes. Sodium urate–induced synovitis causes an acute inflammatory reaction characterized by a dramatic increase in synovial prostaglandin E2 concentration and an initial infiltration of monocytes, macrophages, and mast cells followed by polymorphonuclear leukocytes into the synovial space23,24 and is generally accompanied by signs of pain. The synovitis is transient because the sodium urate crystals are quickly phagocytized by poly-

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morphonuclear leukocytes and mononuclear phagocytes.\textsuperscript{25,26} Therefore, injection of sodium urate into the hip joint of dogs may provide an effective model for examining the efficacy of treatments for hip joint disease.

In the present study, induction of synovitis in the right hip joint resulted in transient lameness and restricted motion in both the right hip and stifle joints. The effect on the right hip joint was likely caused by synovial inflammation and associated signs of pain. Signs of pain can also be associated with spasmodic muscles, especially the adductor and pectineus muscles, which result from a reaction to inflammation and mechanical strain on the affected hip joint capsule.\textsuperscript{27}

The lameness and alterations observed in the instrumented gait analysis variables could also have been caused by the volumetric effect of the intra-articular injection on joint laxity\textsuperscript{28} or stretching of the joint capsule\textsuperscript{29}; however, the associations among joint laxity, lameness, and gait alterations require further investigation. In dogs with sodium urate-induced synovitis of the stifle joint, NSAIDs attenuate the associated signs of pain, which suggests that inflammation plays an important role in synovitis-induced lameness.\textsuperscript{10,30} The transient nature (24-hour duration) of the lameness associated with sodium urate-induced synovitis of the hip joint in dogs was similar to that associated with sodium urate-induced synovitis of the knee in humans and the stifle joint in dogs, although lameness persisting for 72 hours after injection of sodium urate into the knee or stifle joint has been described.\textsuperscript{8,10,25,26,30–32}

All dogs of the present study had complete recovery of hip joint function and were no longer lame within 24 hours after a single intra-articular injection of sodium urate, which suggested that sodium urate-induced synovitis is an ethically acceptable model for canine hip joint disease just as it is for canine stifle joint disease.\textsuperscript{10,30}

Sodium urate-induced hip joint synovitis is probably best used as a model for diseases in which synovitis is the main source of pain such as acute inflammatory hip dysplasia rather than chronic hip dysplasia.\textsuperscript{29} In young dogs with hip dysplasia, signs of pain from synovitis are believed to be associated with acute laxity that causes stretching of the joint capsule, round ligament of the femoral head, and muscles closely associated with the hip joint and microfractures of the dorsal acetabular rim.\textsuperscript{29} Consequently, sodium urate-induced synovitis would not be a good model for those sources of pain or pain associated with acetabular fractures or ischémic bone necrosis and fragmentation of the femoral head (Legg-Calvé-Perthes disease).\textsuperscript{33}

Although all dogs of the present study received the same volume and concentration of sodium urate suspension and intra-articular injection was ultrasonographically confirmed, the signs of pain varied among dogs from persistent mild lameness to complete non-weight-bearing lameness of the affected limb. In 2 dogs, an initial sodium urate injection caused only mild signs of pain during manipulation of right hip joint but did produce discernable lameness during gait analysis, and the injection had to be repeated. Variable response to intra-articular injection of the same volume and concentration of sodium urate suspension has been described between studies and among individual subjects. For example, intra-articular injection of 10 mg of a urate crystal suspension into the stifle joint of dogs resulted in partial weight-bearing lameness in 1 study\textsuperscript{34} and complete non-weight-bearing lameness in another study.\textsuperscript{11} In yet another study,\textsuperscript{31} intra-articular injection of the same volume of a monosodium urate solution into a stifle joint of 60 dogs failed to result in the desired clinical response for 5 dogs (4 dogs had only mild lameness and 1 dog was not discernably lame), and the injection had to be repeated in those dogs to achieve the desired clinical response.

Instrumented gait analysis is an effective and consistent method for diagnosing lameness because functional movement in terms of temporospatial (time and distance), kinetic (force), and kinematic (motion) variables can be quantitatively assessed. In the present study, each dog underwent instrumented gait analysis 5 times before and after sedation and synovitis induction, which allowed us to use each dog as its own control. Variation of PVF cannot be compared among dogs unless it is normalized for body mass or weight. The 6 dogs used in the present study were all hounds of similar body size and weight, so the effect of body weight on PVF was minimal; however, PVF was normalized for body weight (%PVF) and %WD during analysis as recommended.\textsuperscript{20} Also, during each instrumented gait analysis, dogs were kept at a walk (mean constant velocity for all dogs ranged from 0.5 to 1.2 m/s) as recommended.\textsuperscript{12,19,20} The use of standardized trial conditions during instrumented gait analysis is important if data are to be compared among collection sites, times, and individual subjects.

For the dogs of the present study, the most extreme kinetic changes from baseline were observed 4 hours after injection of sodium urate into the right hip joint and presumably coincided with when the signs of pain associated with synovitis were at their maximum. The redistribution of limb forces in quadrupeds is poorly understood.\textsuperscript{33} In the present study, compared with baseline measurements, induction of synovitis in the right hip joint resulted in a decrease in the kinetic forces in the right pelvic limb and a concurrent increase in the kinetic forces in the left pelvic limb, but compensatory kinetic changes in the thoracic limbs were not observed. In another study\textsuperscript{9} in which urate crystals were injected in a stifle joint of dogs, a compensatory increase in the kinetic forces of the contralateral pelvic limb were detected, and compensatory loading of the thoracic limbs varied with severity of lameness and sometimes decreased despite obvious pelvic limb lameness. Following experimental induction of synovitis in a shoulder joint in each of 5 dogs, the kinetic forces for the contralateral thoracic limb were increased from baseline measurements, and the
PVFs of the pelvic limbs were redistributed in a compensatory manner.\(^{46}\)

In the present study, results of the instrumented gait analyses indicated that the kinetic measurements for the right pelvic (affected) limb were generally decreased from baseline measurements at 4 and 8 hours following induction of synovitis in the right hip joint but did not differ significantly from baseline measurements at 24 hours following synovitis induction. A similar pattern was observed in the kinetic measurements for the affected limbs of dogs with experimentally induced synovitis of a stifled joint.\(^{9,10}\) Unfortunately, temporospatial and kinematic variables were not measured in those studies.\(^{9,10}\) Although it is difficult to definitively determine which variables are most useful for lameness detection on the basis of data from the present study, it appears that induction of synovitis in the hip joint in dogs caused the most extreme changes in kinetic measurements followed by changes in temporospatial and kinematic variables. Investigators of another study\(^ {46}\) likewise reported that kinetic variables were more useful for detection of lameness in dogs than were kinematic variables; however, further investigation is necessary to unequivocally determine the sensitivity and specificity of instrumented gait variables for detection of lameness.

Results of the present study provided a basis for characterization of gait abnormalities in dogs associated with signs of pain originating from the hip joint. Scientific literature describing gait abnormalities associated with hip joint disease in dogs is lacking, and most of the literature\(^ {37–40}\) that is available on the subject compares gait characteristics of dogs with hip dysplasia before and after treatment or with clinically normal dogs. Evaluation of kinetic and kinematic gait analyses of dogs with hip dysplasia indicate that, compared with results for clinically normal dogs or with results from dysplastic dogs following treatment, PVFs and peak impulses are decreased and stride length is increased in affected limbs,\(^ {7,38,39}\) with subtle alterations in the dynamic flexion, extension, and angular velocities of the hip, stifle, and tarsal joints.\(^ {7}\) Thus, the gait alterations associated with sodium urate–induced synovitis of the hip joint were similar to those associated with hip dysplasia, and sodium urate–induced synovitis of the hip joint might be a useful model for assessing interventions for hip dysplasia in dogs.

Information regarding the effect of sedation on instrumented gait analysis of dogs is lacking; therefore, it was important for us to evaluate the possible confounding effect of sedation on instrumented gait analysis in the present study. Results indicated that the kinetic and kinematic variables for dogs immediately prior to and 4 hours after sedation with dexmedetomidine followed by reversal with atipamezole did not differ significantly, which suggested that instrumented gait analysis could be reliably performed 4 hours after appropriate reversal of sedation with dexmedetomidine. These results were consistent with information provided in the FDA freedom of information summary for atipamezole. In 55 dexmedetomidine-sedated dogs, reversal of sedation was evident beginning as soon as 5 minutes after administration of atipamezole, and by 15 minutes after atipamezole administration, 53 (96%) were standing, 54 (98%) had a clinically normal response to sound, 47 (86%) had clinically normal jaw muscle tone, and 50 (91%) had a clinically normal pedal reflex.\(^ {41}\) In dogs, the elimination half-life of dexmedetomidine is 40 to 50 minutes and that of atipamezole is 2 to 3 hours.\(^ {42}\)

Results of the present study indicated that injection of a sodium urate suspension into a hip joint of healthy dogs reliably induced synovitis and signs of pain and lameness in the ipsilateral pelvic limb that lasted 24 hours. This model can be used in conjunction with instrumented gait analysis to provide information on gait changes associated with hip joint disease and might be useful for evaluating the efficacy of analgesics or other interventions for the treatment of hip joint disease in dogs.

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Footnotes

b. Dexdomitor, Orion Corp, Espoo, Finland.
c. Antisedan, Orion Corp, Espoo, Finland.
d. Uric acid sodium salt, Sigma-Aldrich, St Louis, Mo.
e. Hydromorphone hydrochloride injection (2 mg/mL), West-Ward Pharmaceuticals Corp, Eatontown, NJ.
f. Rimadyl 100-mg caplets, Pfizer Animal Health, New York, NY.
g. 5/4-inch black LP SAT dots, VELCRO, Manchester, NH.
i. GL2 digital camcorder, Canon, Melville, NY.
j. Scout scA640-120gc, Basler AG, Ahrensburg, Germany.
l. MATLAB, version 7.10.0.499 (R2010a), The MathWorks Inc, Natick, Mass.
m. Microsoft Office Excel 2007, Microsoft Corp, Redmond, Wash.
n. SPSS, version 21.0, IBM Corp, Armonk, NY.
o. A supplemental table of temporospatial and kinetic variables for the thoracic limbs of the study dogs before and at various times after induction of synovitis in the right hip joint is posted with the article at avmajournals.avma.org.

References


