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TITLE: Spontaneous Septic Arthritis of Canine Elbows: Twenty-One Cases

AUTHORS: B. Mielke, E. Comerford, K. English, R. Meeson

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1 **Manuscript Title:**

2

3 *Spontaneous Septic Arthritis of Canine Elbows: 21 dogs*

4 Objective: To provide information on the clinical features, diagnosis and treatment and  
5 associated risk factors of spontaneous septic elbow arthritis in the dog.

6 Methods: Medical records from two referral institutions between March 2007 – June 2015 were  
7 searched for cases of spontaneous septic elbow arthritis with a diagnosis based on clinical signs,  
8 arthrocentesis, cytological and microbiological analysis of elbow joint synovial fluid,  
9 radiography, and outcome following treatment.

10 Results: 21 cases of septic arthritis were identified. Pre-existing chronic osteoarthritis was  
11 present in 93% of elbows for which diagnostic imaging was available. Although all cases had  
12 increased neutrophil count on synovial fluid cytology, culture was only positive in 52.3% of  
13 cases. Despite initial improvement in lameness scores (pre-treatment 7.5/10 (range 1-10) vs  
14 post-treatment 3/10 (range 1-5)), 92% had residual long term lameness based on clinical  
15 records and owner follow-up. Recurrence of infection was noted in 25% of elbows for which  
16 long term (>8 weeks) follow-up was available. There was an acute mortality rate of 2/21 (10%)  
17 associated with severe systemic sepsis.

18 Clinical Significance: Septic arthritis, even in the absence of pyrexia, should be considered as  
19 a major differential diagnosis in middle aged, large breed dogs, with pre-existing elbow  
20 arthritis, that suffer an acute onset lameness, with elbow joint effusion and discomfort.

21 Antibiotic therapy alone is effective for treatment with high initial response rates of 94%.

22 Chronic lameness post-treatment was common, and a high rate of recurrence was seen with  
23 25% of dogs suffering more than one episode.

24

25 **Introduction:**

26 Septic arthritis is considered an uncommon condition that can significantly impact the quality  
27 of a dog's life (1). Septic arthritis is an active joint infection, which is usually bacterial in origin  
28 and results in an acute inflammation of the joint, with swelling, pain and lameness (1, 2).  
29 Bacterial contamination of the elbow may arise from direct inoculation (at surgery or related  
30 to trauma), or by the extension of local infections or by haematogenous localisation (3). The  
31 term spontaneous is used in this report to describe infections in which there has been no known  
32 recent surgical or traumatic episode to the afflicted joint and the infection is presumed  
33 haematogenous in origin (4). The majority of bacterial septic arthritides manifest as a  
34 monoarthropathy, and may be either acute or chronic in onset (3). A clear joint predilection of  
35 septic arthritis in dogs has not been established for cases of spontaneous infection. In the  
36 veterinary literature, in which surgical related infection is variably included, the stifle is most  
37 commonly affected 16.1 – 73.7%, with the elbow showing variable predilection rates of 12.9  
38 – 38.7% (3, 5-7). Pre-existing joint diseases, such as osteoarthritis, and concurrent medical  
39 conditions (diabetes mellitus, skin disease, urinary tract infection, prosthetic joints) may  
40 predispose the joint to opportunistic infection (2, 8). Septic arthritis more often affects larger  
41 breeds, with an apparent over-representation of males (3, 5-7). The definitive diagnosis of  
42 septic arthritis has traditionally relied on the identification of bacteria from the affected joint  
43 by synovial fluid or synovial membrane culture. The difficulty is that bacterial culture is  
44 frequently unsuccessful and diagnosis must often be based on a degree of suspicion (1, 9).  
45 Often a presumptive diagnosis of bacterial infective arthritis is made where synovial fluid from  
46 a monoarthropathy shows very high nucleated cell counts ( $>50 \times 10^9$  cells/ml), predominantly  
47 polymorphonuclear cells and/or the presence of intracellular bacteria on cytology (1).

48

49 Despite several retrospective articles on the subject of septic arthritis, there is limited  
50 information on the signalment, treatment success, recurrence and long term outcome of cases

51 of septic arthritis in the elbow joint of dogs that have not had recent surgery (3 – 7). This study  
52 aimed to review the current literature on septic arthritis and describe cases of septic arthritis  
53 including the history, presenting complaint, underlying disease state, response to treatment and  
54 outcome.

55

#### 56 **Materials and Methods:**

57 The clinical records database of two tertiary-level referral institutions were searched for cases  
58 of septic arthritis or bacterial infective arthritis that had been diagnosed between March 2007  
59 and June 2015 to determine relative joint prevalence. Cases identified for septic arthritis were  
60 then further stratified to identify cases of spontaneous septic arthritis of the elbow. Inclusion  
61 criteria were the diagnosis of a monoarthropathy, where analysis of either the synovial fluid or  
62 membranes was consistent with septic arthritis, and there was no recent surgery of the elbow  
63 joint within one month of presentation or one year if implants were placed (3, 10). Analysis of  
64 synovial fluid or synovium was required to fulfil one or more of the following criteria; highly  
65 cellular appearance observed subjectively on a direct smear, >40% neutrophil population in the  
66 synovial fluid; a total nucleated cell count of more than  $50.0 \times 10^9$  cells/ml; a positive synovial  
67 fluid or membrane bacterial culture (5, 11).

68

69 The medical records, physical examination and recent haematology and blood biochemistry  
70 results from cases were reviewed. Synovial fluid samples had been obtained from the affected  
71 joint by percutaneous arthrocentesis following aseptic preparation in anaesthetised or deeply  
72 sedated patients (12). Synovial fluid samples were submitted for culture and sensitivity after  
73 inoculation into blood culture media. Culture was performed as previously described (3)

74

75 Lameness of the affected limb was extrapolated from clinical records of patients as assessed  
76 and recorded by either RCVS or ECVS board certified veterinarians pre- and post- treatment  
77 using a numerical scoring system (13, 30). Because of the variability of recorded information  
78 between patient and across the time period of the study the following grouping was defined:

- 79 • 0 – Sound, no lameness
- 80 • 1 – Occasionally shifts weight off affected limb
- 81 • 2 - Mild lameness at a slow trot, none whilst walking
- 82 • 3 – Mild lameness visible whilst walking
- 83 • 4 – Obvious lameness whilst walking, but places the foot whilst standing
- 84 • 4-7 - Moderate lameness in degrees of severity
- 85 • 8 - Severe lameness
- 86 • 9 – Places toe when standing, carries limb when trotting
- 87 • 10 – Non weight bearing

88

89 When imaging studies of the elbow was available the plain radiography and CT scans of the  
90 elbow joints were reviewed by two of the authors. Images were assessed for the presence of  
91 osteophytes; at the anconeal process, medial and lateral epicondyles, and radial head; ununited  
92 anconeal process (UAP), fragmented medial coronoid process (fMCP), incomplete ossification  
93 of the humeral condyles (IOHC) and humeral condyle osteochondrosis dissecans (hOCD). A  
94 global assessment of osteoarthritis (OA) was given; none (no osteophytes), mild (small  
95 numbers of osteophytes less than 1 mm in size, moderate (osteophytes at multiple sites, 1-  
96 2mm) or severe (osteophytes larger than 2mm) following consensus between the two authors  
97 (5).

98

99 Short term (defined as a period less than eight weeks) outcome, was recorded as clinically  
100 *successful* where there was a return to the level of ambulation prior to recent episodes of  
101 lameness, clinically *unsuccessful* if there was continued lameness at or to a greater degree than  
102 prior to intervention but with resolution of infection; and as *failed* if the synovial fluid cytology  
103 was not consistent with resolution of the bacterial infection at the last recorded treatment (4,  
104 14). Long term outcome (>8 weeks) was reviewed for ongoing lameness, recurrence of  
105 infection or further surgical intervention and was evaluated by both owner telephone call and  
106 assessment of clinical records where available.

107

108 Statistical analysis was performed by one of the authors using a statistical software package  
109 (SPSS Stat, Version 2.2, IBM Corp). Normality of data was assessed by a Shapiro-Wilk's test  
110 and presented as mean +/- standard deviation when parametric and median +/- range when  
111 non-parametric. The project was ethically reviewed (URN 2015 1359) by the respective  
112 institutional Research Ethical Review Boards

113

#### 114 **Results:**

115 Twenty-seven cases of septic arthritis of the elbow joint were initially identified during the data  
116 collection period. Five elbows were excluded due to a history of recent surgery involving the  
117 septic elbow. One case was excluded based on repeat synovial fluid analysis consistent with an  
118 immune-mediated process (polyarthropathy with non-degenerate neutrophils on synovial fluid  
119 analysis), resulting in a total of 21 elbows meeting the inclusion criteria for spontaneous septic  
120 arthritis, (summary of case details is provided in Appendix 1). Breeds included Labrador  
121 Retrievers (n=11), and one each of English Springer Spaniel, Cross Breed, Munsterlander,  
122 Golden Retriever, Bull Mastiff, Rottweiler, German Shepherd, Saint Bernard, Cavalier King  
123 Charles Spaniel (CKCS), Patterdale Terrier and Staffordshire Bull Terrier (SBT). The mean

124 age of dogs in this report was 6.8 years +/- 2.3. The median body weight was 35.5 kg (9 – 83  
125 kg). The right elbow joint was involved in 10/21 cases, left in 9/21 and 2/21 cases were  
126 bilateral.

127

128 Nine dogs (43%) were receiving treatment for concurrent medical conditions at the time of  
129 initial presentation; idiopathic epilepsy (n=3), diabetes mellitus (n=3), urinary tract infection  
130 (n=2), hypothyroidism (n=1), acute lymphoblastic leukaemia (ALL) (n=1), paraprostatic cyst  
131 (n=1) and anal furunculosis (n=1). Two of these dogs had more than one concurrent disease.  
132 Immunosuppressive therapy was being used in two cases; the patient with ALL was receiving  
133 a chemotherapy protocol combining doxorubicin<sup>a</sup> vincristine<sup>b</sup>, cyclophosphamide<sup>c</sup> and  
134 prednisolone<sup>d</sup> and the anal furunculosis case was receiving cyclosporine<sup>e</sup>

135

136 A history of prior orthopaedic surgery was identified in 11 cases that met our prior inclusion  
137 criteria. Three of these had a history of surgery at a site distant to the infected elbow, (tibial  
138 plateau levelling osteotomy (TPLO) with implants in place). The remaining eight had a history  
139 of surgery on the septic elbow joint; however it was outside of the time frame for exclusion as  
140 a surgical site infection. Seven did not have implants (elbow arthroscopy (n=5, 3-8 years prior),  
141 bilateral forelimb angular limb deformity and ulnar osteotomy (n= 1, 9 years prior), bilateral  
142 elbow hygroma (n=1, 2 years prior), the eight case had a stainless steel transcondylar lag screw  
143 for incomplete ossification of the humeral condyles (, 1 year prior). The median time since  
144 prior surgery was three years (range: two months to eight years). Of the three cases that had a  
145 TPLO procedure performed, two had surgery within two month of presentation for forelimb  
146 lameness. Both of these cases had evidence of surgical site infection of the distant original  
147 surgical site suggesting the possibility of a haematogenous spread to the elbow.

148

149 At presentation, physical examination findings included joint effusion (n=21), pain upon  
150 manipulation of the affected joint (n=21), lethargy (n=8), muscle atrophy (n=6), regional  
151 lymphadenopathy (n=5), pyrexia ( $>39.2^{\circ}\text{C}$  n=5), systemic leucocytosis (n=6). Sixteen cases  
152 were referred as an emergency consultation due to an acute deterioration in lameness. Of these  
153 16 cases, twelve had a chronic ( $>2$  month) history of forelimb lameness prior to deterioration.  
154 The remaining five dogs were presented for an investigation of chronic lameness through  
155 routine referral consultation. The duration of deterioration in clinical signs in all dogs was  
156 median 4.5 days (1 – 120 days) and a lameness score on presentation was median 7.5/10 (range  
157 1-10). The group of dogs (n=5) presenting for investigation of chronic forelimb lameness had  
158 clinical signs of greater than two months and lameness score of median 5/10 (range 1-10).  
159 Routine haematology and serum biochemical results were available for 13/21 cases. A  
160 leucocytosis was present in 4/13 cases with neutrophilia in 5/13. A thrombocytopenia ( $<150$   
161  $\times 10^9/\text{L}$ ) was present in three cases; two of which had concurrent neutropenia ( $<3 \times 10^9/\text{L}$ ). Of  
162 these two cases; one (Case 14) was receiving chemotherapy for ALL; and the other (Case 15)  
163 was euthanatised due to clinical deterioration and signs of suspected sepsis (pyrexia,  
164 tachycardia, neutropenia) (29). Alkaline phosphatase was elevated in three dogs.

165

166 Imaging available for evaluation included orthogonal radiographs in six and computed  
167 tomography (CT) of the elbow joint in nine elbows. Osteophytosis was present in 14/15 elbows,  
168 fMCP was seen in nine elbows, UAP in one, IOHC in one and hOCD in two. Global OA  
169 assessment was severe 11/15, moderate 1/15, mild 2/15 and absent 1/15.

170

171 Synovial TNCC was available for 13/21 elbows, with a mean of  $102.2 \pm 55.8 \times 10^9$  cells/L  
172 (range of 13.7 – 183). The TNCC was below the inclusion level defined in this study for septic  
173 arthritis of  $50 \times 10^9/\text{L}$  in 2/13 (15.4%) cases (cases 14 and 21). In both these cases the



174 polymorphonuclear differential was greater than >90%. Case 14 was included due to resolution  
175 in clinical signs following antibiotic therapy and case 21 subsequently had a positive bacterial  
176 culture. Cytological assessment was available for 20/21 elbows. Based on the differential cell  
177 count, polymorphonuclear cells predominated in all cases (mean 91.4 +/- 5.1% of the TNCC  
178 population). Degenerate neutrophils were present in only one case (1/20) and intracellular  
179 bacteria were seen in five cases (3/5 subsequently having a positive culture result). Synovial  
180 fluid was submitted for culture in 21 cases with a positive culture obtained in 11/21 cases  
181 (52.3%). Bacteria cultured included *Staphylococcus aureus* (n=4), *Staphylococcus*  
182 *pseudintermedius* (n=3), *Streptococcus canis* (n=2), *Streptococcus agalactiae* (n=1) and a  
183 multi-organism culture (*E.coli*, *Enterococcus faecalis*, *Staphylococcus pseudintermedius*)  
184 (n=1). Antibiotic therapy had been given in 3/21 cases prior to referral and subsequent culture  
185 and sensitivity results; two of these (both post-TPLO infection), subsequently had a positive  
186 synovial fluid culture. Urinalysis was performed in 5/21 cases with a positive (*S. aureus* and  
187 *E. coli*) urine culture in two of these (Case 1 and 7). In Case 7, bacteria isolated from the bladder  
188 (*S. aureus*) matched the synovial fluid suggesting a haematogenous origin. Dogs were treated  
189 either medically with antibiotics only (n=16), or surgically by joint lavage and antibiotics (n=2,  
190 cases 5 and 7), or arthroscopy, joint lavage and antibiotics (n=3, cases 6, 9 and 10). Joint lavage  
191 involved placement of an ingress and egress needle and flushing of the joint with 1-2 litres of  
192 isotonic solution. The decision in treatment strategy was determined by the clinician at the time  
193 of diagnosis. In cases for which arthroscopy was performed (cases 6,9 and 10) arthroscopy,  
194 this was justified to manage concurrent medial compartment disease of the elbow. Antibiotic  
195 therapy included amoxicillin/clavulanic acid<sup>f</sup> (n=12), amoxicillin/clavulanic acid<sup>f</sup> and  
196 enrofloxacin<sup>g</sup> (n=6), cephalexin<sup>h</sup> and enrofloxacin<sup>g</sup> (n=1), cephalexin<sup>h</sup> (n=1). For all 11 elbows  
197 with a recorded antibiotic sensitivity, the instigated empirical antibiotic therapy was  
198 appropriate. Antibiotic therapy was continued for a mean of six weeks +/- 1.7 weeks.

199

200 Short-term follow-up information (<8 weeks) was available for 18/21 elbows. Of the dogs for  
201 which further information was not available, two were euthanatised whilst hospitalised due to  
202 deterioration in their condition and one was lost to follow-up. In all dogs that survived to  
203 discharge there was an improvement from pre-treatment lameness score [pre-treatment 7.5/10  
204 (range 1-10) vs post-treatment 3/10 (range 1-5)] within the treatment period. Cases that had  
205 surgical management (n=5) had pre-treatment lameness of 7/10 (range 1 – 10) vs post-treatment  
206 4.5/10 (range 1 – 5). Those that were managed medically had pre-treatment lameness of 9/10  
207 (range 1-10) vs post-treatment 3/10 (range 2-5). Case 9 had an acute deterioration in lameness  
208 five days after cessation of a four week antibiotic course (amoxicillin/clavulanic acid) and a  
209 subsequent repeat culture and sensitivity revealed ongoing infection (*S. pseudintermedius*).  
210 This dog subsequently improved with additional antibiotic therapy (cephalexin<sup>h</sup>) for eight  
211 weeks but had residual lameness (1-2/10) at its last follow-up 12 months after diagnosis.

212

213 Medium to long-term follow (>8weeks) information was available for 12/21 cases (median 57  
214 weeks; range: 14 weeks – 7 years). Recurrence of infection was recorded in 3/12 (25%)  
215 occurring at 14 weeks (Case 4), 1.2 years (Case 1) and 3.8 years (Case 6) after original  
216 diagnosis. Initial treatment in these three cases had included antibiotic therapy only in cases 1  
217 and 4, and arthrotomy, joint lavage and antibiotic therapy in case 6. Residual lameness  
218 attributable to the elbow joint, based on owner follow-up was seen in 11/12 cases. The median  
219 lameness score was 3/10 (range 2 – 5). Case 8 had progressive ongoing lameness that was  
220 treated with total elbow replacement at another referral institution.

221

222 **Discussion:**

223 This is the first retrospective case series to focus solely on spontaneous septic arthritis of the  
224 canine elbow. It was the authors' experience that the elbow is one of the most common joints  
225 to spontaneously develop septic arthritis, when excluding surgical site associated infections  
226 (<1 month prior if no implants, <1 year if implants present) (10). A preliminary review of all  
227 cases of septic arthritis was performed during data collection for this manuscript. Fifty cases  
228 of spontaneous septic arthritis were identified during the study period and the elbow had the  
229 highest prevalence within this group (21/50, 42%). In a similar smaller retrospective series,  
230 when recent surgical cases were removed, the elbow was again the predominant joint, 8/14  
231 cases (57%) (5).

232

233 In people, certain conditions are considered risk factors including rheumatoid arthritis or  
234 osteoarthritis, old-age, skin infection, cutaneous ulcers, diabetes, joint prosthesis, intra-  
235 articular corticosteroid injection and intravenous drug abuse (4, 15-17). These risk factors  
236 appear to be in accordance with our findings in dogs in that 85% of dogs were middle aged or  
237 older (mean age 6.8 years), and pre-existing osteoarthritis was present in 93% of cases in which  
238 imaging of the elbow was available, and concurrent medical conditions in 43% of our case  
239 population. Both ALL and anal furunculosis are treated with immunosuppressive therapy and  
240 it is likely the conditions and/or the treatment had contributed to the risk of septic arthritis  
241 developing in cases 6 and 14 (15). The presence of a transcondylar screw in case 17 potentially  
242 contributed to the development of infection. Surgical implants can act as a nidus for infection  
243 and subsequent removal of the implant and prolonged antibiotic therapy resulted in clinical  
244 improvement in case 17.

245

246 The main clinical signs seen in dogs with spontaneous septic arthritis of the elbow joint was  
247 joint effusion (100%), pain on joint manipulation (100%), and acute deterioration in lameness

248 (76%). Pyrexia was an inconsistent clinical finding (6/21- 29%), similar to a previous case  
249 series (19.4%) (5), although notably lower than post-surgical stifle sepsis (75%) (6). In this  
250 study, large breed dogs and breeds with a susceptibility to elbow dysplasia were most common  
251 (80%), likely reflecting a higher degree of underlying joint disease and osteoarthritis in these  
252 groups. In non-immunocompromised people, pre-existing joint disease is often identified, with  
253 osteoarthritis accounting for 33% of joint disorders (8, 17). Radiographic evaluation was  
254 available for 15 cases in the present series, and of these 14/15 (93%) had evidence of  
255 osteoarthritis. The high prevalence (11/15 cases, 73%) of severe radiographic OA, as found in  
256 our study, is in accordance with previous reports in which severe OA was present in 5/8  
257 (62.5%) elbows (5).

258

259 A positive bacterial culture was obtained for 52% of cases, consistent with previous reports of  
260 variable positive culture rates (20-80%) (3,5,9,18). Interestingly, the use of antibiotic therapy  
261 prior to culture in three cases did not appear to affect outcome. In 2/3 cases given antibiotic  
262 therapy prior to sampling, two still had a positive culture. There is conflicting information in  
263 the literature regarding the influence of antibiotics on culture success. Pre-culture antibiotic  
264 therapy has been linked with false-negative results in several studies, whilst others have  
265 reported no difference in culture success (3,5,9). Despite this, current recommendations are to  
266 perform arthrocentesis prior to initiation of antibiotic therapy. In this study, *Staphylococcus*  
267 *spp.* were the most common bacteria isolated (63.6%) followed by *Streptococcus spp* (27%),  
268 which is similar to previous reports ranging from 42-59% (5-6) and 16-24% respectively (3).  
269 Two dogs had positive urine cultures, with one dog having similar bacteria isolated from both  
270 urine and synovial fluid. This finding highlights the importance of evaluating all potential  
271 sources of bacteria when a haematogenous origin is suspected. Importantly, 48% of elbows in  
272 the present study had a negative culture and relied on a presumptive diagnosis based on high

273 TNCC, predominance of polymorphonuclear cells and response to therapy. In two elbows the  
274 TNCC was below the cut-off value for septic arthritis ( $50 \times 10^9$  cells/L), however they were  
275 included in the study based on other criteria: a high percentage of neutrophils, response to  
276 antibiotic therapy and subsequent culture results in one elbow (11). The presence of a  
277 monoarthropathy with a predominantly neutrophilic cytology from synovial fluid sampling  
278 may be the only indication of septic arthritis/infection. This can make diagnosis and ruling out  
279 conditions like immune-mediated polyarthropathies challenging. To that end, other diagnostic  
280 tests have been sought, such as molecular methods (bacterial rRNA gene sequencing), analysis  
281 of synovial lactate concentration and use of leukocyte esterase and glucose reagent strips (18-  
282 21). However, even these new avenues for diagnosis are not without constraints, with  
283 comparisons between synovial fluid culture and rRNA PCR analysis not being able to  
284 demonstrate improved accuracy in diagnosis, and a wide reported 95% confidence interval in  
285 the sensitivity of lactate to predict septic arthritis (Sensitivity 1.00, 95% CI: 0.63-1.00) (18,  
286 21). Currently, synovial fluid inoculation into blood culture media, synovial biopsy and  
287 cytology examination are recommended (22, 27, 29, 30).

288

289 The vast majority of septic elbows were treated by antibiotic therapy alone. The initial response  
290 to treatment was very good (94% resolution) and there was no difference in the response  
291 between cases treated with antibiotics alone compared to cases that had joint lavage and/or  
292 arthrotomy. This finding concurs with previous studies suggesting non-surgical management  
293 with antibiotic therapy alone (3,6,23) is sufficient due to the excellent blood supply to joints.  
294 Skeletally immature patients, which were not part of this cohort, may have different  
295 considerations due to the vulnerable nature of the open physes to pressure, and hence, we do not  
296 have the evidence here to conclude that surgical management may not be needed. However,  
297 this conclusion should be interpreted with caution due to low case numbers and potential for

298 clinical treatment selection bias. Failure of treatment in case 9 was likely due to insufficient  
299 antibiotic treatment duration (four weeks) or inappropriate initial antibiotic implementation.  
300 Selection of surgical management may also have been reserved for more severely affected  
301 cases increasingly the risk of recurrence. However the retrospective nature of this report does  
302 not allow further investigation of this potential bias. Subsequent extended treatment in case 9  
303 with cephalexin resulted in clinical resolution and a significant improvement in lameness  
304 (20mg/kg orally twice daily for eight weeks). Long term follow up in 12 cases revealed a 25%  
305 recurrence of infection which is higher than that found in a previous smaller case series (5).  
306 The high rate of recurrence in the elbow contrasts to that reported for septic arthritis of other  
307 joints such as the hip joint (0%), stifle (7%), or hock (0%) (4,23). In this series, recurrence  
308 occurred 14 weeks (case 4), 1.2 years (case 1) and 3.8 years (case 6) after initial diagnosis. The  
309 long periods between remission and recurrence are less suggestive of recrudescence of  
310 incompletely resolved infection and more likely a result of renewed inoculation of a vulnerable  
311 and compromised joint. However, it does remain possible that recurrence of infection may be  
312 a result of quiescent bacteria remaining in the joint post-antibiotic treatment, or could represent  
313 haematogenous reseeding from the same or a new focus elsewhere in the body and an  
314 underlying predisposition to infection (24,28). Case 4 may represent a late relapse due to  
315 insufficient antibiotic therapy duration (6 weeks), or represent a recurrence of infection since  
316 deterioration in lameness occurred following a period of eight weeks of minimal reported  
317 lameness. Both cases 1 and 6 had predisposing factors for joint infection (diabetes mellitus  
318 and skin/urinary infection) and likely represent true recurrence in a predisposed joint. It is  
319 postulated that synovial vascular changes present in OA joints predisposes them to initial  
320 colonisation, and re-colonisation post-treatment (11,24,31). In rheumatoid patients and OA  
321 human patients, altered joint structure, including thinner vascular canals associated with  
322 increased subchondral plate thickness, increased osteochondral vascular density may

323 contribute to bacterial seeding and an increased risk of infection (31). Analysis of both the  
324 migratory and phagocytic function of polymorphocuclear cells in the synovial fluid of humans  
325 with osteoarthritis has shown a decreased function compared to rheumatoid patients. The  
326 altered function and potential anomalous joint structure may help to explain a component of  
327 the increased susceptibility of osteoarthritic patients to joint infections (8,25,31), although we  
328 do not know if this is the case in the clinical canine patient.

329

330 A major limitation in this study is the retrospective design and reliance on assessing outcome  
331 from clinical records and low case numbers due to the relatively uncommon nature of this  
332 condition. The assessment of outcome is further compounded by the presence of pre-existing  
333 joint disease in the majority of dogs. Inclusion criteria were chosen to avoid the possible  
334 inclusion of non-infective cases based on previously described criteria (26). However, due to  
335 the low positivity from synovial culture, diagnosis of infection is often presumptive and may  
336 have resulted of inclusion of aseptic joints.

337

338 In conclusion, middle aged, large breed dogs, with pre-existing arthritis, that suffer an acute  
339 onset lameness, with elbow joint effusion and discomfort, even in the absence of pyrexia,  
340 should be considered for septic elbow arthritis. Antibiotic treatment is effective when  
341 prolonged treatment is instigated (6-8 weeks) appropriately however owners should be warned  
342 and veterinarians need to be aware of the potential for recurrence (3,5-6,24). Although there is  
343 evidence supporting a good early/short term response to medical therapy for septic arthritis,  
344 further evaluation of the long term outcome and recurrence rates for dogs treated medically or  
345 surgically is warranted. In addition, improving the ability to rapidly and accurately diagnose  
346 cases is critical to allow appropriate and early implementation of therapy to our patients.

347

348

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419

420 Appendix Legend:

421 Signalment, Presentation, Treatment and Outcome of 21 cases of spontaneous septic arthritis

422 presented to the contributing institutes between March 2007 and June 2015

423

424 Superscript:

425 a. Doxorubicin, Pfizer Ltd, UK

426 b. Vincristine, Hospira UK Ltd, UK

427 c. Cyclophosphamide, Baxter Healthcare Ltd., UK

428 d. Prednidale, Dechra, UK

429 e. Atopica, Elanco, UK

430 f. Noroclav, Norbrook Laboratories Ltd., North Ireland

431 g. Baytril, Bayer plc, UK

432 h. Cephacare, Animalcare Ltd, UK

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