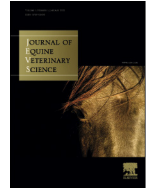
Journal of Equine Veterinary Science 55 (2017) 115–122

Contents lists available at ScienceDirect

Journal of Equine Veterinary Science

journal homepage: www.j-evs.com



Review Article

Update on Managing Serious Wound Infections in Horses: Wounds Involving Joints and Other Synovial Structures

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ARTICLE INFO

Article history:
Received 6 October 2016
Received in revised form 25 January 2017
Accepted 25 January 2017
Available online 2 February 2017

Keywords:
Antibiotics
Horse
Immune system
Infections
Wounds

ABSTRACT

Antibiotics may fail to abolish an infection in synovial structures for several reasons: (1) inherent antibiotic resistance; (2) acquired antibiotic resistance; (3) inappropriate drug dosage, route or treatment duration; and (4) refugia. A strategy to include surgical debridement and ancillary treatments are discussed in eliminating infections of joints and other synovial structures.

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The first article of this series began an exploration of why some wound infections persist and progress despite seemingly appropriate treatment [1]. Examined in the article were the impacts of extensive contamination, bacterial refugia, immunocompromise (intrinsically and extrinsically imposed), and poor perfusion. This article continues with an examination of antibiotic resistance of the wound pathogen(s).

1. Antibiotic Resistance

Antibiotic therapy may fail to resolve an infection for one or more of the following reasons [2]

- Inherent antibiotic resistance—that is, inappropriate drug choice for the pathogen(s) involved.
- Acquired antibiotic resistance—for example, methicillin resistance in *Staphylococcus aureus* and aminoglycoside resistance in *Escherichia coli*; unlike inherent resistance, acquired resistance is unpredictable and may even develop during treatment.
- Inappropriate drug dosage, route, or duration of treatment—each may result in subtherapeutic antibiotic concentrations at the site of infection, even when the pathogen is susceptible in vitro.
- Poor perfusion—may also result in subtherapeutic antibiotic concentrations at the site of infection, even with an appropriate drug choice and dosage.
- Protection from inhibitory or lethal antibiotic concentrations by refugia.

The last two factors were discussed in the first article. The remainder of this paper focuses on antibiotic choices and modes of delivery for optimal effectiveness in horses with synovial sepsis.

1.1. Bacterial Culture

Whenever possible, antibiotic selection should be guided by bacterial culture and antibiotic susceptibility testing:

- Aseptically collect synovial fluid and appropriate tissue samples (e.g., synovial membrane, pannus, fibrinous

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0737-0806/$ – see front matter © 2017 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.jevs.2017.01.016

tags, fibrillated tendon, damaged articular cartilage) from the synovial space and separately from the overlying wound as well
- Submit synovial fluid samples in sterile blood culture tubes
- Request aerobic and anaerobic bacterial culture, and antibiotic susceptibility
- If available, request quantitative antibiotic susceptibility (reported as minimum inhibitory concentration [MIC])
- Repeat culture and susceptibility testing if clinical response is poor or signs of infection recur at any time during prolonged antibiotic therapy (weeks) and within a week of completing antibiotic therapy for polymicrobial or multidrug-resistant infections

Empiric antibiotic therapy is advised, while culture and susceptibility results are pending (see in the following section), but it is unwise to wait until the case is nonresponsive before performing culture and susceptibility testing. Not only does a positive culture and susceptibility result guide antibiotic therapy, but it also aids in prognosis. For example, Taylor et al [3] found that in horses with synovial sepsis, those with a positive synovial fluid culture were 19 times more likely to be euthanized during hospitalization than those with a negative culture.

It is an interesting paradox that synovial fluid culture is not always positive, even when the synovial structure is clearly contaminated (e.g., penetrating injury) or already septic (i.e., elevated synovial fluid white cell count and total protein, bacteria seen on Gram stain). In the clinical studies of synovial sepsis published in the past 15 years, positive culture rates varied from 24% [3] to 100% [4], although in most studies, positive culture rates were in the range of 55%–67% [4–9]. It would be reasonable to assume that positive culture rates would be higher with open wounds (particularly those at or below the fetlock), when there was a treatment delay of more than a day and when no antibiotics had been administered before culture. However, there were no clear patterns linking positive culture rates to cause or site, duration of contamination/sepsis, or prior antibiotic treatment.

Wereszka et al made an interesting observation that argues for in-house Gram staining on all synovial samples collected for culture. (That is, submit the samples as usual for culture and susceptibility but retain a portion for immediate Gram staining and microscopic examination.) In their study of horses with septic tenosynovitis, only 65% of the synovial fluid or tissue samples submitted for culture were positive, but Gram staining showed bacteria in 85% of the samples [7].

The reasons why only some contaminated/infected synovial samples yield positive cultures have not been fully explored, but they may include low numbers of bacteria (small amount of contamination and/or dilution effect of synovial effusion); fastidious organisms that are difficult to grow in culture; sequestration of bacteria in synovial tissues, neutrophils, or fibrin; and partially effective immune response which keeps bacterial numbers or viability low [3,5–7].

1.1.1. Culture Method

Another possible reason why synovial fluid culture may be negative in a horse with evident synovial contamination or sepsis relates to the culture method used. This aspect may be out of our control as clinicians, but it is worth having a basic understanding so that we can have educated discussions and make informed decisions about the microbiology laboratory we use for synovial cultures.

Using synovial fluid samples from horses clinically diagnosed with synovial sepsis, Dumoulin et al [10] compared an automated blood culture system (BACTEC) (BACTEC 9050, Becton, Dickinson and Company, Franklin Lakes, NJ) with four other methods of sample preparation and culture: (1) direct culture onto agar medium and culture onto agar after, (2) lysis and centrifugation, (3) conventional enrichment, or (4) lysis, centrifugation, and enrichment. Significantly more samples were positive with the BACTEC system than with any of the other culture methods; and culture results were available on the same day as culture onto agar and at 1 day sooner than with conventional enrichment.

In a related study, the same authors tested the BACTEC system in the clinical scenario of the severely inflamed, possibly infected joint [11]. Synovial fluid samples were tested from 220 severely inflamed joints, classified clinically as presumably infected ($n = 149$) or not infected ($n = 71$) based on history, clinical signs, and synovial fluid analysis. The samples were also conventionally inoculated into blood culture bottles, incubated, and subcultured onto agar to confirm the results and facilitate full bacterial identification. In the presumably infected samples, both methods yielded similar results (78.5% and 72% positive for automated and conventional culture, respectively). In addition, the median time to detection with the automated system was 14 hours for Gram-positive bacteria and 9 hours for Gram-negative bacteria [11].

As for in-house versus outside microbiology laboratories, Taylor et al [3] showed that culture methods can be more important than the delay caused by having to send a sample to an outside laboratory. Their study of 206 horses with synovial sepsis involved two different veterinary hospitals: H1 had an onsite bacteriology laboratory, whereas H2 used an outside laboratory. At H1, synovial fluid was collected into sterile, plain tubes and immediately cultured using MacConkey, blood, and chocolate agars. A positive culture was found in 24% of samples. At H2, synovial fluid was likewise collected into sterile plain tubes, but in addition, a sample was submitted on a sterile Amies swab. The samples were shipped to the outside laboratory, which used the same methods as H1 but after culture for 24 hours in a nutrient broth. A positive culture was found in 39% of those samples. Even with the shipping delay, the odds of obtaining a positive culture were almost two times greater for the laboratory that used enrichment before plating than for the laboratory that plated immediately after sample collection.

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