Antimicrobial susceptibility patterns of bacterial isolates cultured from synovial fluid samples from horses with suspected septic synovitis: 108 cases (2008–2017)

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OBJECTIVE

To describe the antimicrobial susceptibility patterns of the most commonly isolated bacteria cultured from synovial fluid samples from horses with suspected septic synovitis treated at an equine referral hospital between May 1, 2008, and September 24, 2017.

SAMPLE

131 synovial fluid samples from 108 client-owned horses.

PROCEDURES

A retrospective medical record search was conducted to identify horses with suspected septic synovitis and results of synovial fluid bacterial culture and antimicrobial susceptibility testing. Data collected included signalment, known or suspected origin of synovial contamination, synovial structures affected, antimicrobial treatment, and results of synovial fluid cytologic evaluation and bacterial culture and susceptibility testing. Horses were grouped as adults (≥ 6 months old) or foals (< 6 months old).

RESULTS

Results of bacterial culture were positive for 34 of 70 (49%) and 18 of 61 (30%) samples from 68 adult horses and 40 foals, respectively. Gram-positive bacteria were more common in adult horses, whereas gram-negative bacteria were more common in foals. No multidrug-resistant microorganisms were identified. For adult horses, 92% (23/25) of gram-positive isolates tested with penicillin and gentamicin were susceptible to the combination. For foals, 94% (15/16) of isolates tested with penicillin, gentamicin, or both had susceptibility to 1 or both antimicrobials.

CONCLUSIONS AND CLINICAL RELEVANCE

Periodic review of bacterial profiles and antimicrobial susceptibility in horses with septic synovitis can help to detect early changes in bacterial pressure and antimicrobial resistance. Findings suggested that in the geographic area we serve, a combination of penicillin and gentamicin would be an effective empirical antimicrobial treatment for most horses with septic synovitis while results of bacterial culture and susceptibility are pending. (*J Am Vet Med Assoc* 2020;256;800–807)

Septic synovitis may develop as a result of direct contamination, either through a wound or iatrogenic contamination (eg, with synovial injection or arthroscopic surgery), or as a result of hematogenous spread of infectious agents. The latter occurs more commonly in foals and rarely in mature horses.[1,2] The diagnosis of septic synovitis, whether the affected synovial structure is a joint, tendon sheath, or bursa, is relatively straightforward, and a combination of patient history and results from clinical and cytologic examinations is often enough to reach a diagnosis. Once a diagnosis of septic synovitis has been established, rapid implementation of targeted treatment is essential to eliminate infection and to reduce primary and secondary damage to the synovial structures.[3] However, use of targeted antimicrobial treatment requires bacterial culture and antimicrobial susceptibility testing, which can take days, depending on the growth rate of the bacteria and the culture media used.[4] In addition, positive results for bacterial cultures performed on synovial fluid may vary from 25% (96/379) to 79% (71/90) depending on the culture method used.[1,5–7] Further, the timing in treatment is important in that a poorer prognosis has been associated with treatments started > 24 hours after the onset of clinical signs or after chronic infection is present.[3] For all of these reasons, clinicians treating horses with septic synovitis need to use local and systemic antimicrobial treatment empirically in combination with synovial lavage until results of bacterial culture and susceptibility testing are obtained. Empirical antimicrobial selection is usually made on the basis of clinical experience combined with reported information regarding bacterial isolates commonly involved in septic synovitis and antimicrobial susceptibilities of those isolates. Thus, periodic review of common isolates and suscep-

ABBREVIATIONS

MRSA	Methicillin-resistant *Staphylococcus aureus*
TMS	Trimethoprim-sulfamethoxazole

tibility profiles of etiologic agents of septic synovitis in horses of different geographic regions and hospital settings could be beneficial for the equine community. To the authors' knowledge, the last study[1] that specifically reviewed the antimicrobial profile of bacteria responsible for septic synovitis in adult horses in North America dates from 1992.

The objective of the study reported here was to describe the antimicrobial susceptibility patterns of the most commonly isolated bacteria cultured from synovial fluid samples from horses (adults vs foals) with suspected septic synovitis treated at an equine referral hospital in Quebec, Canada, between May 1, 2008, and September 24, 2017. We hypothesized that the bacterial species isolated would differ between foals and adult horses (consistent with a previous study[1]), the prevalence of *Streptococcus equi zooepidemicus* in adult horses would be higher than previously described,[1,5,6,8] and the bacterial isolates cultured would have low levels of antimicrobial resistance.

Materials and Methods

Case selection

A retrospective search was conducted of the Clinical Bacteriology Laboratory of the College of Veterinary Medicine of the University of Montreal database for records of horses from which a synovial fluid sample had been submitted for bacterial culture and antimicrobial susceptibility testing between May 1, 2008, and September 24, 2017. Data collected from the medical records included signalment (age, breed, and sex), hospital admission date, known or suspected origin of synovial contamination, antimicrobial treatment before admission, synovial structures affected, number of synovial structures from which samples were obtained and submitted for bacterial culture and susceptibility testing, duration of hospitalization, results of synovial fluid cytologic evaluation (if available), and results of bacterial culture and susceptibility testing. For the purpose of the study, horses were grouped as adults (≥ 6 months old) or foals (< 6 months old) because pathophysiologic processes in septic synovitis differ between the 2 age groups.[2]

Bacterial culture and susceptibility testing

Samples of synovial fluid were aseptically collected and placed in a diphasic blood culture system medium[a] or an evacuated glass tube without added anticoagulant. Diphasic medium samples were incubated at 35°C (95°F) for up to 5 days, with a subculture performed on 5% sheep blood agar as soon as bacterial growth was suspected. Between May 1, 2008, and September 1, 2017, bacterial identification was performed with traditional biochemical analysis and analytic profile index identification systems.[b,c] After September 1, 2017, a mass spectrophotometer[d] with matrix-assisted laser desorption ionization time-of-flight spectrometry was used. Susceptibility of all isolates was tested by use of an equine antimicrobial susceptibility panel with the Kirby-Bauer disk diffusion method, and interpretation of susceptibility results was performed according to standards.[9] Selection of the antimicrobial disks used in each test was based on the bacterial species isolated and current recommendations[9] at the time of the test.

Statistical analysis

Data collected were tabulated in a spreadsheet,[e] and calculations of descriptive statistics were performed. Two-sided confidence interval was set at 95% and calculated with a Wilson score interval for distribution of affected synovial structures, bacterial isolates, and antimicrobial susceptibility in each group (adults and foals).

Results

Samples

During the study period, 131 synovial fluid samples from 108 horses (68 adults and 40 foals) were submitted. Of these, 120 (92%) synovial fluid samples were submitted in a diphasic blood culture system medium, and 11 (8%) were submitted in evacuated glass tubes without added anticoagulant. Aerobic incubation was performed on samples from all 108 horses, and anaerobic incubation was also performed on samples from 3 horses. Of the 50 horses for which notation in the medical records addressed whether antimicrobials had been used for the condition before admission, 14 (28%; 12 adult horses and 2 foals) had received antimicrobials before admission to our facility.

Adult horses—From the 68 adult horses (median age, 5.0 years [range, 1.2 to 22.2 years]), 70 synovial fluid samples from 70 separate synovial structures were submitted for bacterial culture and susceptibility testing, and the overall period prevalence for positive results was 49% (34/70 synovial structures sampled) in adult horses (33/68 [49%]; **Table 1**). Alternatively, when only those samples that had results of cytologic

Table 1—Distribution of the 34 affected synovial structures in 33 adult horses (≥ 6 months old) with septic synovitis and positive results on bacterial culture of synovial fluid between May 1, 2008, and September 24, 2017.

Synovial structure	No. of synovial structures	Percentage (95% CI) of synovial structures
Tarsocrural joint	10	29 (17–46)
Metacarpo- or metatarsophalangeal joint	5	14 (6–30)
Digital flexor tendon sheath	4	12 (5–27)
Tarsal tendon sheath	4	12 (5–27)
Calcaneal bursa	4	12 (5–27)
Distal interphalangeal joint*	3	9 (3–23)
Femoropatellar joint	1	3 (1–15)
Femorotibial joint, medial aspect	1	3 (1–15)
Lateral digital extensor tendon sheath	1	3 (1–15)
Radiocarpal joint*	1	3 (1–15)

*One adult horse had a radiocarpal joint and a distal interphalangeal joint affected.
CI = Confidence interval.

evaluation compatible with septic synovitis (presence of bacterial elements alone or in combination with the presence of ≥ 2 of the following criteria: cellularity ≥ 30 X 10^9 cells/L, cellularity with ≥ 90% neutrophils, or total protein concentration ≥ 30 g/L) were considered, the period prevalence for positive results was 58% (32/55 synovial structures).

Of the 33 adult horses with positive results for bacterial culture and susceptibility testing on synovial fluid samples, 16 (48%) were geldings, 13 (39%) were mares, and 4 (12%) were stallions. Median age was 8.3 years (range, 1.2 to 22.2 years). On the basis of breed, horses were grouped as warmbloods (10/33 [30%]), American Quarter Horses (8 [24%]), Standardbreds (4 [12%]), Thoroughbreds (3 [9%]), draft breeds (2 [6%]), or other (6 [17%]). One female had 2 synovial structures (radiocarpal joint and distal interphalangeal joint) from which samples yielded positive results on bacterial culture and susceptibility testing.

Thirteen of 34 (38%) synovial structures from which bacteria were isolated had been infected for > 48 hours. Of the 9 samples submitted for joints recently treated with arthroscopy, 6 had positive results for bacterial culture and 5 were from tarsocrural joints. Two of these 5 horses had signs of colic and problems with their arthroscopic bandages before being readmitted for suspected septic arthritis. Origins of synovial contamination were attributed to penetrating wounds to synovial structures (25/34 [73%]), arthroscopy (6 [18%]), or intra-articular injection (3 [9%]).

Foals—From the 40 foals (median age, 21.7 days [range, 2 to 176 days]), 61 synovial fluid samples from 61 separate joints were submitted for bacterial culture and susceptibility testing, and the overall period prevalence for positive results was 30% (18/61 joints) in foals (17/40 [43%]; **Table 2**). However, the period prevalence was 58% (32/55) when limited to samples with cytologic evidence compatible with septic synovitis.

Of the 17 foals with positive results for bacterial culture and susceptibility testing on synovial fluid samples, 11 were fillies and 6 were colts. The median age was 14.6 days (range, 2 to 109 days). On the basis of breed, foals were grouped as warmbloods (n = 6), Standardbreds (4), draft breeds (4), American Quarter Horses (2), or Thoroughbred (1). Similar to the adult horses, 1 filly had synovial fluid samples from 2 joints (the radiocarpal joint and tarsocrural joint) that yielded positive results on bacterial culture. Origins of synovial contamination for the 18 affected joints in foals with positive results on bacterial culture were attributed to hematogenous spread (n = 13), penetrating wounds to a joint (4), or arthroscopy (1).

Table 2—Distribution of the 18 affected joints in 17 foals (< 6 months old) with septic synovitis and positive results on bacterial culture of synovial fluid between May 1, 2008, and September 24, 2017.

Synovial structure	No. of synovial structures	Percentage (95% CI) of synovial structure
Midcarpal or radiocarpal joint*	6	33 (20–50)
Tarsocrural joint*	5	28 (16–44)
Elbow joint	3	16 (8–32)
Femorotibial joint, medial aspect	2	11 (4–26)
Metacarpo- or metatarsophalangeal joint	1	6 (1–19)
Distal interphalangeal joint	1	6 (1–19)

*One foal had a radiocarpal joint and a tarsocrural joint affected.
CI = Confidence interval.

Bacterial isolates

Adult horses—Thirty-six bacterial isolates were cultured from 34 synovial fluid samples from adult horses, with pure growth of a single isolate in 32 (94%) samples **(Table 3)**. Gram-positive bacteria accounted for 30 of the 36 (83%) isolates, with the most common being *Streptococcus* spp (13/36 [36%]) and *Staphylococcus* spp (11/36 [31%]). Among the *Staphylococcus aureus* (4/36 [11%]) isolates, 1 MRSA was suspected because of the isolate's resistance to cefoxitin.[10] Of the gram-negative bacteria (5/36 [14%]) isolated from adult horses, those in the Enterobacteriaceae family (4/36 [11%]), particularly *Escherichia coli* (3/36 [8%]), were most common.

Foals—Bacterial culture performed on synovial fluid samples obtained from foals yielded a pure growth of a single isolate in each of the 18 samples that had positive results **(Table 4)**. Most of the isolates were gram-negative bacteria (13/18 [72%]), with the most common being *Actinobacillus* spp (8/18

Table 3—Summary results of bacterial cultures performed on synovial fluid samples of synovial structures with suspected septic synovitis in adult horses described in Table 1.

Bacterial identification	No. of adult horses	Percentage (95% CI) of adult horses
Gram-positive	30	83 (68–92)
Streptococcus spp	13	36 (22–52)
β-Hemolytic *Streptococcus* spp	10	28 (16–44)
Streptococcus equi subsp *zooepidemicus*	9	25 (14–41)
Streptococcus dysgalactiae subsp *equisimilis*	1	3 (0–14)
α-Hemolytic *Streptococcus* spp	3	8 (3–22)
Staphylococcus spp	11	31 (18–47)
Coagulase-positive *Staphylococcus* spp	7	19 (10–35)
Staphylococcus aureus	4	11 (4–25)
Coagulase-negative *Staphylococcus* spp	2	6 (2–18)
Enterococcus spp	5	14 (6–29)
Enterococcus faecium	1	3 (0–14)
Rhodococcus spp	1	3 (0–14)
Gram-negative	5	14 (6–29)
Enterobacteriaceae	4	11 (4–25)
Escherichia coli	3	8 (3–22)
Hemolytic *E coli*	1	3 (0–14)
Klebsiella oxytoca	1	3 (0–14)
Bacillus spp	1	3 (0–14)
Unknown	1	3 (0–14)

CI = Confidence interval.

[44%]) and bacteria in the Enterobacteriaceae family (5/18 [28%]). *Streptococcus* spp (4/18 [22%]) were the most commonly isolated gram-positive bacteria from affected joints in foals.

Antimicrobial susceptibility

Adult horses—Results of susceptibility testing of gram-positive bacterial isolates cultured from synovial samples from adult horses indicated that most had susceptibility to β-lactam antimicrobials (18/23 [78%] susceptible to penicillin and 19/21 [90%] susceptible to ceftiofur; **Table 5**). Further, results for 23 of 25 (92%) gram-positive isolates tested with the combination of penicillin and gentamicin indicated susceptibility to the combination. Results indicated that *Streptococcus* spp, the most commonly identified bacteria cultured from synovial fluid of adult horses, were particularly susceptible to β-lactam antimicrobials, with 10 of the 11 tested isolates susceptible to penicillin and all 11 tested isolates susceptible to ceftiofur. Susceptibility of *Streptococcus* isolates to aminoglycosides was not tested because of the intrinsic low-level resistance of *Streptococcus* spp to aminoglycosides.[11] Of the *Staphylococcus* spp (the second most common isolates cultured from adult horses), 5 of 8 tested isolates had susceptibility to penicillin and 7 of 8 tested isolates had susceptibility to ceftiofur. However, all isolates of *Staphylococcus* spp tested with amikacin (n = 8) or TMS (8) had susceptibility to the drugs. Among all *S aureus* isolates (n = 4), results indicated that only 1 isolate was resistant to cefoxitin, which is a surrogate marker for MRSA identification.[10] None of the other isolates cultured from the adult horses was suspected to have had multidrug resistance.

No susceptibility to erythromycin or rifampin was detected among the gram-negative isolates tested (Table 5). Further, only 1 of 3 gram-negative isolates tested had susceptibility to ampicillin, and only 2 of 3 gram-negative isolates tested had susceptibility to TMS. Because of the small number of gram-negative bacterial isolates and tests performed, further statistical analysis was not practical.

Foals—Results indicated that 15 of the 16 isolates tested with penicillin, gentamicin, or both had susceptibility to 1 or both antimicrobials **(Table 6)**. Antimicrobial susceptibility of gram-negative isolates (most commonly cultured from the synovial samples from foals) to β-lactam antimicrobials was detected in 8 of 10 isolates tested with penicillin

Table 4—Summary results of bacterial cultures performed on synovial fluid samples obtained from the foals described in Table 2.

Bacterial identification	No. of foals	Percentage (95% CI) of foals
Gram-positive	5	28 (12–51)
Streptococcus spp	4	22 (9–45)
β-Hemolytic *Streptococcus* spp	3	17 (6–39)
Streptococcus equi zooepidemicus	2	11 (3–33)
α-Hemolytic *Streptococcus* spp	1	6 (1–26)
Gram-positive coryneform bacilli	1	6 (1–26)
Gram-negative	13	72 (49–88)
Enterobacteriaceae	5	28 (12–51)
Escherichia coli	1	5 (1–26)
Hemolytic *E coli*	1	5 (1–26)
Enterobacter spp	3	17 (6–39)
Enterobacter cloacae	2	11 (3–33)
Proteus mirabilis	1	6 (1–26)
Actinobacillus spp	8	44 (25–66)
Actinobacullus equuli	7	39 (20–61)
Unknown	0	0 (0–18)

CI = Confidence interval.

Table 5–Summary results of Kirby-Bauer disk diffusion testing antimicrobial susceptibility of the bacterial isolates cultured from synovial samples from adult horses described in Table 1.

	Streptococcus spp			*Staphylococcus* spp			Other gram-positive spp			Enterobacteriaceae		
Antimicrobial	T	S	Percentage S (95% CI)	T	S	Percentage S (95% CI)	T	S	Percentage S (95% CI)	T	S	Percentage S (95% CI)
Amikacin	—	—	—	8	8	100 (68–100)	2	1	50 (9–91)	3	3	100 (44–100)
Ampicillin	2	2	100 (34–100)	11	5	46 (21–72)	5	3	60 (23–88)	3	1	33 (6–79)
Cefazoline	—	—	—	11	5	46 (21–72)	1	1	100 (21–100)	1	1	100 (21–100)
Cefoxitine	—	—	—	4	3	75 (30–95)	—	—	—	1	1	100 (21–100)
Ceftiofur	11	11	100 (74–100)	8	7	88 (53–98)	2	1	50 (9–91)	3	3	100 (44–100)
Chloramphenicol	6	4	67 (30–90)*	8	7	88 (53–98)	5	4	80 (38–96)	3	3	100 (44–100)
Clarithromycin	—	—	—	1	1	100 (21–100)	—	—	—	—	—	—
Enrofloxacin	—	—	—	8	7	88 (53–98)*	5	2	40 (12–77)*	3	3	100 (44–100)
Erythromycin	11	8	73 (43–90)*	8	7	88 (53–98)	5	2	40 (12–77)*	2	0	0 (0–66)
Gentamicin	—	—	—	8	6	75 (41–93)	2	1	50 (9–91)	3	3	100 (44–100)
Oxacillin	—	—	—	4	3	75 (30–95)*	1	1	100 (21–100)	—	—	—
Penicillin	11	10	91 (62–98)	8	5	63 (31–86)	4	3	75 (30–95)	2	0	0 (0–66)
Rifampin	—	—	—	8	8	100 (68–100)	5	1	20 (4–62)*	3	0	0 (0–56)
Tetracycline	7	2	29 (8–64)	4	3	75 (30–95)	1	1	100 (21–100)	2	2	100 (34–100)
TMS	11	6	55 (28–79)	8	8	100 (68–100)	1	1	100 (21–100)	3	2	67 (21–94)

*Intermediate susceptibility was considered as resistance.
— Not tested. CI = Confidence interval. S = Number of isolates with susceptibility. T = Number of isolates tested.

Table 6—Summary results of Kirby-Bauer disk diffusion testing antimicrobial susceptibility of the bacterial isolates cultured from synovial samples from foals described in Table 2.

	Streptococcus spp			Enterobacteriaceae			*Actinobacillus* spp		
Antimicrobial	T	S	Percentage S (95% CI)	T	S	Percentage S (95% CI)	T	S	Percentage S (95% CI)
Amikacin	—	—	—	5	4	80 (38–96)	8	7	88 (53–98)*
Ampicillin	1	1	100 (21–100)	5	1	20 (4–62)	8	8	100 (68–100)
Cefazoline	—	—	—	5	1	20 (4–62)	4	4	100 (51–100)
Ceftiofur	3	3	100 (44–100)	5	3	60 (23–88)	8	8	100 (68–100)
Chloramphenicol	2	2	100 (34–100)	5	2	40 (12–77)*	8	8	100 (68–100)
Clarithromycin	—	—	—	2	0	0 (0–66)	1	0	0 (0–79)*
Enrofloxacin	—	—	—	5	4	80 (38–96)*	8	8	100 (68–100)
Erythromycin	3	3	100 (44–100)	—	—	—	7	2	29 (8-64)*
Gentamicin	—	—	—	5	4	80 (38–96)	8	8	100 (68–100)
Oxacillin	—	—	—	2	1	50 (9–91)	1	0	0 (0–79)
Penicillin	3	3	100 (44–100)	2	0	0 (0–66)	8	8	100 (68–100)
Rifampin	—	—	—	5	0	0 (0–43)	8	6	75 (41–93)*
Tetracycline	2	0	0 (0–66)*	1	0	0 (0–79)	5	5	100 (57–100)
TMS	3	2	67 (16–95)	5	4	80 (38–96)	8	8	100 (68–100)

See Table 5 for key.

and in 11 of 13 isolates tested with ceftiofur. Results for all isolates of *Actinobacillus* spp (n = 8) tested with penicillin (8), ceftiofur (8), gentamicin (8), enrofloxacin (8), TMS (8), or tetracycline (5) indicated susceptibility to the drugs. Of the Enterobacteriaceae isolates, 3 of the 5 isolates had susceptibility to ceftiofur, and 1 of 2 isolates tested with oxacillin was susceptible to it.

In foals, the only isolates of gram-positive bacteria (n = 5) tested for antimicrobial susceptibilities were isolates of *Streptococcus* spp (4). Of these, all isolates tested with penicillin (n = 3), ceftiofur (3), erythromycin (3), or chloramphenicol (2) had susceptibility to the drugs. However, neither of the 2 isolates of *Streptococcus* spp had susceptibility to tetracycline.

Discussion

Results of the present study provided updated information regarding the antimicrobial susceptibility patterns of bacterial species identified in horses with suspected septic synovitis treated at a referral hospital in Quebec, Canada, between May 1, 2008, and September 24, 2017, and, by extension, updated previously reported[1] bacterial profiles for septic synovitis in horses in North America. Our findings could guide clinicians in their empirical antimicrobial choice to treat septic synovitis in horses during the crucial period when bacterial culture results are pending.

Our findings indicated that a positive result for bacterial culture was obtained for 49% (34/70) of synovial structures with suspected septic synovitis in adult horses. The low period prevalence was compatible with findings in previous studies[1,5–7] (25% [96/379] to 79% [71/90]), among which study design seems to be the main reason for the wide variation in prevalence reported. The present study, as did other studies[5,6] with comparatively low prevalences (25% [96/379] to 33% [67/206]), included all synovial fluid samples sent for bacterial culture and susceptibility testing. It was therefore understandable that some samples were of noninfected synovial structures, resulting in a reduced proportion of positive results on bacterial culture. Conversely, studies[1,7] with higher prevalences only included synovial samples obtained from horses with septic synovitis confirmed with clinicopathologic results. However, when we considered bacterial culture results for those synovial structures with documented cytologic characteristics compatible with sepsis in the present study, the period prevalence for positive results on bacterial culture would have been 58% (32/55). Unfortunately, the retrospective nature of our study prevented us from accurately determining the status of cytologic criteria compatible with septic synovitis for all horses and structures sampled. In addition, duration of the condition might have affected the number of positive results for bacterial culture in the present study. Although, to our knowledge, there was no information in this regard for horses, chronicity of sepsis in humans seems to worsen the diagnostic sensitivity for septic synovitis by 34%.[12] In our study, 38% (13/34) of the synovial structures sampled in adult horses had been infected for > 48 hours. Furthermore, 28% (14/50) of all horses in the present study received antimicrobials before hospital admission, which could have further affected bacterial culture results. In addition, we used culture medium that did not contain antimicrobial-absorbing resin or sodium polyanethole sulphonate, and use of such may have also affected bacterial culture results for horses previously treated with antimicrobials.[13] In contrast, the use a diphasic blood culture system[f] that includes antimicrobial-absorbing resin may increase the proportion of synovial fluid samples with positive results for bacterial culture.[7]

For foals of the present study, the period prevalence of positive results on bacterial culture of synovial structures with suspected septic synovitis was 30% (18/61), which was markedly lower than pre-

viously reported prevalences (83% [33/40] to 86% [60/70]).[1,14] Our refrain from using antimicrobial-absorbing resin nor agitating the culture medium during the culture process could partially explain the difference; however, further investigation is needed to better explain the difference.

Not surprisingly, our hypothesis that the bacterial species isolated would differ between foals and adult horses was confirmed with our finding that isolates were mainly gram-positive (30/36 [83%]) for the adult horses, compared with mainly gram-negative (13/18 [72%]) for foals. Differences in pathogenesis of septic synovitis in foals versus adult horses could have explained this. In foals, privileged hematogenous dissemination of bacterial emboli to joints may occur because of the presence of transphyseal vessels that allow spreading of bacteria into the joints,[2,14] especially in joints with close contact to ≥ 1 physes, such as the 5 tarsocrural joints and 2 joints in the stifle region affected with septic synovitis in foals of the present study.

The origin of septic synovitis was a wound to the synovial structure in 74% (25/34) of affected structures in adult horses of the present study. Previous studies[5,6] also highlight wounds as the main underlying factor in 75% (155/206) to 86% (82/95) of adult horses; however, septic synovitis after intra-articular injection seems to be more predominant in previous literature.[1] Findings for adult horses in the present study indicated that septic synovitis occurred after arthroscopy for 18% (6/34) of the synovial structures with positive results on bacterial culture, which was higher than previously reported (4% [4/95] to 13% [25/192]).[1,5] Five of the 6 synovial structures with postoperative septic synovitis in the present study occurred after surgery at our institution; however, these 5 affected structures (1 structure each in 5 horses) represented approximately 0.5% of all arthroscopic procedures performed (approx 1,080 joints treated in 954 horses) in our hospital during the study period, and the proportion of affected joints was similar to proportions previously described (0.5% [3/636] to 0.9% [8/932]).[15,16] Therefore, the high proportion of septic synovitis identified following arthroscopy in the present study could have been because of the relatively low proportion of samples overall with positive results for bacterial culture (49% [34/70]) or the high proportion of samples from synovial structures treated with arthroscopy that later had positive results for bacterial culture (6/9 [67%]).

Our results regarding the most commonly affected synovial structures in adult horses were in concordance with previous studies.[1,5,6,15] The tarsocrural joint, metacarpo- or metatarsophalangeal joint, and digital flexor tendon sheath were overrepresented. This was not surprising because these locations are commonly affected in horses with penetrating wounds. In addition, the finding that most (5/6) joints affected with septic synovitis following arthroscopy were tarsocrural joints was consistent with results of a previous study[15] and has been suggested to be associated with difficulties in maintaining bandages over the treated joint after surgery, as was noted in 2 of the 5 horses in the present study.

Our finding that *S equi zooepidemicus* accounted for 25% (9/36) of the isolates from the adult horses was markedly higher than proportions previously reported (0.9% [1/114] to 10% [7/67]),[1,5,6,8] with the exception of a study[17] from western Canada, in which 50% (6/12) of isolates following orthopedic surgery (eg, fracture fixation, arthroscopy, and arthrocentesis) and intra-articular injections were *S equi zooepidemicus*. This discrepancy could have been explained by differences in geographic conditions or bacterial populations (alone or in combination) present in Canada. Another possible explanation could have been a consequence of organizational differences among veterinary care systems (primary or secondary referral) in various countries. For instance, a higher proportion of isolates cultured from synovial fluid may be *Staphylococcus* spp (41% [48/116] to 42% [48/114]) at tertiary care institutions in the United States or Europe, owing to progressive bacterial selection.[1,5,6]

Most of the gram-positive bacterial isolates cultured from synovial fluid samples obtained from adult horses in the present study had susceptibility to penicillin or aminoglycosides, which supported the use of this antimicrobial combination as first-line treatment for horses with septic synovitis. In fact, results of Kirby-Bauer antimicrobial susceptibility testing suggested that the combination of penicillin and gentamicin would be effective in vitro against 92% (23/25) of the isolates tested with both antimicrobials. In healthy horses, there is good intrasynovial diffusion of β-lactams and aminoglycosides, yet with a slight delay to peak plasma concentration after IV administration.[18] In contrast, antimicrobials administered IV to horses with inflamed synovium penetrate synovial structures quicker and achieve higher antimicrobial concentration in the synovial fluid, probably because of the higher blood flow in affected joints (versus heathy joints),[19] and this phenomenon is further enhanced when antimicrobials are administered with IV regional limb perfusion.[20]

Important to note was that in the adult horses, results of culture and susceptibility testing indicated that all 8 *Staphylococcus* isolates tested with TMS were susceptible to the drug, whereas 5 of the 11 *Streptococcus* isolates tested with TMS were resistant to the drug. In addition to this in vitro resistance, it is important to recall that TMS is unlikely to have appropriate in vivo activity against *Streptococcus* spp and is therefore not usually recommended. The efficacy of TMS decreases in purulent medium owing to such medium's generally low pH and high concentrations of *p*-aminobenzoic acid.[21]

Most isolates cultured from synovial fluid samples from foals in the present study were gram-negative bacteria that were *Actinobacillus* spp (n = 8) or bacteria in the Enterobacteriaceae family (5). For unknown reasons, these findings were opposite of

findings in previous studies[1,14] in which Enterobacteriaceae isolates are more common than *Actinobacillus* spp. Results of susceptibility testing on isolates of *Actinobacillus* spp and bacteria in the *Enterobacteriaceae* family cultured from foals had susceptibility to most of the antimicrobials tested and commonly used in equine practice. However, Enterobacteriaceae isolates generally have an unpredictable resistance profile, are not host specific, and can transfer numerous mobile genetic elements, conferring resistance between bacteria of the same or different species.[22] Our findings on susceptibility testing indicated that 15 of the 16 isolates cultured from foals and tested with penicillin, gentamicin, or both had susceptibility to 1 or both antimicrobials. This proportion of isolates with susceptibility to a combination of penicillin and gentamicin was higher in the present study than previously reported.[14]

No multidrug-resistant bacteria were detected in the present study; however, 1 instance of MRSA was suspected because of an isolate's resistance to cefoxitin.[10] These findings were consistent with a recent study[23] that shows no increase in antimicrobial resistance, except for an increase in resistance of coagulase-positive *Staphylococcus* spp to TMS, over 3 time periods spanning from 1986 to 2013 at our hospital.[23] A previous Canadian study[17] also shows that antimicrobial resistance is not common and that multidrug-resistant bacteria are rare. Nonetheless, the risks and consequences of MRSA outbreaks in veterinary hospitals are still present and should not be underestimated, particularly in view of the close proximity of horses and people in the provision of veterinary care to horses.[24,25]

Results of the present study indicated that septic synovitis in foals was primarily from hematogenous spread of gram-negative bacteria, with a predominance of *Actinobacillus* spp and bacteria in the Enterobacteriaceae family, whereas the condition in adult horses was mainly from wounds that inoculated gram-positive bacteria in synovial structures in the distal aspects of the limbs. S*treptococcus* spp (especially *S equi zooepidemicus*) and *Staphylococcus* spp were overrepresented. Results of antimicrobial susceptibility testing indicated that antimicrobial resistance was not a problem with the bacteria isolated in the present study. Our findings suggested that in the geographic area we served, a combination of penicillin and gentamicin would be an effective empirical antimicrobial treatment for most horses with septic synovitis while results of bacterial culture and susceptibility are pending. Periodic review of bacterial profiles and antimicrobial susceptibility in horses with septic synovitis can help to detect early changes in bacterial pressure and antimicrobial resistance in different geographic locations or hospital settings, alone or in combination.

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Footnotes

a. BC0102M, Oxoid, Thermo Fisher Scientific Inc, Whaltham, Mass.
b. API 20E, bioMérieux SA, Marcy-l'Etoile, France.
c. API Strep, bioMérieux SA, Marcy-l'Etoile, France.
d. Microflex LRF, Bruker Scientific LLC, Billerica, Mass.
e. Excel, Microsoft Corp, Santa Rosa, Calif.
f. BACTEC Peds Plus/F, Becton, Dickinson and Co, Sparks, Md.

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From this month's *AJVR*

Evaluation of dose-response effects of short-term oral prednisone administration on clinicopathologic and hemodynamic variables in healthy dogs

Rebecca L. Tinklenberg et al

OBJECTIVE
To determine whether a dose-response relationship exists between short-term oral prednisone administration and common clinicopathologic variables, cardiovascular biomarkers, and systolic arterial blood pressure (SAP) in healthy dogs.

ANIMALS
8 healthy Beagles.

PROCEDURES
Dogs underwent five 5-day experiments (no prednisone treatment [control condition] and prednisone administration at 0.5, 1, 2, and 4 mg/kg, PO, q 24 h), with a 9-day washout period between protocols. Analyses performed before and after treatments included a CBC, serum biochemical analysis, and determination of SAP, fractional excretion of electrolytes, urine protein-to-creatinine ratio, glomerular filtration rate (GFR), serum N-terminal pro B–type natriuretic peptide (NT-proBNP) and plasma cortisol concentrations, and plasma renin activity. Linear mixed-effects modeling was used to compare changes in variables from baseline (day 1 for the same experiment) among treatment conditions.

RESULTS
Changes in serum glucose concentration and GFR were significantly greater after administration of prednisone at 4 mg/kg than for the control condition. Fractional excretion of sodium was decreased from baseline when dogs received 0.5, 1, or 4 mg of prednisone/kg, compared with results for the control condition. Several expected changes in clinicopathologic values were observed after prednisone administration at any dosage. Changes in serum NT-proBNP concentration, plasma renin activity, and SAP did not differ from changes for the control condition at any prednisone dosage.

CONCLUSIONS AND CLINICAL RELEVANCE
Oral prednisone administration did not affect SAP, NT-proBNP concentration, or measures of renin-angiotensin-aldosterone system activation in healthy laboratory-housed dogs but was associated with relative increases in GFR and serum glucose concentration. (*Am J Vet Res* 2020;81:317–325)

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