



UNIVERSITY OF CALGARY FACULTY OF VETERINARY MEDICINE

This review accompanies the relevant episode of the Cutting Edge veterinary podcast. In each episode of this podcast, 3rd year students in the University of Calgary's veterinary medicine program fill you in on the most up-to-date literature and evidence-based practices on topics that matter to you, the practising veterinarian.

How Can Practitioners Improve Outcomes for Horses with Synovial Sepsis Using Evidence-Based Methods?

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Introduction

Equine synovial sepsis is a high priority condition for emergent diagnosis and treatment, with associated mortality ranging from 10-55%.¹ Any veterinarian working with horses must be equipped to recognize and manage synovial sepsis. Focusing on sepsis arising from traumatic wounds; we will outline how to identify patients at risk, further options for diagnostics, and some key prognostic indicators. We will also explore how field practitioners can guide owners by outlining gold standard practices. Finally, we will explore the role of the field practitioner and how they can improve the outcome for their synovial sepsis patients.

Identifying Contaminated/Septic Wounds

When faced with a wound near a joint, tendon sheath or bursa, all practitioners should be able to confidently assess when there is a risk for synovial sepsis. This is best done through a thorough physical examination, history, and good understanding of anatomy.² Wounds with extensive punctures, laceration tracts, deep pockets or overt gross contamination are obviously of concern, and require presumptive treatment for sepsis. However, smaller wounds cannot be overlooked. If the wound is within the anatomical region of a synovial structure, it must be thoroughly explored through probing, pressure lavage or imaging.² Depending on the chronicity, sepsis may already be present in the joint. These horses are severely lame, with heat, effusion and sensitivity in the region.² When synovial involvement is in question, the practitioner should utilize additional diagnostics, including synovial fluid or serology sampling for markers of infection. If a joint may be compromised, it is the veterinarian's responsibility to confidently rule out this possibility or be prepared to treat on assumption of synovial contamination.

Diagnostic Indicators of Septic Wounds

With suspicion of a contaminated synovial structure wound, accurate and early diagnosis is important for the best outcome.³ Traditionally, veterinarians have relied on the clinical index of suspicion. The patient may have effusion, heat, pain or swelling, and marked lameness in the associated limb.² In combination with a history of trauma or joint entry, one can reasonably expect that treatment for a septic wound is required. Another well-established diagnostic indicator; microbial culture remains the most specific gold standard test at our disposal.⁴ The issue with microbial culture is that it has very low sensitivity (only 34% of highly suspect sepsis cases will have a positive culture result).⁴ In addition, microbial culture results can take 3-4 days or longer, delaying the emergent diagnosis for these wounds that is necessary for the best prognostic outcome.³ Synovial fluid analysis is another established approach for diagnosis of septic joints. Fluid obtained from the synovial structure will be evaluated by total nucleated cell count (TNCC), % neutrophils, and total protein.⁵ These values are elevated in septic pathologies, with marked neutrophilia, percentage of neutrophils over 80-90% and total protein above 40 g/dL.⁴ While synovial fluid analysis is a good inflammatory indicator, it can be altered by synovial lavage or intrasynovial use of antimicrobials.⁶ Similarly increased parameters can also be seen in cases of sterile synovitis.⁷ Finally, sampling the synovial fluid requires synovial entry, which could contaminate a previously sterile joint.⁶ Due to this, the decision to sample must be made with an understanding of the risks and benefits.

Another adjunctive approach that shows good evidence for diagnosis of septic joints is the measurement of serum or synovial fluid serum amyloid A (SAA). SAA is an acute-phase protein present in early inflammation that is primarily synthesized by the liver and the synovial membrane in cases of injury.⁶ SAA synthesis is triggered by pro-inflammatory cytokines in the bloodstream, regardless of the site of injury.⁸ Multiple studies have shown significant SAA increases in serum and synovial fluid in cases of equine septic synovitis.^{6,7} The SAA level changes in proportion to the degree of insult, offering a great advantage for serial monitoring.⁷ Equally advantageous, it is available as a stall-side test that is validated against the highly sensitive and specific ELISA lab test.⁹ It is important to consider that SAA elevations can be seen with concurrent inflammatory conditions, large wounds, or extensive soft tissue damage.⁶ Additionally, the effect of treatment on SAA markers is not fully understood.⁶ Overall, SAA can be a powerful tool in recognizing septic joint involvement, with the recognition that the test is not specific to infection.

There is always ongoing research for better ways to diagnose synovial sepsis. For example, D-lactate has also been explored as an alternative option for diagnosis. D-lactate is a stereoisomer of mammalian L-lactate, produced exclusively by bacterial fermentation.⁶ It is elevated in the peritoneal fluid of horses with septic peritonitis, suggesting it may also become elevated with joint bacterial contamination.⁶ However, this hypothesis has not been supported in research, as there were no significant increases of D-lactate in either serum or synovial fluid of horses with septic synovial pathology.⁶ It could be that the bacterial population in these wounds are not significant D-lactate producers, unlike those found in septic peritonitis. Another recent study

looked at the use of synovial fluid metabolites for diagnosis. In this research, the primary determinant of sepsis was an elevated glucose level in the synovial fluid.¹⁰ However, the technology used for this analysis is complex and not readily available. While the early results suggest that this may be a future diagnostic indicator, metabolic analysis has not yet been used in practice.¹⁰

Key Determinants of Outcome

Wounds that are found to be septic can come at a high cost, both in regards to treatment and prognosis. Research dedicated to prognostic indicators can guide us as veterinarians in educating our clients, dictating aggressiveness of treatment, and electing when to consider euthanasia. Poor survival is colloquially correlated with many factors, but consensus between studies shows only two definitive indicators. First, any bone or tendon involvement is a negative indicator for survival, or return to function.^{11,12} This finding supports the importance of a full diagnostic work-up to determine the true extent of the patients' injuries. Second, staphylococcal infection, especially with *S. aureus*, is associated with persistent sepsis, putting the animal at a higher risk of uncontrolled disease and potential euthanasia.^{3,11}

Beyond survival, clients need to be informed of the horse's chance for return to function. One study found that horses who required an increased number of repeated treatments, or the use of multiple drugs, had poor return to function.¹² Another study suggests that extreme lameness on presentation is also a negative indicator for return to function.¹³ The author suggests that this may be due to intractable pain, more extensive injury or higher levels of bacterial invasion. The same paper also found that smaller wounds and hindlimbs were associated with worse outcomes.¹³ In another study population, a negative prognostic indicator for return to function was multiple joint involvement, with exponential decreases in treatment response with each additional affected joint.³ They also found an association with poor performance outcome and gram-negative

bacterial infections, as well as staphylococcus species infections.³ These findings provide a basis for client and colleague discussion when looking at options for treatment, referral or euthanasia.

Many clinicians believe that there is a "golden hour" of treatment when it comes to synovial sepsis. While initiation of treatment within 24 hours of injury is associated with a positive prognosis,³ there is no robust evidence that treatment onset timing is essential to survival. In fact, a 2021 meta-analysis provided evidence that only 2 of 61 studies found a difference between time to treatment and survival.¹⁴ This means that even older wounds can have a positive prognosis, if appropriately treated. Another common misconception is that white blood cell count is positively correlated with decreased survival. This has been invalidated by multiple studies, finding no correlation between white blood cell count and response to treatment or

survival to discharge.¹⁵ Being educated on these common misconceptions can provide a field practitioner with the confidence to attempt treatment on an appropriate candidate.

Treatment Options – Referral

Referral center treatment is considered the gold standard for synovial sepsis. As such there are many in-hospital options available associated with good outcomes. For example, negative pressure wound therapy can be an option for extensive wounds that cannot be closed by primary intention.¹⁶ This therapy can also be used for prevention of infection in acute wounds, as well as acceleration of healing.¹⁶ Endoscopic lavage of joints, or arthroscopy, is currently the gold standard of care for synovial sepsis. It is often followed by a course of repeated intravenous regional limb perfusion with broad-spectrum antimicrobials. There is good evidence that this protocol is associated with positive outcomes in horses.¹⁷ However, such care is expensive and not always available to clients. While there has been a recent shift towards arthroscopy as the preferred treatment, there is a lack of research directly comparing arthroscopy to field alternatives, such as through and through lavage.¹⁷ More studies are needed to compare the value of arthroscopy over field treatments so that veterinarians can ethically decide on a treatment plan based on their abilities, available facilities, finances, and equipment.

Indwelling catheters of the cephalic or saphenous vein are another aspect of synovial sepsis management that can be performed in referral centers.¹⁸ They can be used for regional limb perfusion with antimicrobials repeatedly over the course of treatment. These catheters offer another advantage as they can be placed in sites away from swelling over the wound, where edema has been shown to reduce the absorption of the local antimicrobial.¹⁸ This is considered a referral-level treatment, because in some cases, horses require casts to stabilize the catheters, and require more intensive care than most general practices can provide.¹⁸ For example, during a 2018 study utilizing indwelling catheters, most of the horses received amikacin and required multiple perfusions in order to achieve resolution of clinical signs.¹⁸ While theoretically offering the best outcome for return to function, referral comes at a financial cost, and treatments may be drawn out over the course of several weeks. These studies and referral treatments might not always be techniques used by general practitioners themselves, but they offer guidelines that veterinarians can use to better understand and communicate about the options available to their client.

Treatment Options – Field

Synovial sepsis is often a daunting condition for field practitioners to deal with. However, there are many techniques that can be used in the field that carry good prognoses for patients. These same methods can be used for general practitioners to delay or reduce infection while horses are being transported to referral care. First, it has been found that there is no increased risk of infection when comparing field and hospital condition joint injections.¹⁹ This information can be extrapolated and used for evidence that through and through lavage in the field for horses with

synovial wounds does not carry an increased risk for further iatrogenic contamination. Through and through lavage can be an effective means of reducing or even preventing infection in horses with contaminated synovial wounds.¹⁷ There is also evidence that a single lavage treatment used in conjunction with regional limb perfusion can be sufficient for horses presented acutely after synovial structure injury.²⁰ This is more evidence supporting the importance of the field veterinarian and their actions on initial presentation of the horse for providing the best outcome.

In terms of regional limb perfusion in the field, amikacin has been shown to be an accessible and appropriate antimicrobial choice.²¹ In addition, the use of amikacin is associated with good long-term outcomes for the patient.²⁰ It is also important for veterinarians to take a culture of the synovial fluid before any treatments are performed to aid with determining prognosis for horses with synovial sepsis.^{3,11} The culture will also guide further antimicrobial choice in the case of amikacin resistance. Additionally, administration of systemic antibiotics is indicated for reduced mortality.¹ Systemic antibiotics can be used prior to referral if that is the chosen plan or in conjunction with field methods discussed previously.

In conclusion, field practitioners can have a large impact on the outcome of horses with synovial sepsis. Field practitioners do not need special equipment or techniques to have a positive effect. Whether the owners choose referral or pursue treatment with a general practitioner, there are many steps that can be taken on initial presentation that will affect the long-term prognosis of the patient. As such, an understanding of the available diagnostics, treatments, and prognostic indicators is crucial to the equine field practitioner to best help patients with synovial sepsis.

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