

# Septic arthritis: diagnosis, management and prognosis

**Septic arthritis is an uncommon but potentially devastating condition of small animal patients; Ben Mielke BVSc MANCVS (Surgery) MRCVS and Ignacio Calvo Ldo Vet CertSAS DipECVS FHEA MRCVS, the Royal Veterinary College, UK, outline the common features of this condition and the recommended treatment strategy**

Septic arthritis is an active joint infection, typically bacterial in origin (subsequently often referred to as bacterial infective arthritis), that results in variable degrees of inflammation, pain, joint swelling and lameness.<sup>1,2</sup> Bacterial contamination may be directly introduced into the joint; at surgery or from local trauma/tissue damage; or be haematogenous in origin having spread from distant sites.<sup>1,2,3</sup> Septic arthritis typically manifests as a monoarthropathy, with variable joint predilection reported.<sup>3,4,5,6</sup> Early recognition and diagnosis of septic arthritis is crucial to ensure an optimal outcome for affected patients, as delayed or inadequate treatment of septic arthritis can lead to irreversible joint destruction and in very severe cases, death.<sup>9</sup> The difficulty in early recognition and diagnosis is a large part attributable to the cross over in clinical features of common arthropathies; septic arthritis, degenerative arthropathies and immune mediated processes.<sup>1,2</sup> This is particularly true when recent surgery is not part of a patient's clinical history. This article reviews current diagnostic strategy, treatment options and prognosis for animals with septic arthritis.

Synovial effusions develop following cartilage or synovial membrane insult. This injury results in the release of an array of inflammatory cytokines causing synovial capillary vasodilation and subsequent increased vascular permeability. These leaky synovial vessels allow the extravasation of fluid, protein and inflammatory cells into the joint. The relative number and type of leukocytes that arrives dictates the categorisation, diagnosis and subsequent treatment strategy. The important point to consider in the physiology of joint effusion is the considerable overlap in the response of the joint to insult.<sup>25</sup> The identification of septic arthritis cases in the veterinary literature, has spread from a modified criteria used in human, requiring one of four points to be met: 1. Isolation of the pathogenic organism from the affected joint; 2. Isolation of a pathogenic organism from another source; 3. Typically synovial-fluid features (reduce viscosity, increased



turbidity/cloudiness, automated cell count greater than  $50 \times 10^9$  cells/L and greater than 40% neutrophils when turbidity, reduced viscosity); and 4. Post-mortem or pathological features consistent with septic arthritis diagnosis.<sup>9,25</sup>

## SIGNALMENT

Older, large-breed males are overrepresented in all studies. Similar to people, septic arthritis has been typically confined to older populations and young animals.<sup>3-6,9</sup> Pre-existing joint pathology is a very common finding amongst older animal's patients. In one veterinary study, all of the cases of septic arthritis that had no history of trauma or local surgery had evidence of joint disease,<sup>4</sup> which is similar to the finding of joint disease in 73% of non-immunocompromised adult patients. In people, pre-existing osteoarthritis, prosthetic joints, low-socioeconomic status, drug abuse, diabetes and previous intra-articular corticosteroid injections have been identified as risk factors for septic arthritis.<sup>7,9</sup> This suggests that abnormalities in the normal cartilage and synovium combined with a compromised immune response may predispose these animals to developing infection.

## GENDER

Males are overrepresented in the veterinary literature of septic arthritis 92/138 cases (66.7%). In the one study that had an even distribution of sexes, a large percentage 14/19 cases were secondary to surgical infection following cruciate surgery, a disease that female are predisposed to.<sup>5</sup> Large-breed dogs are most commonly reported; particularly German Shepherds, Labradors and Boxers.<sup>3</sup>

**JOINT INVOLVEMENT**

The most commonly reported joints involved included: stifle 47/99; carpus 28/99; elbow 26/99; hock 15/99; and the hip 9/99 and 7/99 shoulder.<sup>3-6</sup> Post-operative infection following articular surgery likely represents the most common cause of infection in companion animals. Infection rates following surgery have been established between 0-2.7% at one referral institute (C4). There is considerable variation between different studies and procedure types that needs to be considered.<sup>1</sup> When cases that had recent surgery were removed, a haematogenous aetiology is most likely. In the same studies when surgical cases were excluded the carpus was most common joint infected, followed by the elbow and then the stifle. Typically, animals will present with a single joint involved (monoarthropathy) but occasional animals will present with multiple joint involvement. These cases are typically observe in younger or immunocompromised individuals.

**ACUTE VERSUS CHRONIC**

Animals may present with an acute onset (<1 week – 32-70%) or chronic history (>1 week – 30-68%) of variable lameness severity. The severity of lameness is also variable, with animals presenting acutely typically being more severely affected.<sup>3-6</sup> The large percentage of animals that present with a chronic history highlights the importance of considering a chronic-infectious process in animals that have lingering lameness following a pain management trial. The most common clinical sign in a painful, swollen joint. In general, it is recommended that any swollen

joint should be sampled; however, if none exist, then at least two to three different joints should be sampled.<sup>25</sup> Based on the prevalence; carpus and elbow in thoracic and tarsus and stifle in the pelvic limbs; would be recommended.

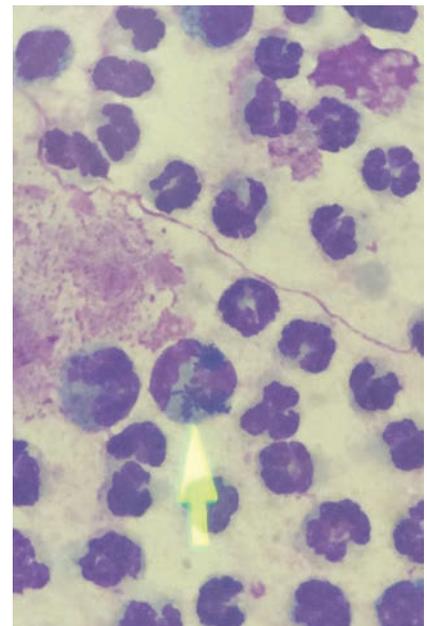
**INVESTIGATION OF SUSPECTED SEPTIC ARTHRITIS**

Diagnosis of septic arthritis relies upon collection and analysis of synovial fluid. A discussion of the techniques of arthrocentesis are beyond the scope of this discussion but several useful resources are available.<sup>26</sup> Initial assessment of synovial fluid can be based on volume, colour, turbidity and viscosity (see Table 1). Normal synovial fluid should be clear, colourless, free of flocculent material and 'stringy' compared to the typically watery and cloudy appearance of septic synovial fluid.<sup>25</sup> Inflammation results in a reduction of hyaluronic-acid content within synovial fluid leading to reduced viscosity. A simple test of viscosity can be performed by placing a drop of synovial fluid between the thumb and finger – a strand of at least 2.5cm should be produced. Analysis of synovial fluid should include immediate assessment by in-house cytology to subjectively assess the cell population, collection of a sample for further pathological interpretation (either direct smear or ethylenediaminetetraacetic acid [EDTA] sample if sufficient quantity), and sample for culture.

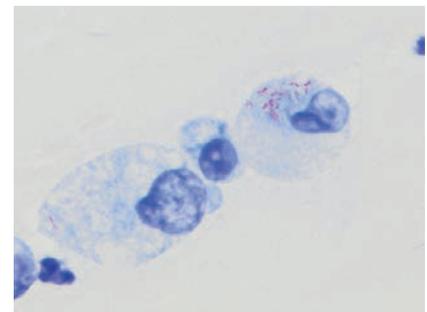
**ANALYSIS OF SYNOVIAL FLUID**

**1. Cytology:**

The relative cell population of a synovial fluid sample can be used to indicate the likely underlying



**Figure 1: Intracellular bacteria on a Diff-Quick stained cytological sample from septic arthropathy.**



**Figure 2: Intracellular bacteria (Mycobacteria spp) identified on Ziehl-Neelson acid-fast stain from coxofemoral synovial fluid.**

disease process. Differentiation of osteoarthritis, immune-mediated disease and septic arthritis is often based upon differential cell counts, the presence of degenerative neutrophils or the presence of intracellular bacteria. The relative cell population of different disease states is summarised in Table 1.

Condition	Volume (ml)	Colour	Clarity	Viscosity	Nucleated cell count (x 10 <sup>9</sup> /L)	Mononuclear cells (% total cells)	Neutrophils (% total cells)
Normal	0.24	Colourless to straw	Clear	High	<2	94-100	0-6
Degenerative	Normal to ↑	Colourless to yellow	Clear	Normal to ↓	2-5	88-100	0-12
Immune Mediated Arthropathy	Normal to ↑	Yellow to bloody	Hazy or cloudy	↓	4-370	5-85	15-95
Septic Arthritis	Normal to ↑	Yellow to bloody	Cloudy to opaque	↓	40-267	1-10	90-99

**Table 1: Characteristic of synovial fluid from a normal joint, degenerative arthropathy, immune mediated disease and septic arthritis.**

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There is considerable overlap between categories and variation within categories, consequently it is generally not possible to differentiate between immune-mediated and infective disease, or between normal joints and joints with osteoarthritis based on relative cell counts.<sup>21</sup> If possible, a total nucleated cell count should be performed, to allow both immediate classification and for ongoing monitoring of response to treatment. Although bacteria may be directly visualised (see Figures 1 and 2) on smears, this is infrequently documented (8/27 samples, 4/20 samples, 6/13 samples if gram stain used),<sup>4,6,5</sup> and the absence of visible bacteria does not preclude a diagnosis of septic arthritis. An important differentiation between cytoplasmic granules in neutrophils; which represent phagocytosed droplets of nucleoprotein; seen in immune-mediated disease and intracellular bacteria should be noted for the inexperienced clinician to avoid incorrect classification.<sup>25</sup>

**2. Culture:**

The definitive diagnosis of septic arthritis relies on the isolation of bacteria from the affected joint, however bacterial culture is frequently unsuccessful (positive culture in 40-68.4% of cases) and diagnosis must often be based on a degree of suspicion.<sup>1,8</sup> Of the four largest veterinary case series of septic arthritis, the most commonly isolated bacteria included *Staphylococcus* spp. (46/99 – 46.5%), *Streptococcus* spp (22/99 – 22.2%), *Coliforms* (8/99 – 8%) and *Pseudomonas* spp (5/99 – 5.1%).<sup>3,6</sup> This is similar to the disease in people, where staphylococci or streptococci account for 91% of cases<sup>9</sup> No association has been found between the use of antibiotics prior to sample collection and ability to obtain a positive culture.<sup>4,8</sup> Inoculation of sample onto both culture swab and into a blood-culture bottle may reduce the false-negative culture results.<sup>17</sup> Samples are initially plated from a culture swab and if there is no observed growth after 24 hours, the blood culture medium is plated onto an appropriate medium, serving as a 'back-up' sample. The blood culture medium is thought to prevent coagulation of fluid, dilutes bacterial inhibitors and limits in vitro phagocytosis of bacteria.

**ADDITIONAL SYNOVIAL FLUID ANALYSIS OPTIONS**

**1. Synovial fluid total protein:**

Inflammation in the joint typically results in increased total protein concentrations. However results should be interpreted with caution as inadequately filled EDTA sample (ie excessive EDTA to sample), which can often occur due to small sample size, can result in false increases.

**2. Mucin clot test:**

The mucin clot test is a semi-quantitative test for the amount of hyaluronic acid content in sample. Poor clot formation is associated with inflammation within the joint. Relies on sample to be in plain tube or heparin tube (therefore, limited utility when insufficient sample).

**3. Polymerase chain reaction:**

Because of the frequency of unsuccessful culture, polymerase chain reaction (PCR) has been explored as an additional test in the identification of bacterial components in synovial samples. PCR is a rapid molecular diagnostic

technique that allows early detection of bacteria and may also allow detection of difficult organisms to culture. This technique does not replace traditional culture techniques and in one study there was no improvement to diagnostic accuracy with 16S rRNA PCR, however further research and consideration of this modality is certainly warranted.<sup>13,15</sup> PCR is, therefore, considered a more useful complementary tool in the identification of seldom identified or fastidious organism.

**4. Lactate levels:**

Lactate levels increase as a result of inflammation. Lactate level assessment may be considered as an adjunctive/ ancillary test if hand-held meters are available.<sup>18</sup> When lactate level cut-off was set at  $\geq 6.5$ mmol/L the test had a high specificity estimate 1.0 (95% CI 0.95 – 1.00) and therefore, may be useful to rule out septic arthritis when concentrations are low. However, this study should be interpreted with caution as in humans the utility of lactic acid to discriminant between different types of inflammation has not be established.<sup>9</sup>

**5. Urine dipstick analysis:**

Leukocyte esterase and glucose-reagent strips on a urine dipstick may be used to investigate suspicion of septic arthritis. A leukocyte esterase reading of ++ or +++ combined with a negative glucose result yielded a sensitivity of 89.5% (95% CI 72.7 – 99.9%) and specificity of 99.2% (95% CI 95.7 – 99.9%).<sup>14</sup>

In addition to assessment of synovial fluid, in cases in which a haematogenous aetiology is suspected, further diagnostics are warranted. A minimum database, including haematology, biochemistry and urinalysis is recommended. The lack of leucocytosis does not preclude a diagnosis of septic arthritis.<sup>9,20</sup> Particular attention on physical examination should be paid to the skin, ears, oral cavity, thorax and urinary system.<sup>10,11,12</sup> Cultures of the urine are recommended as the urinary tract has been observed as a nidus for systemic spread of septic arthritis.<sup>10</sup>

**MANAGEMENT FOR SEPTIC ARTHRITIS**

At this stage, no investigation can be considered more reliable in the diagnosis of septic arthritis than professional opinion. Therefore, management often relies on a treatment trial and assessment of clinical response. Many treatment recommendations exist but no consensus as to the most appropriate has been determined for veterinary patients. At present treatment recommendations are extrapolated from other species and small case series and retrospective studies.<sup>3-6,9,11,19</sup> Prompt treatment with antibiotics together with removal of any purulent material is the currently accepted mainstay of treatment of septic arthritis.

**Antibiotic selection (see Figure 3):** Based on the

**Treatment protocol for suspect septic arthritis:**

**First 24-48 hours: IV cefuroxime or amoxicillin/clavulanic acid 20mg/kg q8h**

**Oral antibiotics (based on culture and sensitivity): six to eight weeks**

**Figure 3: Treatment algorithm for cases of septic arthritis.**

most common bacterial isolates in veterinary patients; *Staphylococcus* and *Streptococcus* species; the use of B-lactam antibiotics as firstline treatment is recommended (see protocol below). Intravenous antibiotics are instituted until there is a clinical improvement in the patient. At this point, the patient is switched to oral antibiotics for an extended period of between six to eight weeks. There is limited evidence as to the appropriate antibiotic duration, with wide ranges reported in veterinary studies (10 days – three months).<sup>3-6</sup> However, recurrence of infection was noted in one of the patients given the shortest recorded duration and therefore we extrapolate advice from human recommendation.<sup>9</sup>

### NEEDLE DRAINAGE AND SURGICAL INTERVENTION

There has recently been a shift away from aggressive surgery management (arthrotomy/synovectomy) of septic arthritis cases based on the reported successful treatment of animals with suspect haematogenous aetiology with antibiotics alone and the findings of no difference in the outcome of combined surgical and medical management and medical management alone.<sup>3,9,19</sup> In the human literature there is no clear consensus on the best treatment strategy but successful treatment includes removal of purulent material from the joint space. Needle aspiration of synovial fluid appears to be a preferable initial management mode, despite a lack of significant results.<sup>9</sup> However, the utility of surgical drainage via arthroscopy or revision surgery for implant removal should not be overlooked; case history (ie. recent surgery, surgical implants) and joint involvement should be considered when deciding on management

strategy Post-operative infections frequently required a combination of implant removal combined with extended antibiotic therapy.<sup>5</sup> Timing of implant removal needs to be based upon assessment of fracture healing and may need to be delayed.

**Prognosis and recurrence:** There is considerable variation in the outcome for patients and results often depend on the degree of pre-existing disease, chronicity and development of recurrence. Complete resolution of lameness is reported between 40-80% of cases<sup>3-6,19,20</sup> at a timeframe of 24 hours – one month. There is variable levels of residual lameness reported in the remaining cases; in the elbow joint severe osteoarthritis was observed in 5/8 cases that had no history of recent surgery.<sup>4</sup> Recurrence rates of 0-11% are reported and the authors recommend repeat synovial assessment immediately following antibiotic cessation, combined with long term surveillance and follow-up.

Interestingly in a small subset of patients with long-term lameness, treatment with corticosteroids results in clinical improvement.<sup>3,9</sup> It is possible that these cases represent either an initial misclassification of a reactive immune mediated arthropathy or are the result of antigenic response to remaining bacterial components.<sup>4</sup>

Septic arthritis represents an uncommon but potentially life-threatening condition for animals and needs to be appropriately managed by rapid diagnosis and prompt treatment to ensure an optimal outcome. The clinician should have this as a differential for any animal presenting with lameness and consider arthrocentesis and cytology as a routine part of their arsenal.

### REFERENCES ON REQUEST

## READER QUESTIONS AND ANSWERS

### 1. WHAT IS THE NORMAL TOTAL NUCLEATED CELL COUNT IN NORMAL SYNOVIAL FLUID?

- A <2.0 x 10<sup>9</sup> cells/L
- B >250 x 10<sup>9</sup> cells/L
- C 2-5 x 10<sup>9</sup> cells/L
- D 50-60 x 10<sup>9</sup> cells/L

### 2. HOW FREQUENTLY IS SYNOVIAL FLUID SUCCESSFUL/ POSITIVE IN CASES OF SEPTIC ARTHRITIS?

- A 10-20%
- B 20-40%
- C 40-70%
- D 70-80%

### 3. WHAT IS THE MOST COMMONLY ISOLATED SPECIES IN CASES OF SEPTIC ARTHRITIS?

- A *Staphylococcus* spp
- B *Streptococcus* spp
- C *Pseudomonas* spp
- D *Coliform* spp

### 4. WHICH OF THE FOLLOWING GROUPS IS THE MOST APPROPRIATE FIRST LINE ANTIBIOTIC SELECTION PRIOR TO CULTURE RESULTS?

- A Carbonpenems
- B Metronidazole
- C Flouroquionlone
- D First-generation cephalosporin

### 5. WHAT DURATION OF ANTIBIOTICS IS RECOMMENDED FOR MANAGEMENT OF SEPTIC ARTHRITIS?

- A Five to seven days
- B 10-14 days
- C Three weeks
- D Six to eight weeks

ANSWERS: 1:A; 2:C; 3:A; 4:D; 5:D