EQUINE PROCEEDINGS

June 4–6, 2023

2023 ANNUAL CONFERENCE

KANSAS STATE UNIVERSITY | College of Veterinary Medicine

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Compounding and ELDU

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KANSAS STATE UNIVERSITY | College of Veterinary Medicine

EXTRA LABEL DRUG USE AND COMPOUNDING

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TYPES OF DRUGS:

FDA approved drugs include pioneer ("legend") and generic drugs. Pioneer drugs are the first approved version of a new drug. These compounds have been subject to extensive testing to ensure safety and efficacy. Additionally, the manufacturer is required to demonstrate that the manufacturing process is consistent, that sterility is maintained, that the concentration and purity of the product does not change from batch to batch and that labeling and advertising are accurate and complete. Generic medications may be produced once the patent has expired on a pioneer product. Manufacturers are required to demonstrate that the generic product is bioequivalent to the pioneer product. Both pioneer and generic drugs are subject to adverse event reporting, and this is public record. FDA approved pioneer drugs are issued a New Animal Drug ("NADA") number and a generic drug an Abbreviated New Animal Drug ("ANADA") number. These can be found on the drug container and are an indicator that the product is an FDA approved product.

In contrast to pioneer and generic drugs, compounded drugs are not FDA approved. Compounding is the manipulation of an approved drug by a veterinarian or pharmacist upon the prescription of a veterinarian, to meet the needs of a particular patient. By this definition, actions such as mixing of two drugs in the same syringe, preparing a suspension from crushed tablets, or adding a flavoring, are considered compounding.

EXTRA LABEL DRUG USE:

Extra Label Drug Use (ELDU) is the use of a medication in a manner other than that defined on the label. This includes using the drug in a species other than that for which it is approved, using a different dose, different route of administration or different dosing interval. Prior to 1994 and the passage of the Animal Medicinal Drug Use and Clarification Act (AMDUCA), extra-label drug use in veterinary medicine was technically Illegal. The passage of AMDUCA allows for ELDU where the animal's health is threatened, or the animal may suffer or die without treatment and provided one of the following conditions is met:

- No animal drug approved for the intended use OR
- There is an approved animal drug for the intended use, but it does not contain the active ingredient that is needed OR
- There is an animal drug approved for the intended use, but the approved drug is not in the required dosage form OR
- There is an animal drug approved for the intended use, but the approved drug is not in the required concentration OR
- In the context of a valid veterinary client patient relationship (VPCR), the approved drug has been deemed clinically ineffective when used as labeled.

In non-companion animals it is considered acceptable to prescribe an approved human drug for ELDU even if an approved animal drug is available. Economic reasons are considered acceptable justification for this.

COMPOUNDING:

Compounding whereby the active ingredient is an FDA approved product is permitted under the Food, Drug and Cosmetic (FD&C) Act and AMDUCA, provided ELDU requirements are met.

Compounding is the modification of an approved drug to sufficiently treat a patient and increase the likelihood of efficacy. Compounding should NEVER be done to mimic a commercially available product and cost is not considered an acceptable reason for using a compounded product. Using a compounded product that mimics a commercially available product is acceptable if the approved form is not available (i.e. there is a shortage). Additional examples of appropriate compounding include adding flavorings to increase the palatability of the drug, formulation of a different strength or changing the form to make it easier to administer.

In contrast to compounding from an FDA approved product, compounding from bulk substances is not permitted under the FD&C Act. A bulk substance is a substance that is used to make a drug that becomes an active ingredient in the finished dosage form of the drug. These are not FDA approved as they have not been reviewed by the FDA for safety, efficacy, proper manufacturing or accurate packaging and labeling. Additionally, there is no requirement for reporting of adverse effects to the FDA.

Although compounding from an FDA approved product is preferred to a bulk substance, the FDA does recognize that in some cases it may be necessary to compound from the latter. However, an FDA approved product is preferable because a bulk substance does not have the same assurance of safety, efficacy, and quality as FDA-approved and indexed products. Additionally, the bulk substance used in the approved version of a drug has passed stringent tests of analysis regarding drug ingredients and presence of contaminants but the same may not be true for compounded substance made from bulk substances. In 2022, after a public comment period, the FDA finalized and released the Guidance for Industry (GFI) #256 which addressed compounding of animal drugs from bulk substances. Under GFI#256, the following conditions should be met:

- By/under supervision of vet or pharmacist in licensed pharmacy
- Should only be done if FDA-approved drugs are not medically appropriate to treat the animal.
- All substances meet USP standards.
- Should not be a copy of an approved marketed drug.
- Office stock should not be compounded from bulk substances except in limited instances.
- Specific labeling requirements: “This is a compounded drug. Not an FDA approved drug.”
- Report adverse events to FDA

Office Use of Compounded Products:

Under AMCUDA, compounding is meant to be for an individual patient to address that specific patient’s need. Office use, however, is obtaining a compounded medication not pursuant to a patient-specific prescription. The FDA frowns on this because of the lack of regulation of compounded products but does recognize that sometimes it is necessary to start therapy immediately, using a compounded product. This should only be used when no other option is available. Under GFI #256, the FDA permits compounding from bulk drug substances nominated and approved for use as office stock under these circumstances. These substances are listed on the “List of Bulk Drug Substances for Compounding Office Stock Drugs for Use in Nonfood-Producing Animals.”[1] Veterinarians may nominate substances to this list.

Expiration versus Beyond Use Dates:
An expiration date is the time during which a conventionally manufactured drug product may be expected to maintain its labeled identity, strength, purity, and quality if stored as labeled. A conventionally approved product is an FDA approved product. Establishing expiration dates involves product specific studies. These studies evaluate the specific formulation, in the specific container it is stored in, under the storage conditions listed on the label. A beyond-use-date is the time period beyond which a compounded product should not be used. For most compounded products, an expiration date is not appropriate because these drugs have not undergone full stability studies to determine expiration dates. Beyond-use-dates are based on data for similar products or United States Pharmacopoeia (USP) default dates and are estimated using the date and time the preparation is made. Regardless of the USP default date, the beyond-use-date should not be beyond the expiration date of any component of the product.

Risks of compounded products
Although compounding is a necessary component of veterinary medicine, use of compounded medications is not without risks. These include (1) concentrations that differ from the label dose (greater or lesser than), (2) lack of stability, (3) toxic excipients and (4) pharmacokinetic concerns (i.e. poor absorption of oral formulations).

Selection/Evaluation of Compounding Pharmacies
Choosing a quality compounding pharmacy can be challenging. State Pharmacy Boards can provide lists of licensed compounding pharmacies. Another resource for selection of a compounding pharmacy is the Pharmacy Accreditation Board.[2] This organization assesses pharmacies for compliance with USP standards. Accreditation is voluntary but shows the pharmacy is committed to meeting standards for quality and safety. Accreditation involves an inspection and a fee. Warning letters can be found on the FDA-CVM's website.[3] Word of mouth is also an excellent way to find a quality compounding pharmacy.

VETERINARY MEDICAL DEVICES:
Although some companies may market veterinary drugs as veterinary devices, they are not the same. The product is a drug if (1) it relies on a chemical action in or on the animal's body to achieve its effect or (2) If it needs to be metabolized by the animal's body to work. It is important to note that veterinary medical devices are not FDA approved products. The FDA does **NOT** require formal pre-market approval of devices. Manufacturers are **NOT** required to list their products with the FDA-CVM and there are **No** mandatory adverse event reporting requirements for veterinary medical devices. It is the responsibility of the manufacturer to assure safety, effectiveness, and proper labeling.

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1. https://www.fda.gov/animal-veterinary/animal-drug-compounding/list-bulk-drug-substances-compounding-office-stock-drugs-use-nonfood-producing-animals.
2. https://www.achc.org/compounding-pharmacy/
3. FDA Website (https://www.fda.gov/animal-veterinary/compliance-enforcement/cvm-warning-letters)

ADDITIONAL RESOURCES:

1. USP Compounding Compendium (http://www.usp.org/products/usp-compounding-compendium)
2. AVMA Website (https://www.avma.org/resources-tools/animal-health-and-welfare/animal-health/compounding)
3. Current Animal Drug Shortages: https://www.fda.gov/animal-veterinary/product-safety-information/current-animal-drug-shortages

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Pharmacology of Antimicrobials I & II

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OVERVIEW OF ANTIBIOTIC USE IN HORSES

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RATIONAL USE OF ANTIBIOTICS:

The goal of antibiotic therapy is to administer doses sufficient to reach concentrations at the site of infection that can kill or suppress microbes to the extent that they can be eliminated by the animal's immune system. The following should be considered when developing a treatment plan:

- Does the diagnosis warrant antibiotic therapy?
- What is the likely causative organism?
- What is the *in vitro* antibiotic susceptibility of the organism?
- Where is the infection located and will the antibiotic penetrate the infection?
- Will the antibiotic be effective in the local environment of the organism?
- What antibiotic formulation/dose regimen is necessary to reach/maintain the appropriate concentration for an appropriate duration of time?
- What are the potential adverse drug effects and do the benefits of treatment outweigh the risks?
- Is there an FDA approved product that can be used as labeled? Can you determine an appropriate withdrawal time for performance horses?

SUSCEPTIBILITY TESTING:

It is not always necessary to culture samples from patients with an infectious disease as often times the practitioner can base a diagnosis on clinical experience. Susceptibility testing should be considered for complicated, chronic, or recurrent infections, or a nonresponsive infection with a history of previous antibiotic therapy. Although susceptibility testing is not a perfect tool and is only one of several tools, it can be useful in designing an effective treatment plan. In most cases, antibiotic susceptibility testing determines and reports the concentration of an antibiotic that is necessary to inhibit the growth of bacteria (minimum inhibitory concentration; MIC). The MIC represents what is needed at the site of infection to treat the causative organism but does not take into consideration the pharmacokinetics of the drug.

Different tests are available for determining antibiotic susceptibility with each offering advantages and disadvantages. The disk diffusion (Kirby Bauer) method utilizes antibiotic impregnated disks that are placed on an agar, previously inoculated with the bacterial isolate. Each disk contains a single concentration of an antimicrobial. The antimicrobials diffuse outward from the disk into the agar with the concentration of drug decreasing as the distance from the disk increases. If growth of the microbe is inhibited by the drug, an area of no growth (area of inhibition) around the disk will be observed. After 24 hours, the diameter of the zone of inhibition is measured and the isolate is deemed "susceptible" (S; large zone of inhibition), "intermediate" (I) or "resistant" (R; growth inhibited only in close proximity to the disk). The diameter sizes corresponding to these classifications are established by the Clinical and Laboratory Standards Institute (CLSI). A "R" classification suggests that it is unlikely the concentration can be reached in the patient at the recommended dose. This method is considered qualitative as an MIC value is not provided.

In contrast to disk diffusion, the broth dilution assay is a quantitative test that does generate an MIC value. With this method, a series of test tubes or wells on a plate containing

increasing concentrations of a drug (twofold dilutions), are inoculated with a standard number of organisms. After a standard period of time, the tubes or wells are evaluated, using an analytical instrument, for detectable growth of the organism. The MIC of the drug is the lowest concentration necessary to inhibit bacterial growth.

A third test utilized for susceptibility testing is the E-Test (Epsilon test). This method utilizes a strip that contains increasing concentrations of a drug. The strip is placed on an agar plate inoculated with the causative organism. The point at which the zone of inhibition intersects with the strip is read as the MIC. Although more expensive, this method tests a larger range of MICs compared to the broth dilution assay.

Interpretation of Susceptibility Testing:

Designation by the diagnostic lab as "S," "I," or "R" is based on likelihood of susceptibility, which is based on whether the recommended (label) dose is likely to generate plasma drug concentrations that will equal or exceed the MIC of the causative organism. The "SIR' designation reflects how close the MIC is to the breakpoint (MIC_{BP}). The MIC_{BP} is established by the CLSI. The MIC_{BP} is determined by the pharmacokinetics of the drug (i.e. C_{max}), using the recommended dose of the drug, the MIC of the organism, and the clinical response to the drug as observed in a population of patients. The MIC_{BP} is specific for the animal species, disease, pathogen, antimicrobial, and dosage regimen. If the MIC of the infecting organism is less than the breakpoint it is deemed "S", if it is close to or equal to the breakpoint it is classified as "I" and if it is greater than the MIC it is considered "R." Using these criteria, a microbe is considered "S" when it is inhibited by a concentration of drug that is readily achievable in plasma after administering recommended doses. A drug deemed "I" would be less desirable than one designated as "S", as therapeutic efficacy is less predictable and only likely to be achieved if the infection is in a site where the drug is concentrated. Breakpoints are updated periodically by CLSI, as new information regarding organism susceptibility and drug pharmacokinetics becomes available. It is important to note that equine specific MIC_{BP} don't exist for every drug and therefore may be extrapolated from human data. While in some cases this might be comparable (i.e. IV administered drugs), in other cases, because of pharmacokinetic differences, the MIC_{BP} may not be appropriate (i.e. oral drugs). In this case, having the actual MIC value from the diagnostic lab to compare to results from pharmacokinetic studies can be helpful. Some suggested susceptibility breakpoints for oral antimicrobials as recommended in another publication[1] are listed below. Please note these are for adult horses and NOT foals.

1. Chloramphenicol: ≤ 1 µg/mL after a dose of 50 mg/kg PO, q 6-8 hours.
2. Enrofloxacin: ≤ 0.12-0.25 µg/mL after oral dosing at 7.5 mg/kg once a day (CLSI, 2020 for ≤ 0.12 µg/mL, (0.25 µg/kg considered I); Magdesian, 2019 for ≤ 0.25 µg/mL).
3. Trimethoprim-sulfamethoxazole or trimethoprim-sulfadiazine: ≤ 0.5 µg/mL for the trimethoprim/≤ 9.5 µg/mL for the sulfonamide component. [Some labs report the combined MIC as ≤ 10 µg/mL]. These recommendations are for doses of 30 mg/kg PO, q 12 h, except for Equisul SDT, which is dosed at 24 mg/kg q 12 h [Aurora Pharmaceutical, LLC].
4. Minocycline ≤ 0.12 µg/mL after a dose of 5 mg/kg PO, q 12 h; Minocycline ≤ 0.25 µg/kg, after a dose of 4 mg/kg PO, q 12.

5. Doxycycline ≤ 0.12 µg/mL after a dose of 20 mg/kg PO, q 12 h. Note, this dosage regiment is not recommended in horses due to risks of adverse effects, including fatal enterocolitis; Doxycycline ≤ 0.25 µg/mL after a dose of 10 mg/kg PO, q 12 h.

ANTIBIOTICS

Availability and Extra-label Use of Antibiotics:

There are a limited number of antibiotics that are Food and Drug Administration (FDA) approved specifically for use in horses and those that are labeled for use in this species have limited label indications (specific bacterial pathogens) or are approved for administration via a single route. Antibiotic formulations approved for use in horses include amikacin, gentamicin, trimethoprim-sulfadiazine, penicillin, ampicillin, and ceftiofur. The limited number of antibiotics approved for use in horses, necessitates extra-label use and although this is permitted under the Animal Medicinal Drug Use and Clarification Act (AMDUCA), it is the responsibility of the clinician to ensure appropriate and judicious use. This includes knowledge of the MIC for the organism to be treated, as this may differ from the MIC for the organism that the drug is labeled for, and an understanding of the pharmacokinetics of the antibacterial agent in the horse, especially if the drug is labeled for use in a different species.

Aminoglycosides, such as amikacin and gentamicin, are important therapeutics in equine medicine. They are effective against *Enterobacteriaceae* and *Pseudomonas* and are sometimes used in the treatment of methicillin-resistant *Staphylococcus aureus* (MRSA; extra-label use). It is important to note that aminoglycoside antibiotics exhibit age-dependent pharmacokinetics with lower peaks, higher troughs, and longer elimination half-lives in foals less than 2 weeks of age. This may necessitate increasing the dose and possibly extending the dosing interval in this age group, compared to adult horses. Although FDA approved equine formulations of amikacin and gentamicin are available, the approved route of administration is limited to intra-uterine infusion and as such extra-label administration, including systemic or intra-articular, is common. Systemic administration is necessary to reach common sites of infection outside of the uterus. Intra-articular administration, in the case of amikacin, allows for attainment of higher therapeutic concentrations in synovial fluid in the case of a septic joint, as compared to systemic administration. Regional perfusion has proven effective in achieving high local concentrations of amikacin in the distal limb [2–4]. An advantage to intra-articular and regional perfusion includes a reduction in required doses as compared to what would be needed if administered systemically to reach these sites, thereby decreasing the potential for adverse effects.

Potentiated sulfonamides are broad-spectrum antibiotics and commonly used in veterinary medicine. While some of the more common equine pathogens, such as *Enterobacteriaceae,* are often resistant, other organisms such as *Staph aureus*, including some strains of MRSA, and *Streptococcus zooepidemicus* are usually susceptible to potentiated sulfonamides. Sulfonamides are ineffective in pus and necrotic tissue. A powder and oral suspension, as well as tablets are available, however, only the powder and oral suspension are FDA approved for use in horses; therefore, the use of trimethoprim-sulfamethoxazole tablets would constitute extra-label use. The use of these tablets in equine medicine has become a point of debate. According to AMDUCA, extra-label administration is only warranted if there is no approved drug that is labeled for such use in that species or that contains the same active ingredient in the required dosage form and concentration. Since the oral trimethoprim-sulfadiazine suspension and powder are FDA approved for use in horses, justifying tablet administration should be for a medical and not economic reasons. Although many veterinary

formulations are labeled for once daily administration, published reports indicate that twice daily administration is better for achieving effective concentrations[5,6].

Ceftiofur, also frequently used in equine medicine, is labeled for use in the treatment of respiratory infections caused by *Streptococcus equi subspecies zooepidemicus* in horses. It is also used extra-label to treat *Enterobacteriaceae* and other Gram-negative infections. Currently there are two FDA approved equine ceftiofur formulations, including a sterile sodium powder and a sustained release crystalline free acid suspension, both labeled for intramuscular administration. Extra-label administration (IV or SQ) of ceftiofur, at higher than label doses, has been reported for foals [7] with concentrations exceeding the MIC in nearly 79% of susceptible bacteria commonly isolated from neonates. There are also reports of administration via regional intravenous perfusion (2 grams of ceftiofur sodium). Investigators reported concentrations exceeding the MIC of common pathogens for greater than 24 hours in synovial fluid [8] and subcutaneous tissue [9].

Penicillin is used at extra-label doses to treat susceptible infections, including *Streptococcus equi* subsp. *zooepidemicus and Streptococcus equi* subsp. *equi*. Potassium (IV) and procaine (PPG; IM) penicillin formulations are the two formulations most used, with the latter being the FDA approved formulation for horses. An advantage to the PPG formulation is that less frequent administration is required, the disadvantages are injection site reactions and the potential for adverse effects (i..e. CNS stimulation with inadvertent intravascular administration) associated with procaine administration. It should be noted that for many bacterial species that affect horses, the label dose of 6000 IU/kg IM q 24 h for PPG is inappropriate, and the clinical standard has dictated a dose of 22,000 IU/kg IM q 12. Recently, one group of investigators described a hybrid protocol, whereby potassium penicillin was administered IV at 0 and 6 hours followed by IM administration of PPG at 12 hours [10]. Although there was variability between horses, concentrations exceeded the MIC_{90} for *Streptococcus spp*. for >50% of the 24 hour testing interval [10]. In humans, carbapenems, such as imipenem and meropenem, are used for infections caused by organisms resistant to other antimicrobial agents. There are anecdotal reports of their use in veterinary medicine for the treatment of neonatal sepsis caused by organisms resistant to other antibiotics, as well as published reports describing pharmacokinetics following both systemic administration and regional limb perfusion in adult horses [11–13]. Although effective concentrations are reportedly achieved following administration via these routes of administration and extra-label use would be permitted under AMDCUA, because of the importance of these drugs in human medicine, use in veterinary medicine should be reserved for the treatment of bacterial infections where there is documented resistance to all other antimicrobials.

Tetracyclines (doxycycline and minocycline), rifampin and macrolides (erythromycin, azithromycin and clarithromycin) are also commonly used extra-label in equine medicine. Doxycycline is available in a suspension formulation and as tablets and is administered orally. Concentrations adequate for killing susceptible intracellular bacteria (MIC <=0.25 uμ/mL) has been achieved following administration of 20 mg/kg PO once a day,[14] though it is usually administered at a dose of 10 mg/kg PO twice a day in practice. Minocycline has been studied in adult horses (2.2 mg/kg IV and 4 mg/kg IG) [15] and foals (4 mg/kg IG route)[16]. In both, drug concentrations in pulmonary epithelial lining fluid (PELF) and bronchoalveolar lavage (BAL) cells were determined to be sufficient to be effective against susceptible bacteria, including pneumonia caused by Strep spp. There are currently no veterinary labeled rifampin products, which necessitates the use of human labeled products in horses. In foals, extra-label

administration of rifampin capsules (10 mg/kg PO administered once per day) resulted in concentrations 1.5-2.4 times the MIC_{90} of rifampin alone in PELF and 2.0-3.3 times the MIC_{90} in BAL cells for *Rhodococcus equi* [17]. While the MIC of rifampin is unknown in the presence of macrolides or azalides, it would be expected to be lower than that of rifampin alone due to synergism, which has been demonstrated between rifampin and azithromycin or clarithromycin (Giguere et al., 2012). Rifampin is often administered at a dose of 5-10 mg/kg PO, q 12 h in clinical practice. For the treatment of *Rhodococcus equi* or *Lawsonia intracellularis* in foals, macrolides or azalides are commonly administered along with rifampin.

Compounding:
Chloramphenicol oral suspension or paste is commonly compounded for administration to equine patients. Although there are FDA approved tablets for use in dogs, ease of administration as well as the safety to both the horse and handler can arguably be used as justification for choosing a compounded chloramphenicol paste or suspension. Use of these compounded formulations, however, must be weighed against the potential risks of compounded drugs. Reported risks include actual concentrations that are not in agreement with the label concentration which in extreme cases can lead to death (Desta et al., 2011; Thompson et al., 2011), changes in the concentration of the same compounded formulation over time and variable pharmacokinetics [18,19].

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Analgesic Pharmacology & Pain Management

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KANSAS STATE UNIVERSITY | College of Veterinary Medicine

PHARMACOLOGICAL TREATMENT OF PAIN

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NOCICEPTION AND PAIN:

Pain is defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage." Perception of pain begins with stimulation of nociceptors located in tissues. Stimulation of these nociceptors, whether from chemical or physical (heat, cold, or mechanical pressure) signals generates an impulse that travels to the dorsal horn, where it stimulates second-order neurons in the spinal cord gray matter. Signals are transmitted to the second-order neurons through fast-conducting (Aδ) or slow-conducting (C) fibers. Finally, the signal is transmitted through specific pathways to the thalamus, brainstem, and limbic system. Chemical mediators, released in response to stimulation of the pain pathways, function in transmission of peripheral pain as well as signal processing in the dorsal horn. Glucocorticoids, endogenous opioids, catecholamines, endorphins and enkephalins, substance P, excitatory and inhibitory neurotransmitters (aspartate, γ-aminobutyric acid, and prostaglandins), and monoamines appear to be the most prominent. These mediators serve as important targets for pharmacologic intervention.

Resolution of acute pain states may occur with discontinuation of the stimulus and appropriate intervention. Descending inhibitory pathways originating from the brain or the use of alternate non-painful afferent input, such as ice, at the site of injury may also lead to modulation of neuronal input. Without these, nociceptive input can result in continued peripheral and central sensitization which can lead to hypersensitivity (reduction in the intensity of the stimulus required to cause pain), allodynia (typically non-painful stimulus is now perceived as pain), hyperalgesia (exaggerated response to a noxious stimuli) and hyperpathia (persistence of pain after removal of a noxious stimuli).

ASSESSMENT OF PAIN:

Assessment of pain in horses can be challenging and to most effectively recognize pain, a multi-faceted approach may be necessary. Over the last several years, there has been significant efforts to develop tools that consider physiologic (heart rate, respiratory rate, etc) and behavioral indices for horses in different clinical situations (e.g. orthopedic pain, colic). Scales have been developed for various parameters to assess not only the presence or absence of pain but also the severity. The AAEP lameness and the horse Grimace Scale are examples of approaches to assessing pain. The Grimace Scale, originally developed in horses undergoing castration, correlates six facial expressions with the degree of pain.[1] It is important to note that many of the pain scales assess acute or nociceptive pain in adult horses. Other tools may be necessary to assess chronic pain or pain in foals.

THERAPY:

With surgical or acute pain, nociception is considered an adaptive, protective strategy. The associated inflammatory response is a necessary part of the healing process. In this scenario, the goal of therapy is to normalize pain sensitivity and prevent it from progressing to a maladaptive state. Early treatment and the use of multiple drugs that target different sites in the nociceptive pathway (multimodal therapy; Figure 1) can help minimize development of a chronic condition and prevent less severe adverse effects. The most used classes of drugs for the treatment of pain include anti-inflammatory drugs, opioids, α_2- adrenergic agonists and local anesthetics.

Additional drugs that are less studied but that may have a place in pain management for horses includes tramadol, gabapentin, and ketamine.

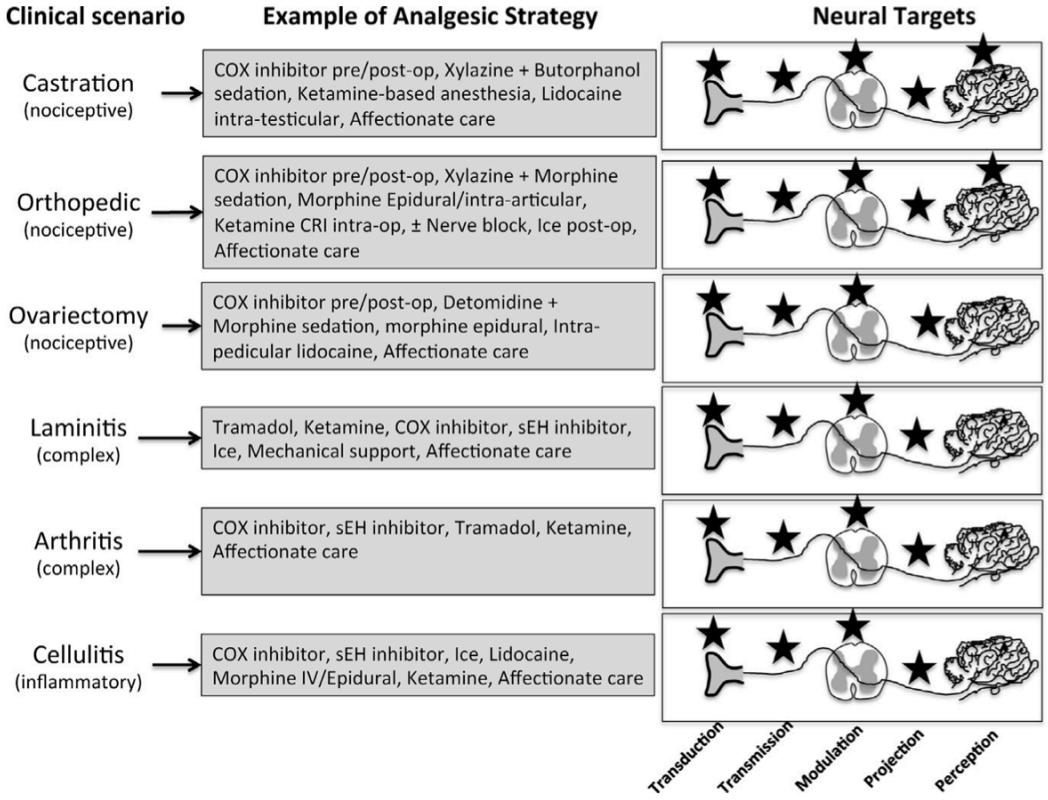

Figure 1. Examples of multimodal approaches and neural targets (stars) to maximize the management of conditions characterized by nociceptive, inflammatory, or complex pain in horses. *Note*. Reprinted from "Pain Management in Horses" by Guedes, A., 2017, *Veterinary Clinics of North America: Equine Practice (Equine Pharmacology)*, *33*, p. 181-211.

Opioids:

Opioids are potent analgesic agents used in horses, primarily for management of intraoperative and postoperative pain or in combination with a sedative to provide chemical restraint for procedures conducted on standing horses. Excitement is often observed when opioids are administered as sole agents to pain-free horses; however, stimulation is rarely observed when opioids are administered with sedatives or in horses undergoing surgery. It's important to note though that the lack of excitement while undergoing surgery may be simply because of the lower doses that are often administered.

Opioid receptors, classified as μ, κ, or δ, are found at both spinal and supraspinal levels and in peripheral tissues such as the synovial membrane and cornea. In the brain, binding of an agonist to an opioid receptor releases the inhibition of adrenergic and serotonergic pathways, ultimately increasing the activity of descending inhibitory pathways. In peripheral tissues, opioids modulate the actions of C fibers already sensitized by inflammation. Commonly used opioids in the horse include butorphanol (agonist-antagonist) and morphine (agonist), and to a lesser extent, fentanyl (agonist) and tramadol (agonist). More recently, hydromorphone administration to horses has

been reported.[2,3] Butorphanol is arguably the most commonly used opioid in the horse. It is effective for treatment of mild to moderate pain and is used frequently in combination with other sedatives, such as α_2-adrenergic agonists, for standing chemical restraint and as part of a preanesthetic protocol. Its excitatory effects are believed to be less than those of pure μ-receptor agonists, but this may also be a result of the dose administered. When administered alone at the label dose (0.1 mg/kg), ataxia, increased locomotion, tachycardia, and muscle fasciculations develop.

Morphine is the prototypical opioid, however, it is used less frequently in horses because of reports of excitation, behavioral changes, and increased locomotor activity when used at higher doses. Another concern regarding the use of morphine in horses lies in its effects on gastrointestinal motility and the increased potential for colic. Like butorphanol, morphine is often used in combination with a sedative for chemical restraint in the standing horse or as part of a preanesthetic protocol. Non-systemic routes of administration (epidural or intraarticular) appear to reduce the severity of the adverse effects observed with systemic administration. Opioid receptors have been identified in the equine joint and intraarticular injection of 0.05 mg/kg of morphine appears to induce long-lasting analgesia (up to 24 hours) in experimentally induced synovitis.[4]

Tramadol is a synthetic opioid agonist as well as a neuronal serotonin and norepinephrine reuptake antagonist. It is used to treat mild to moderate pain in small animal species but studies describing its analgesic effects in the horse are limited. In one study in horses, IV doses of 2 and 3 mg/kg did not result in an antinociceptive effects and higher doses resulted in excitation. Part of the analgesic effect of tramadol has been attributed to its O-desmethyltramadol metabolite, which appears to be 200 times as potent as tramadol. Although the horse is adept at rapidly generating the active metabolite, the rate at which the O-desmethyltramadol metabolite is conjugated for elimination is just as rapid and may limit any associated analgesic effects accompanying tramadol administration.

α_2-adrenergic receptor agonists

α_2-adrenergic receptor agonists provide sedation, muscle relaxation and are potent analgesic agents, especially in the treatment of visceral pain. In most cases, the sedative effects of the α_2-adrenergic agonists will outlast the analgesia. The most used α_2-adrenergic agonists in equine medicine are xylazine and detomidine, and, to a lesser extent, romifidine and dexmedetomidine. The overall effects of the drugs are the same, with the differences being with respect to α_2:α_1-adrenergic receptor selectivity, chemical structure and pharmacokinetics. Of the α_2-adrenergic agonists used most commonly in horses, xylazine (160:1; α_2:α_1) is the least selective for the α_2-adrenergic receptor and is considered to be the least potent of the α2-adrenergic agonists. Relative to xylazine, detomidine (260:1) has a higher α_2:α1-adrenergic receptor selectivity. The α_2:α_1-adrenergic selectivity for romifidine has not been reported, but clinically it appears to fall between that of xylazine and detomidine. Many of the adverse effects associated with α_2-adrenergic agonist administration have been attributed to the α_1-adrenergic receptor. Adverse effects include bradycardia, atrioventricular blockade, transient hypertension (followed by hypotension), and a transitory decrease in respiratory rate with a mild increase in $PaCO_2$ and decrease in PaO_2. Additional effects include decreased gastrointestinal motility and colic, hyperglycemia, hypoinsulinemia, increased micturition, and profuse sweating.

α_2-Adrenergic receptors are found in both the brain and the spinal cord, and the analgesic effects of α_2-receptor agonists are seen after both parenteral and epidural administration. Although α_2-receptor agonists are most commonly administered systemically (intravenous or intramuscular), epidural administration can minimize (but not necessarily alleviate altogether) the sedative and cardiovascular effects of this class of drugs. After epidural administration, xylazine has a faster onset of effect and longer duration of action, and it appears to be effective at lower doses than other α_2-receptor agonists. With respect to systemic doses, epidural doses of xylazine (0.17 to 0.25 mg/kg) tend to be lower, whereas detomidine (0.02 to 0.06 mg/kg) requires a similar dose for both routes of administration.

Detomidine can also be administered sublingually. Although the pharmacokinetics and the sedative and cardiac effects have been reported, at present no information is available regarding the analgesic effects of this formulation. Cardiac effects appeared to be less after sublingual administration, compared with intravenous administration.

Local Anesthetics

Local anesthetics (lidocaine, mepivacaine, bupivacaine, ropivacaine) block nerve conduction and are administered in a localized region or in some cases systemically (lidocaine). When administered in a localized region of the body, they induce a loss of sensation without the loss of consciousness or alteration in CNS activity that is observed after systemic administration of other sedatives and anesthetic agents. They not only act on pain fibers, but also produce loss of sensation of temperature, touch, and pressure. Adverse effects of systemic overdoses of local anesthetics include CNS toxicosis, ranging from depression to excitation to muscle twitching and convulsions, and cardiovascular reactions including bradycardia, conduction disturbances, myocardial depression, hypotension, and cardiovascular collapse in extreme cases.

Local anesthetics are commonly used in the horse is for diagnostic purposes as part of a lameness evaluation to localize the source of pain. However, local infiltration of this class of drugs can also provide pain control, either before or after surgery. Mepivacaine tends to be longer lasting and less irritating than lidocaine. If a longer-term effect is desired, bupivacaine administration can provide up to 4 to 6 hours of analgesia. Intraarticular administration of local anesthetics is used for the diagnosis and management of lameness and surgery of the joints. Chondrotoxicity has been reported in an *in vitro* study in horses but in an *in vivo* study no increase in collagen degradation biomarkers were noted following intra-articular administration of lidocaine and bupivacaine. Until more data is available, it would be prudent to assess each clinical situation individually and weigh potential risks with benefits.

Epidural administration is another common route for administration of local anesthetics. Onset of analgesia is rapid (within 15 minutes), and the duration of analgesia is about 3 hours for the perineal region. Moderate hind limb ataxia has been observed with this route of administration but appears to resolve within an hour of administration. Systemic administration of lidocaine for analgesic purposes has also been reported.

Gabapentin:

Gabapentin is a first-line drug for the treatment of neuropathic pain in humans. It inhibits high voltage activated calcium channels by interacting with the $\alpha_2\delta$-1 subunit, which is upregulated in chronic and neuropathic pain. Oral bioavailability in horses is poor (~16%). Reports describing the efficacy of gabapentin as an analgesic in horses are conflicting. The drug was not effective at

decreasing lameness in chronically lame horses[5] but was reportedly effective for the treatment of neuropathic pain in one case report.[6]

Ketamine:
NMDA receptor activation can lead to the development of hyperalgesia and central sensitization. Ketamine is an NMDA receptor antagonist and is commonly used as an anesthetic induction and maintenance agent but that also has analgesic properties. Although there is limited evidence of its antinociceptive effect and very few clinical reports in horses, infusions of subanesthetic doses may be effective as adjunctive treatment for the management of laminitic pain (see below).[7]

Acetaminophen:
Acetaminophen affects serotonergic, opioid, nitric oxide, and cannabinoid pathways. There are also reports that it is a weak prostaglandin inhibitor. Studies suggest that at doses of 20-30 mg/kg PO, it is comparable to flunixin and phenylbutazone in experimental models of lameness.[8,9] In another study, acetaminophen (20 mg/kg PO) had a significant and sustained thermal anti-nociceptive effect.[10] Studies assessing GI effects appear to be favorable with no evidence of gastric ulceration noted following administration of 30 mg/kg q12h for 21 days.[11]

PHARMACOLOGIC TREATMENT OF NOCICEPTIVE PAIN:
Activation of high-threshold peripheral nociceptors can lead to nociceptive pain. The most effective method for managing nociceptive pain is to interrupt neurotransmission near the injury or surgical site by administering local anesthetics (Table 1). α_2-receptor agonists, which decrease afferent activity and activate descending inhibitory neurons and opioids, which decrease Aδ and C-fibers neurotransmitter release resulting in reduced responsiveness of projection neurons, can also be used to modulate nociceptive pain. The two drugs in combination, provide greater sedative and analgesic effects and are commonly used for perioperative pain control.

PHARMACOLOGIC TREATMENT OF INFLAMMATORY PAIN:
With inflammatory pain, changes in central and neural pathways occurs due to sensitization and lowering of the activation threshold of peripheral nociceptors by inflammatory mediators. Treatment options for inflammatory pain are listed in Table 1.

PHARMACOLOGIC TREATMENT OF NEUROPATHIC PAIN:
Pain Control for Laminitis
The pain associated with laminitis is a result of inflammation, facilitation of central nerve transmission and neuropathic pain. Inflammatory pain is a result of peripheral sensitization because of enhanced responsiveness of high threshold C fibers by chemical mediators released as part of the inflammatory process. The pain observed within the first 48-72 hours of clinical signs, is primarily attributed to inflammation. Facilitation of pain transmission within the central nervous system and the increase in excitability of spinal synapses are caused by the release of excitatory chemicals. Neuropathic pain results from the presence of chemical markers of nerve injury in the lateral digital nerve. Peripheral and central sensitization and neuropathic pain become more important as contributors to laminitis pain as the disease progresses.

Several classes of drugs are used for the treatment of pain associated with laminitis including NSAIDs, α_2-receptor agonists, opioids, lidocaine, gabapentin, and ketamine. More recently, published reports suggest that soluble epoxide hydrolase inhibitors may have a role in the treatment of pain from laminitis.[12] Starting NSAID (phenylbutazone, flunixin meglumine)

therapy early on during the developmental stage has been shown to be most beneficial. The addition of other analgesics to NSAID based treatment helps to address other aspects of pain and may allow for administration of a lower NSAID dose, thus decreasing the risk of NSAID-related side effects. The long-term use of opioids in the treatment of laminitis induced pain must be weighed against the potential for decreased gastrointestinal motility, which may predispose horses to colic. Regional administration (perineural or epidural) of opioids my decrease the likelihood or severity of adverse effects, such as decreased gastrointestinal motility. Tramadol has been assessed for pain management in horses with chronic laminitis. While improvement in off-loading frequency was noted at 10 mg/kg q12h PO, this dose was also associated with signs of colic.[13,14] When tramadol was administered at a dose of 5 mg/kg q12 hours PO for 7 days, a transient (3 days) improvement was noted.[7] When tramadol (5 mg/kg q12h PO for 7 days) was combined with a subanesthetic dose of ketamine (0.6 mg/kg/h IV for 6 hours) for the first 3 days of treatment, an improvement was noted for up to 3 days after discontinuing tramadol.[7] These results suggest that tramadol alone may not be satisfactory as a monotherapy for the treatment of chronic laminitis and that ketamine may be a useful component of a multimodal approach for the treatment of chronic laminitis.[7] In one case report, gabapentin (2.5 mg/kg PO) had good efficacy as an adjunctive analgesic for the treatment of laminitis pain.[6]

Table 1. Treatment options for nociceptive, inflammatory, and nociceptive pain.

Type of Pain	**Treatment Options**
Nociceptive	Local or general anesthetics Opioids α_2-adrenergic agonists
Inflammatory	COX inhibitors (NSAIDs) Soluble epoxide hydrolase inhibitors Local anesthetics Opioids
Neuropathic	Tramadol Ketamine Soluble epoxide hydrolase inhibitors Gabapentin Local anesthetics

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EQUINE PROCEEDINGS

June 4–6, 2023

NSAIDs in Horses I & II

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NON-STEROIDAL ANTI-INFLAMMATORY DRUGS IN EQUINE MEDICINE

Heather Knych, DVM, PhD, DACVCP

INTRODUCTION:

Inflammation occurs as a result of damage to tissue. In the early (acute) stages, the body attempts to return normal function to the injured tissue. However, over time and with chronic inflammation, detrimental effects can occur. The release of arachidonic acid is the first step in the inflammatory cascade. This initiates what is referred to as the arachidonic cascade. As part of this cascade, cyclooxygenase (COX) and lipoxygenase (LOX) enzymes generate several eicosanoids (thromboxane, prostaglandins, and leukotrienes) which play a key role in the inflammatory process. It is important to note, that although eicosanoids participate in the inflammatory cascade, some are also necessary for normal cellular function and maintaining homeostasis.

It is well established that PGE_2 lowers nociceptor thresholds and can therefore potentiate the effects of substances that cause pain. During inflammatory pain, prostaglandins (primarily PGE_2) are generated at peripheral terminals of sensory neurons causing hyperalgesia. In addition to acting at peripheral sites, there is evidence that Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) also act centrally to reduce hyperalgesia. In addition to inhibition of PGE_2 production in the CNS, other central mechanisms mediated by endogenous opioid peptides as well as inhibition of serotonin or excitatory amino acids have been proposed.

Non-Steroidal Anti-Inflammatory Drugs are effective for the treatment of soft tissue, musculoskeletal and abdominal inflammation, and pain. These drugs are potent anti-inflammatory drugs by virtue of their ability to decrease the production of inflammatory eicosanoids (prostaglandins and leukotrienes), through inhibition of cyclooxygenase (COX-1 and COX-2) enzymes. Traditionally, compounds that have a greater selectivity for COX-2, which is often associated with the signs of inflammation, relative to COX-1, the so-called "housekeeping enzyme," have been thought to have a better safety profile. However, it is important to note that COX-2 is also constitutively expressed in several tissues (i.e. brain, spinal cord, kidney, etc) and plays a role in normal cellular processes. It is now widely accepted that both COX-1 and COX-2 play a role in maintaining mucosal integrity in the upper GI tract as well as renal perfusion[1,2].

There are currently six Food and Drug Administration (FDA) approved NSAIDs labeled for use in the horse, including flunixin meglumine (FM), phenylbutazone (PBZ), ketoprofen, diclofenac, meclofenamic acid and firocoxib (Table 1). While all are effective anti-inflammatory agents, they vary with respect to their COX-1: COX-2 selectivity, as well as pharmacokinetic properties.

GENERAL PROPERTIES AND PHARMACOKINETICS:

Most NSAIDS are weak acids and are well absorbed following oral administration. They are highly plasma protein bound and are predominately distributed to extra-cellular fluid (ECF) with only low concentrations found in normal tissue and joint fluid. However, in damaged joints and tissues, NSAID concentrations can reach therapeutic concentrations. Persistence of the drug in inflammatory exudate can be prolonged compared to plasma concentrations, explaining the prolonged duration of anti-inflammatory effect, relative to the plasma pharmacokinetics. Most NSAIDs undergo hepatic metabolism followed by renal elimination.

CLINICAL INDICATIONS:

Musculoskeletal Inflammation and Pain:

Phenylbutazone and FM are the most prescribed NSAIDs in equine medicine. It is thought that PBZ is best for orthopedic pain and FM for colic and visceral pain. Phenylbutazone is effective for the treatment of orthopedic pain in horses. The recommended dose of PBZ for the treatment of orthopedic pain is 4.4 mg/kg q12h for the first dose, followed by 2.2 mg/kg q12h on consecutive days. Both PBZ (4.4 mg/kg IV SID for 4 days) and FLU (1.1 mg/kg IV SID for 4 days) significantly improved lameness scores and force plate evaluations in navicular syndrome.[3] Administration of 2.2 mg/kg IV ketoprofen and 4.4 mg/kg IV PBZ resulted in comparable improvements in hoof pain indices and lameness scores in horses with chronic hoof pain.[4] In another study, PBZ (4.4 mg/kg IV) was found to be superior to ketoprofen (2.2 mg/kg IV) in reducing lameness in a model of acuate synovitis. The authors concluded that PBZ may be more useful than ketoprofen in the treatment of acute synovitis or joint inflammation.[5]

The COX-2 selective NSAID, firocoxib, is effective in the treatment of naturally occurring osteoarthritis with improved lameness scores and mobility observed following chronic administration (0.1 mg/kg q24h x 14 days).[6] In a clinical trial, PBZ (4.4 mg/kg PO q 24 h) and firocoxib (0.1 mg/kg PO q 24 h) administration resulted in comparable improvements in lameness parameters (lameness score, joint swelling, joint circumference and range of motion) in horses with osteoarthritis.[7]

Diclofenac is a NSAID used extensively in human medicine. Currently the only DLC product approved for use in veterinary medicine is a topical liposomal preparation (Surpass®), labeled for the control of pain and inflammation associated with osteoarthritis in horses. The label instructions indicate that a 5-inch ribbon should be applied over the affected area twice daily for up to 10 days. The reported benefit to a topical formulation such as this one, is the lack of systemic absorption. It is applied and acts locally, decreasing systemic concentrations, thereby decreasing the likelihood of adverse side effects reported for systemic administration of NSAIDs. The efficacy of this preparation in the treatment of inflammatory conditions in the horse has yielded highly variable results and may be dependent on the inflammatory model utilized. Prostaglandin E2 (PGE_2) production in transudate was significantly decreased following a single topical administration of DLC in carrageenan-induced inflammatory model.[8] Application of diclofenac liposomal cream resulted in significant improvement in lameness in an experimental model of osteoarthritis.[9] Conversely, DLC did not appear to have an effect in an acute synovitis model.[10] The investigators also noted an increase in PGE_2 concentrations, compared to the control group.

Although not FDA approved for use in horses in the United States, meloxicam is commonly used in equine practice in other countries. It is effective for the management of orthopedic post-operative pain and inflammation.[11] Experimentally, meloxicam administration (0.6 mg/kg PO q 24 h x 7 days) significantly reduced lameness and effusion and decreased synovial fluid biomarkers of inflammation, matrix metalloproteinase activity and cartilage turnover in the treatment of acute synovitis.[12]

Recently, a new transdermal flunixin meglumine product labeled for use in cattle has been approved by the FDA. As transdermal administration is non-invasive, the purported benefits of this product include reduced handling of animals and ease of administration (Banamine Transdermal® label). This formulation is not approved for use in horses, however, there is one report describing the pharmacokinetics and effects on inflammatory biomarkers (eicosanoids)

following administration of a 500 mg dose.[13] Serum concentrations were lower than that described following intravenous administration of a comparable dose but still resulted in concentrations adequate to elicit an anti-inflammatory effect for 24-72 hours utilizing a well-established *ex-vivo* model of inflammation.[13] The terminal half-life following transdermal administration was prolonged (24.3 ± 9.17 hours) compared to oral, intramuscular and intravenous administration suggesting that absorption is rate limiting process following administration by this route.[13]

Grapiprant (Galliprant®) is a prostaglandin E_2 receptor antagonist that has been found to be an effective anti-inflammatory in dogs and that is devoid of some of the adverse effects associated with traditional NSAIDs that elicit their effects through inhibition of PGE_2 production. Although the therapeutic concentration is unknown for horses, administration of the label dose for dogs (2 mg/kg oral) did not achieve levels determined to be therapeutic in dogs. [14,15]. Using an ex vivo EP4 receptor assay, administration of an oral dose of 15 mg/kg suggests a short duration of EP4 receptor engagement (2-4 hours).[16] Assuming a correlation between the EP4 receptor assay and clinical effects, the short duration of EP_4 receptor antagonism is not likely to be clinically beneficial in horses. Administration of a much higher dose would be necessary, which is not practical using currently available formulations (60 and 100 mg tablets) and would likely be cost prohibitive.

Colic:

Non-Steroidal Anti-Inflammatory Drugs are routinely used to reduce the effects of endotoxemia and visceral pain in patients with colic and colitis. Clinically, FM is the most used NSAID for the treatment of colic and associated endotoxemia. Experimentally, both FM and PBZ have been shown to be effective in preventing adverse effect associated with endotoxemia.

While FM remains one of the mainstays for the treatment of colic, inhibition of repair mechanisms in the injured intestine, as well as a reduction in intestinal motility, following administration of non-specific COX inhibitors has been well established.[17–19] While non-selective NSAIDs such as FM, slow mucosal recovery in ischemic-injured jejunum, the COX-2 selective NSAID, firocoxib does not appear to affect recovery.[19] Since the degree of visceral analgesia was comparable between FM and firocoxib, firocoxib may be advantageous in horses recovering from ischemic intestinal injury.

Pyrexia:

A dipyrone formulation (Zimeta®) was recently approved by the FDA for use in the horse. The label indication is for the treatment of pyrexia, however, dipyrone is also thought to have mild analgesic and anti-inflammatory properties. Dipyrone is not as effective as FM for the treatment of visceral pain.

ADVERSE EFFECTS:

Non-Steroidal Anti-Inflammatory Drugs are relatively safe at therapeutic doses, however, adverse effects can occur in susceptible populations, at high doses or with long-term administration. Gastrointestinal effects, such as gastric ulcers, right dorsal colitis and renal toxicity are the most common adverse effects associated with NSAID administration. The likelihood of gastric ulcer formation increases with higher doses. Administration of a proton pump inhibitor, such as omeprazole has been shown to be effective in preventing and treating gastric ulceration associated with NSAID administration. Recently a group of investigators

demonstrated that horses treated with omeprazole in combination with PBZ (4.4 mg/kg PO q12 h) had an increased incidence of intestinal complications (colic, impactions diarrhea, enterocolitis and typhlocolitis).[20]

Right dorsal colitis is most common with excessive or prolonged PBZ administration, however cases have been reported with FM, firocoxib and meloxicam. Acute signs of right dorsal colitis include colic, anorexia, lethargy, depression, fever, and diarrhea. The chronic form may manifest as intermittent colic episodes, ventral edema, and weight loss. Laboratory findings include hypoalbuminemia. In the case of right dorsal colitis, all NSAIDs should be discontinued, and alternate analgesics (opioids, alpha-2-agonists, or lidocaine) administered for pain management.

Renal papillary necrosis can occur with NSAID administration, particularly with PBZ, due to inhibition of the synthesis of prostaglandins that play key roles in renal blood flow, water excretion and electrolyte balance. In the hydrated animal, COX inhibition by NSAIDs likely has little effect on renal hemodynamics, however, when an animal is hypovolemic, dehydrated or has renal disease, loss of prostaglandin production can result in vasoconstriction of the afferent arteriole, loss of medullary perfusion and redistribution of blood flow to the renal cortex.

USE OF ANTI-INFLAMMATORY DRUGS IN PERFORMANCE HORSES:

While the administration of therapeutic substances, such as anti-inflammatory drugs, is necessary for effective treatment of equine athletes, equally as important is ensuring the safety and welfare of the horse. Non-Steroidal Anti-Inflammatory Drugs are highly regulated in equine competition because of their potential to mask injuries during performance and in the case of horseracing, interfere with detection of lameness during pre-competition fitness and lameness examinations. In the United States, controlled therapeutic medication and anti-doping is regulated as part of the Horseracing Integrity and Safety Act (HISA). In other equine disciplines, oversight of medication monitoring may be under the purview of The United States Equestrian Federation (USEF) or the International Equestrian Federation (FEI). Under HISA, PBZ, FM and ketoprofen are the only permitted controlled therapeutic NSAIDs with a restricted administration time (RAT) of 48 hours. This corresponds to a laboratory screening limit (SL) of 300, 4.0 and 2.0 ng/mL in blood for PBZ (4.4 mg/kg IV single dose), FM (1.1 mg/kg IV single dose) and ketoprofen (2.2 mg/kg IV single dose), respectively. The USEF does not permit administration of approved NSAIDs within 12 hours of competition and does not allow administration of a second NSAID within 72 hours of competition.

CONCLUSION:

While the use of this class of drugs is imperative in veterinary medicine, for the effective treatment of pain and inflammation in equine patients, it is important that they be used judiciously. Administration at recommended dose rates and avoidance of "stacking" of NSAIDs, along with careful monitoring, especially with chronic administration is suggested to decrease the likelihood of the development of adverse effects.

Table 1. Food and Drug administration approved non-steroidal anti-inflammatory drugs approved for use in horses.

Drug	Formulation	Route	Dose (mg/kg)
Phenylbutazone	Tablets, Paste, Powder	PO	4.4 mg/kg q24h 2.2 mg/kg q12h
	Injectable	IV	2.2- 4.4 mg/kg q12h
Flunixin meglumine	Injectable	IV, IM	1.1 mg/kg q24h
	Paste, Granules	PO	1.1 mg/kg q24h
Ketoprofen	Injectable	IV	2.2 mg/kg q24h
Firocoxib	Injectable	IV	0.09 mg/kg q24h
	Tablets, Paste	PO	0.1 mg/kg q24h
Diclofenac	Liposome-cream	Topical	73 mg (5 inch strip) q12h
Meclofenamic Acid	Granules	PO	2.2 mg/kg q24h
Dipyrone	Injectable	IV	30 mg/kg q12h or 24h

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EQUINE PROCEEDINGS

June 4–6, 2023

Orthopedic Infection: Diagnosis, Treatment, & Recent Literature

Haileigh Avellar, DVM, MS, DACVS-LA, Kansas State University

KANSAS STATE UNIVERSITY | College of Veterinary Medicine

EQUINE PROCEEDINGS

June 4–6, 2023

Management of Equine Heel Bulb Lacerations

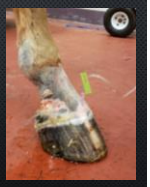
Dylan Lutter, DVM, MS, DACVS-LA, CERP, CAC, Kansas State University

KANSAS STATE UNIVERSITY | College of Veterinary Medicine

Managing Equine Heel Bulb Lacerations

Dylan Lutter DVM, MS DACVS-LA
Kansas State University

Heel Bulb Laceration Overview



- Common occurrence with potentially devastating consequences
- Surprisingly is sparsely addressed in the literature
  - Conflicting information regarding prognosis
  - No prognostic factors have been evaluated
- Janicek, et al. JAVMA 2005; v226 p418-423
  - 83% return to use; DIP involvement carries poor prognosis
    - 101 cases treated by Texas A&M VMC
- Ketzner, et al. Aus Vet J 2009 v87 no 9 p363-368
  - 89% return to soundness; Synovial involvement did not affect outcome
    - 50 cases, multicenter
      - 3 university hospitals- Cornell, Illinois, Kansas State

Equine heel bulb lacerations: 62 cases (2004-2018)

Seen at Kanas State University VHC JAVMA 2022 v260 n12 p1541-1546

- Study prompted by my observations during my time as KSU VHC Large Animal Emergency Clinician
- Many horses did well despite apparent severity, chronicity, and synovial involvement
  - A subset of horses do terribly
- Created a desire to identify prognostic factors that could aid practitioners and owners in making treatment decisions

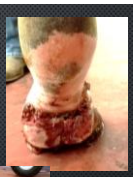
Patient Evaluation on Presentation

- 75-85% Quarter Horse
- Roughly even split male/female
- 50/50 or 60/40 front limb to hind limb split
  - Wire or metal reported causes
- Variable range of duration
  - 40%<24 hr; most 1-2 day range
  - ~30% present >2 days, several multiple weeks
- 30-40% show no lameness on presentation
  - Is that because they aren't painful or because they have transected the PD nerves?

My Initial Steps in Patient Evaluation

- Establish weight
- Perform general physical exam, assess degree of lameness
- Draw blood
  - PCV/TP- especially for acute or sub-acute
  - Same needle stick administer sedation- often xylazine +/- butorphanol
  - May administer NSAID but rarely at this stage
- Immediately prep & perform nerve block
  - Minimum of abaxial sesamoid
  - Often Low 4-point
- Clip hair fetlock to coronary band, clean skin, prep for synoviocentesis
  - #1 factor in affecting my plan & client cost

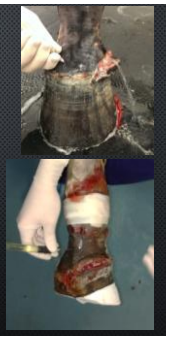
Wound Evaluation on Presentation



- Orientation
  - Transverse, directly palmar/plantar
  - Sagittal, medial or lateral
    - May wrap palmar
    - May include dorsal structures
- Contamination
  - 70% grossly contaminated
- Depth
  - 60% involve more than just skin

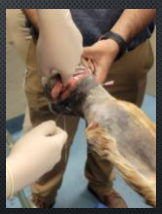
Arthrocentesis

- 17-34% overall synovial involvement
- Up to 50% require arthrocentesis to determine synovial involvement
  - Based on depth of wound & digital evaluation
  - ~70% of arthrocentesis confirm synovial involvement
- DIP joint involved in 60% of cases
- DFTS involved in 25-40%
- PIP & Navicular Bursa <15%
- 15-20% have >1 synovial structure involved
  - Most commonly DFTS & DIP



Initial Steps in Wound Evaluation

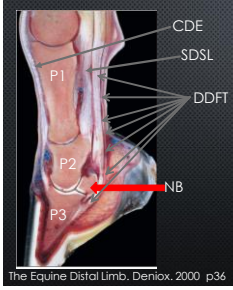
- Once blocked & prepped
  - Sterilely digitally palpate- weight bearing & non weight bearing
- Change gloves & perform synoviocentesis
  - Multiple saline-filled syringes for joint distension
    - 2 each of 6, 12, & 20/35 cc
  - Empty syringes for synovial fluid sample
  - Amikacin drawn for IA administration if no communication present
  - DIP- performed first weight bearing
  - PIP, DFTS performed second with limb held
  - NB performed last with limb held

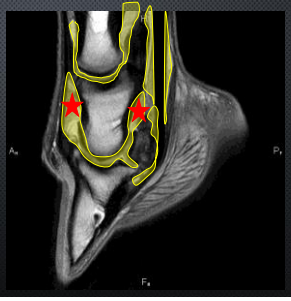


Synoviocentesis of Coffin joint

- Supplies
  - 3 to 5 -18 ga 1.5 in hypodermic needles
  - At least two 20 ml syringes filled with saline (or LRS)
    - I prefer slip tip over luer lock
  - 2 empty 3 ml syringes- for synovial sampling
    - Sample acquired <30 % of the time
- Approaches:
  - Dorsal approach- almost always an option
  - Palmar approach- more difficult but more consistent fluid sample
    - Rarely needed
    - May not be possible due to wound location

Distal Limb Anatomy

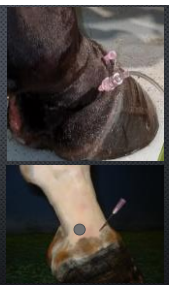




The Equine Distal Limb. Denoix. 2000 p36

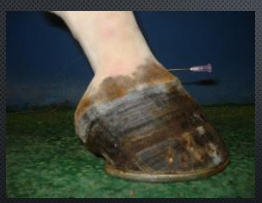
Coffin Joint

Dorsal approach

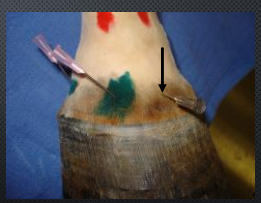


Lateral approach (needle)
Palmarolateral (dot)

Coffin Joint



Dorsal Horizontal approach

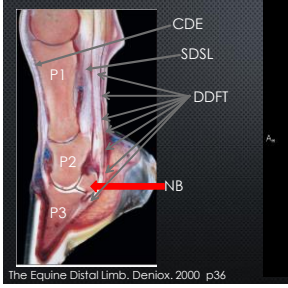


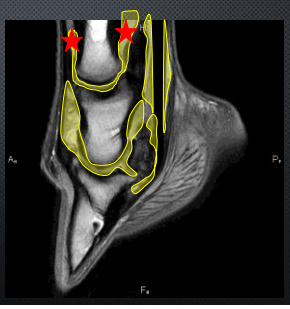
All 4 approaches
(Arrow = Dorsal Perpendicular)

Synoviocentesis of PIP

- Supplies
  - 3 to 5 -18 ga 1.5 in hypodermic needles
  - At least two 12 ml syringes filled with saline (or LRS)
    - I prefer slip tip over luer lock
  - 2 empty 3 ml syringes- for synovial sampling
    - Sample acquired <30 % of the time
- Approaches:
  - Dorsal approach- almost always an option but more difficult
  - Palmar approach- larger pouch but requires practice
    - May not be possible due to wound location

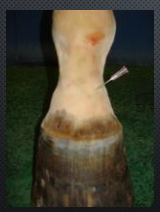
Distal Limb Anatomy





The Equine Distal Limb. Deniox. 2000 p36

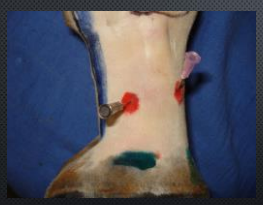
Pastern Joint

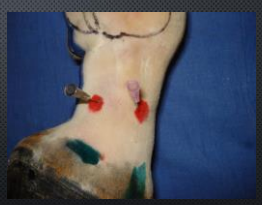


Dorsal approach

Palmar approach

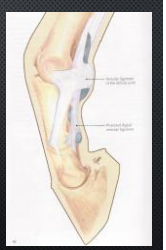
Pastern Joint





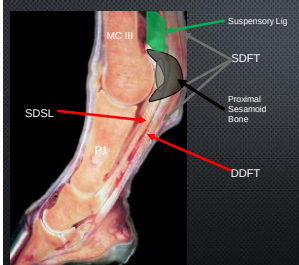
Synoviocentesis of DFTS

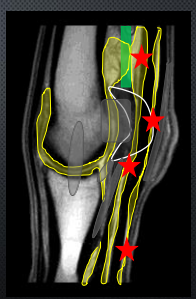
- Supplies
  - 3 to 5 -18 ga 1.5 in hypodermic needles
  - At least 2, preferably 3 or 4, 20 ml syringes filled with saline (or LRS)
    - I prefer slip tip over luer lock
  - 2 empty 3 ml syringes- for synovial sampling
    - Sample acquired <30 % of the time
- Approaches:
  - Basisesamoid
  - Proximal pouch
  - Peri-Sesamoidean
  - Distal Pouch
- Lavage & communication confirmation is difficult



A Guide to Equine injection and Regional Anesthesia p32

DFTS ANATOMY

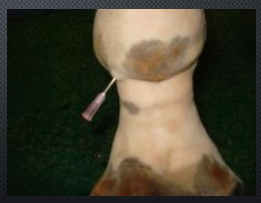




The Equine Distal Limb. Deniox. 2000 p280

FLEXOR TENDON SHEATH

Peri-Sesamoidean approach

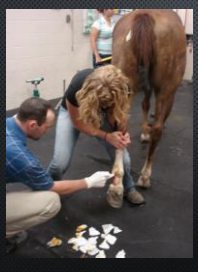


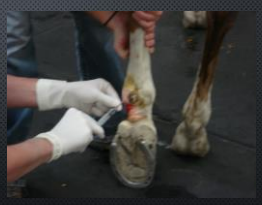
Basilar Sesamoidean approach

FLEXOR TENDON SHEATH

- All 4 approaches
- Proximal is at the top
- Top circle is the proximal pouch approach
- Bottom circle is the distal pouch approach

FLEXOR TENDON SHEATH

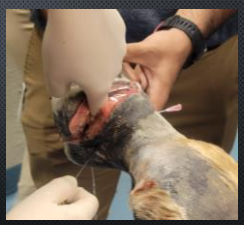




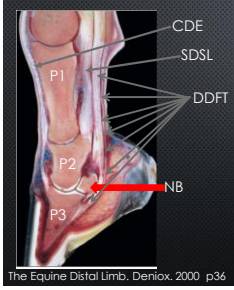
Clinical use of the basilar sesamoidean approach

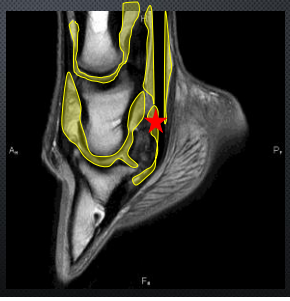
Synoviocentesis of Navicular Bursa

- Supplies
  - 2-18 ga 3 in spinal needles
  - At least two 12 ml syringes filled with saline (or LRS)
    - I prefer slip tip over luer lock
  - 2 empty 3 ml syringes- for synovial sampling
    - Sample acquired <30 % of the time
- Approaches:
  - Palmar approach- trans-tendinous
    - Blind or radiographically guided
  - US-guided Lateral approach
    - May not be possible due to wound location



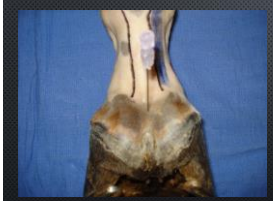
Distal Limb Anatomy



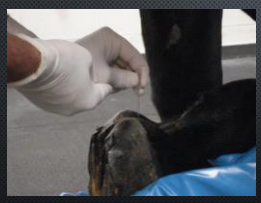


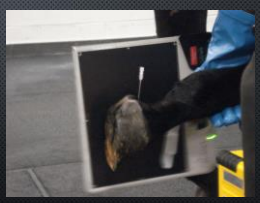
The Equine Distal Limb. Deniox. 2000 p36

Navicular Bursa

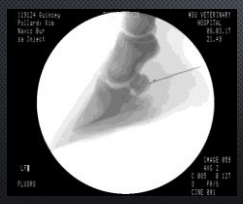


Navicular Bursa

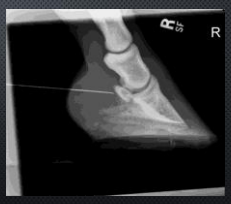




Navicular Bursa



Fluoroscopy

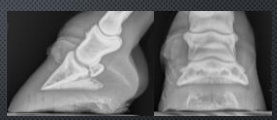


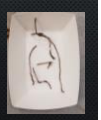
Radiography

Imaging- Radiographs & US

- Arguably indicated in every case
  - Particularly if wire is involved
- Reality: 25-40% of cases are radiographed
  - Often clinician discretion
  - Dictated by client finances
  - Vast majority have no lesions beyond ID of the wound
    - When present damage is often substantial
      - Osteomyelitis, bone defect, joint subluxation
- Ultrasound rarely performed
  - Degree of trauma?
  - Digital palpation instead

- Views:
  - Standard foot views +/- oblique views
  - Lateral & Horizontal DP likely most useful





HEEL BULB LACERATION MANAGEMENT

Synovial Lavage

- Arthroscopy is indicated in any joint with traumatic compromise
  - Removal of pannus & debris
  - High volume lavage
  - Assessment of damage
- Through & through needle lavage can be effective
  - Introduces element of risk to case management
  - Multiple large bore needles preferred
  - Anesthetized with pressurized pump best
  - Standing lavage with pressure bag often the only option
    - Target 1 L lavage
- Joint distension & fluid egress through single needle stick
  - Surprisingly effective in the short term if no other options possible
  - Often only 50-100 ml is possible/practical

Antimicrobial Choices & Routes

- Systemic- Clinician discretion & wound dependent
  - Reported 15-40% do not receive antibiotics- no negative effect on outcome
  - ~ Half immediately placed on Trimethoprim Sulfa
    - 15-30 mg/kg PO BID. Uniprim powder or TMS tablets
    - Preferred oral administration vs top dressing on feed
    - Oral tetracyclines also options but not reliably cost effective
  - ~ Half receive parenteral antibiotics
    - 22,000 IU/kg IV QID Potassium Penicillin/ 6.6 mg/kg SID IV Gentamicin
      - Standard top tier option
    - 2.2 mg/kg IV BID Ceftiofur Sodium/ 6.6 mg/kg SID IV Gentamicin
      - More cost effective upper tier option, some spectrum limitations
    - 2.2 mg/kg IV or IM BID Ceftiofur Sodium alone
      - Not preferred option, as some spectrum coverage deficits
      - May be reasonable if finances or drug availability present limitations
    - 6.6 mg/kg IV BID Oxytetracycline IV
      - Very cost effective option, particularly with financial limitations & synovial contamination but not outright infection
      - Some risk involved with this option- bacteriostatic

Antimicrobial Choices & Routes

- Intra-articular
  - Indicated following synovial lavage with wound communication
  - Prophylactically due to proximity or if communication suspected but not confirmed
- Amikacin remains the most broadly effective choice for common equine synovial pathogens

- Potential concern with IA antibiotic use
  - In vitro & In vivo dose dependent cytotoxicity, joint inflammation, & cartilage breakdown
    - Aminoglycosides among the most toxic
      - Even at the lowest commonly used clinical doses- 125 mg
      - 31.25 mg (1/8ml) amikacin administered IA still reached MIC levels of 100x those of common equine pathogens
    - Beta-lactams potentially least toxic

Pezzanite et al Equine Vet J 2020 v52 p713-724
Pezzanite et al Front Vet Sci 2021 doi: 10.3389/fvets.2021.676774
Pezzanite et al Equine Vet J 2022 v54 p24-38

Antimicrobial Choices & Routes

- Regional Limb Perfusion
  - Clinician discretion
  - Indicated due to large degree of soft tissue damage & contamination

- Concentration dependent antimicrobials preferred- q48 hrs
  - Amikacin, Gentamicin
- Time dependent antimicrobials are an option but require q12 to q 24 administration
  - Limited objective data on a per drug basis

- Wide tourniquet (Esmarch best) with 22 g catheter, needle or butterfly catheter into PD vein at fetlock or cephalic/saphenous
  - Nerve block above tourniquet maintain for 20-30 minutes
- 1 g amikacin QS to 60 cc if fetlock or below, 2 g QS to 120 cc if carpus/tarsus or below
  - Slow administration to avoid blowing the vessel

Wound Management

- Debridement- contaminated & devitalized tissues
  - Judicious debridement- highly vascular, lots of important structures
  - Bandage facilitated debridement is a reasonable option

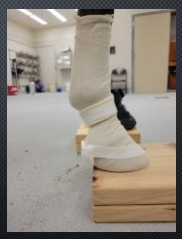
- Wound closure
  - Dictated by duration & wound condition
  - Primary closure preferred for cosmesis & time to healing
    - Closure has no effect on outcome

Bandaging vs Casting

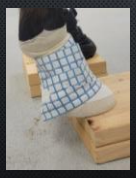
- Bandaging frequently required for initial management
  - Synovial lavage/antibiotic administration
  - Wound debridement
  - Typically until wound is healthy & synovial structures are healed
  - Mean of 4 to 8 days prior to casting

- Phalangeal Casting
  - Limits motion of hoof capsule, heel bulbs, and phalanges
  - Speeds healing & limits development of exuberant granulation tissue
    - 2.8 mean weeks for cast vs 4.1 mean weeks to healing for bandage alone
      - Half require some bandaging after cast removal
    - Improved cosmesis, especially with primary closure
  - Initial cost is higher but eliminates workload on owners for bandage changes

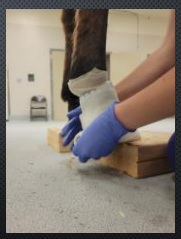
Phalangeal Casting Procedure



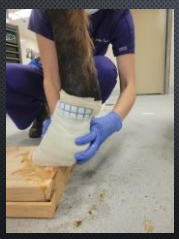
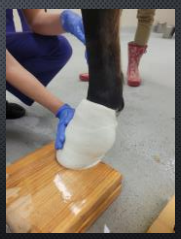
Phalangeal Casting Procedure



Phalangeal Casting Procedure

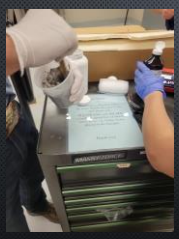



Phalangeal Casting Procedure

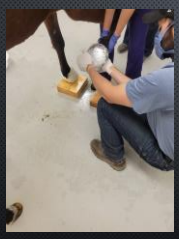



Phalangeal Casting Procedure

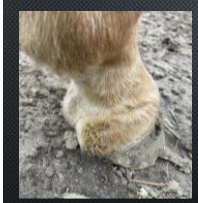

Phalangeal Casting Procedure

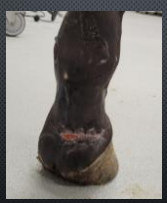


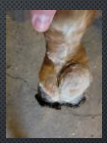
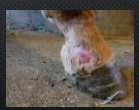

Phalangeal Casting Procedure




Appearance following casting


Sutured


Sutured



Sutured, patient removed cast q 1 week, dehisced, then bandaged 1 week

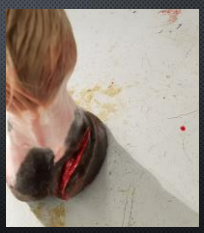
Outcome

- Morbidity- 5-10% reported persistent lameness
  - Some may be addressed by therapeutic shoeing
- Mortality- 2-5% mortality
  - Chronic synovial sepsis; Severe co-morbidities
- 85-95% Survival to discharge
  - Synovial involvement does not appear to affect survival- Sloan & Ketzner studies
  - DIP involvement negatively associated with outcome/survival in Janicek study
    - More associated with degree of damage/wound severity?
      - My hypothesis- joint collapse from chronic open joint or joint instability form CLL laceration
- Return to intended use
  - 75-85% reported return to previous level of use
    - With or without continuing therapy- unknown from literature
  - Time to return to use- not reported; dependent on level of wound healing

Predicting prognosis

- Sloan et. al JAVMA 2022 v260 n12 p1541-1546
  - 41 horses lost to follow up
    - Our records were not up to date or no return call from owners
  - 18 available: 5 with synovial involvement & 13 without
    - Mean 108 months to follow up
    - 11/18 had good outcome (score 3)- return to intended use with no residual lameness
    - Wound duration < 2 days sig associated with higher outcome score
    - Treatment with foot cast did not affect outcome
    - Synovial involvement did not affect outcome
- There is room for additional work to aid in predicting prognosis
  - Time to healing, time to return to work, better characterization of damage to predict poor outcomes

Questions?



EQUINE PROCEEDINGS

June 4–6, 2023

Field Management of Equine Fractures

Dylan Lutter, DVM, MS, DACVS-LA, CERP, CAC, Kansas State University

KANSAS STATE UNIVERSITY | College of Veterinary Medicine

Field Management of Equine Fractures

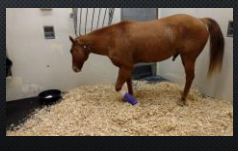
Dylan Lutter DVM, MS DACVS-LA
Kansas State University

Challenges of Equine Distal Limb Fractures

- Large fractious animals
- Little to no surrounding musculature
  - Open fractures are common
- Adequate stabilization absolutely required prior to transport
- Frequently occur in sub-optimal locations
  (Geographic & Anatomic)

Clinical Presentation

- Non-weight bearing lameness
  - Differentials: Fracture, Septic joint, Hoof abscess, Tendon/Ligament rupture, Solar foreign body penetration
- Associated trauma
  - Car accident
  - Natural disaster
  - Athletic/Sporting accident
  - Unknown cause



Initial Assessment

- Goals
  1. Determine the cause clinical signs
  2. Stabilize the patient
     - Systemically & locally
  3. Identify & address soft tissue injury
     - Wound/laceration
     - Tendon/ligament rupture
  4. Make appropriate treatment recommendations
     - Local/on the farm
     - Referral
     - Euthanasia

Initial Stabilization

- De-escalate the situation
- Control hemorrhage
- External limb coaptation of obvious fractures
- Physical exam
- Diagnostic imaging as indicated
- Systemic stabilization as indicated
- Initial wound management
- Fracture coaptation revision if needed
- Discussion of prognosis & treatment options as appropriate

Stabilization of a Fracture

- Goals
  - Facilitate partial weight bearing
  - Prevent further tissue damage
  - Immobilize adjacent joints
  - Reduce pain & anxiety

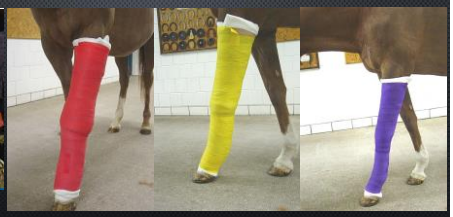
Types of Stabilization

- Robert Jones Bandage
  - Very thick & heavy
    - 3 one inch thick layers cotton padding, each compressed with brown gauze, then secured with cohesive bandage
      - Bandage 3x the diameter of the limb
    - Idea is that the bulk stabilizes the limb
  - Provides insufficient stabilization
    - Padding compresses with time & loading
  - Modified vs unmodified
    - Confusing



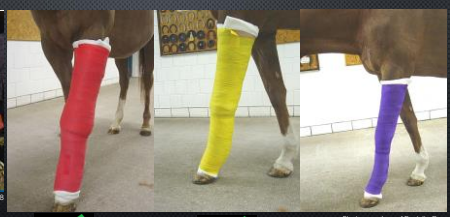
RJB vs modified RJB

Robert Jones Bandage


Photos courtesy of Dr. Julie Cary

These are all just variations of a single layer full limb bandage.
AKA a single stack bandage

RJB vs modified RJB


Photos courtesy of Dr. Julie Cary

Types of Stabilization

- Bandage/Splint Combination
  - Method of choice for emergency stabilization
    - Relatively fast application & inexpensive
    - Materials more readily available
  - Blankets, towels, bed sheets, jackets will work in an emergency
  - Pillows are too bulky and compress too easily yet not enough
  - Splint materials
    - PVC pipe section, board, broom handles, +/- metal bars
    - Kimzey Leg Saver

Is there benefit to a Robert Jones-type (ie. multi-layer) bandage?

Multiple layers do not apply significantly more pressure to the limb

- Canada et al. Vet Surg 2018 47:640-647
  - Mean sub-bandage pressure for standard equine compression bandages
    - Distal Limb Compression: 165 mm Hg*
    - Double Layer Compression: 146 mm Hg
- Granello et al. Vet Comp Orthop Traumatol 2023 36(2):82-86
  - Mean sub-bandage pressure for ex vivo MC III fracture model
    - Single layer full limb vs full limb RJB with 2 orthogonal splints
    - Dorsal pressure: 123.5 mm Hg (SS)* vs 102.5 mm Hg (RJB)
    - Lateral pressure: 109.3 mm Hg (SS)* vs 81.5 mm Hg (RJB)

How effective is a single layer bandage vs a RJB?

- Lutter et al. J Vet Emerg Crit Care 2015 25(3): 379-387
  - Simulated MCIII fracture model, bending only
  - Mean deflection 92.5 mm (SS) vs 93.5 mm (RJB)
    - RJB deflection decreased as bandager experience increased
      - Approached but did not reach significance (p = 0.072)
  - Stretching the elastic bandage to 94% vs 80% of maximum
    - Applied significantly more force 39 N vs 19.5N, respectively, with significantly less deflection†
    - <80% results in substantially more deflection†
  - It is difficult to achieve >80% of maximum stretch when bandaging a live, normal horse
    - Experienced bandagers approached 80% stretch†
    - Novice bandagers reached 60-70% stretch as a maximum†
      - Some as low as 47%

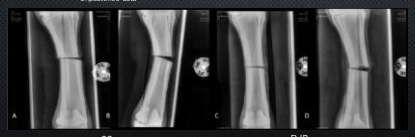

†Unpublished data

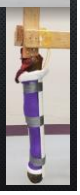
How effective is a single layer bandage vs a RJB?

- Bandage/splint stiffness (bending) of a single stack bandage is not significantly different than a RJB.
  - Experimental model only; SS not superior to RJB; RJB not ineffective
- How tightly you apply the bandage material significantly affects the stiffness of the bandage, regardless of SS or RJB.
  - ie. in a fracture situation, apply the bandage as tightly as possible
    - Nearly to the point of ripping

How effective is a single layer bandage vs a RJB?

- Granello et al. Vet Comp Orthop Traumatol 2023 36(2):82-86
  - Ex vivo MC III fracture model
  - SS deflection not significantly different than RJB
  - Radiographic total deflection angle not significantly different
    - SS fracture fragments were significantly less aligned (ie. larger angle)
  - Optimum % stretch threshold was not achieved
    - Mean stretch RJB: 83.9% stretch, SS 76.3% stretch
      - †Unpublished data





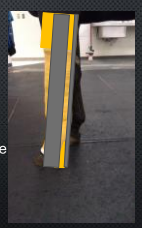
SS RJB

How effective is a single layer bandage vs a RJB?

- SS/splint as effective as RJB/splint and reducing bending in cadaver limbs
  - Not directly applicable to clinical fracture situations
- 94% stretch not necessary to produce an adequately stiff bandage
  - 80% appears adequate but low threshold is not known
  - It is difficult to tightly bandage real horse legs too tightly.
- Effect of the radiographic angles is unknown
  - RJB limbs were more cylindrical & fit the splints better
  - Strategically adding padding to fill gaps may be beneficial
    - Hypothesize to improve patient comfort through improved anatomical alignment?

Application of the Bandage

- Bandage stability is of utmost importance
  - Use only enough padding to make the limb a cylinder
    - Protects the soft tissues
    - Allows uniform pressure distribution of the splint
    - Can always add more bandage on top of the splint
  - Apply the bandage material as tightly and uniformly as possible
  - Excessive padding & inadequate tension in application will allow the fracture to move



Application of the Splint

- The splint becomes the load bearing structure
  - Apply the splint after the first layer of bandage material
  - Must immobilize the joint above and all joints below
  - Always extend the splint from the ground to the proximal aspect of the adjacent long bone
  - Always apply two splints at 90° to each other, when use of 2 splints is indicated
  - Secure the splint with non-elastic tape
    - Duct tape
    - 2" White athletic tape

Specific applications to the horse

Fracture Regions:

Front Limb

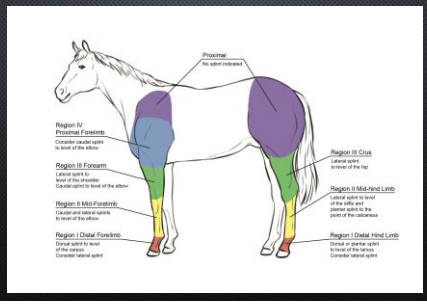
1. P1, P2, +/- P3, Sesamoid bones
   - Suspensory apparatus breakdown
2. MC III & Carpal bones
3. Radius
   3b. Ulna
4. Humerus & Scapula

Hind Limb

1. Same
2. MT III & Tarsal bones
3. Tibia
4. Femur

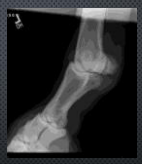
Bramlage Comp Cont Educ 1983 v5 no 10 p564-574

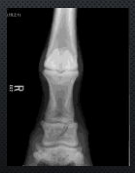
Specific Splinting Applications to the Horse



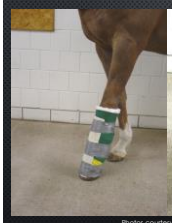
Region 1: Phalanges & Sesamoids

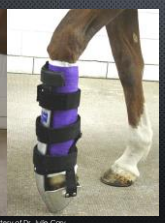
- Must align the dorsal cortices
  - Removes the lever arm from the fetlock joint
  - One dorsal (required)
  - One Lat/Med splint (situation dependent)
  - Heel wedge may be applied to the foot
    - Gives the horse a toe touching appearance
  - Kimzey splint with bandage achieves this
    - Does not perfectly align the phalanges



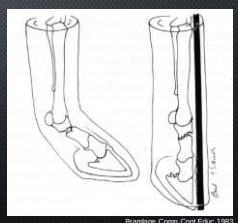


Region 1



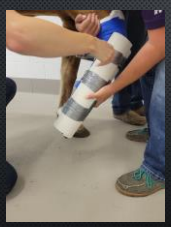


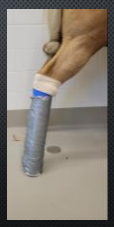
Photos courtesy of Dr. Julie Cary

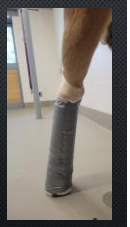


Bramlage Comp Cont Educ 1983

Region 1



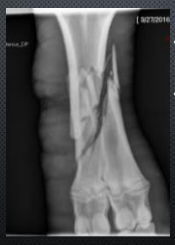




Region 2: MC/MT III, Carpal/Tarsal Bones

Front limb

- One splint lateral
- One caudal
- Extends to the point of the elbow
  - Locks carpus in extension



Hind Limb

- Lateral splint to the level of the stifle joint
- Plantar splint to the point of the calcaneus
  - May only need to the calcaneus if fracture is in distal MTIII

Region 2 Front Limb

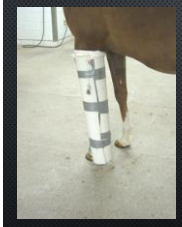
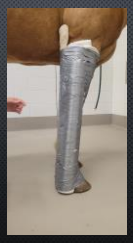
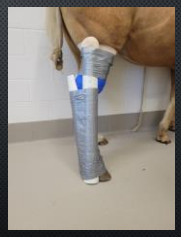
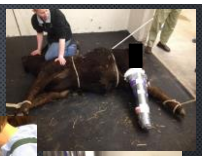


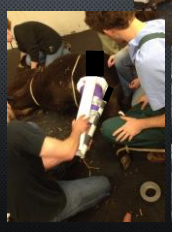
Photo courtesy of Dr. Julie Cary

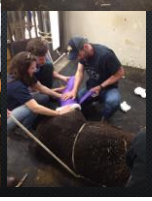




Region 2 Rear Limb



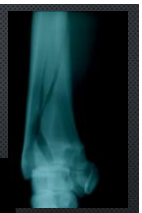


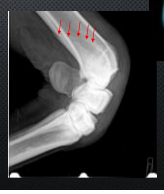


Region 3: Radius and Tibia

Front Limb

- Lateral splint to the level of the withers
  - Prevents abduction of the distal limb & subsequent open fracture
- Caudal splint to the point of the elbow

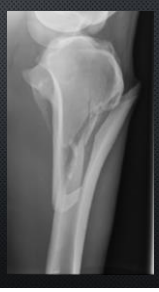




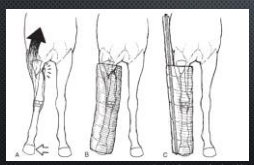
Region 3: Radius and Tibia

Rear Limb

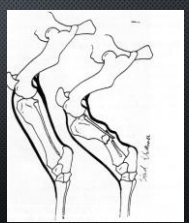
- Difficult to splint
  - Consider a cast
  - Reciprocal apparatus
- Single lateral splint to the level of the coxofemoral joint
  - Ideally contoured to the limb
  - Caudal splinting not possible



Region 3

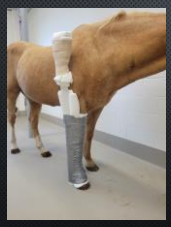
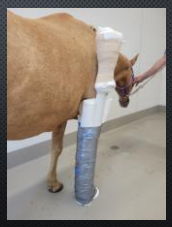


Equine Surgery 4th ed p 1021

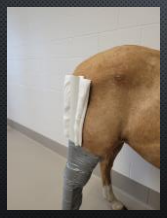


Rhamtags Comp Cont Educ 1983

Region 3: Radius

Region 3 Tibia

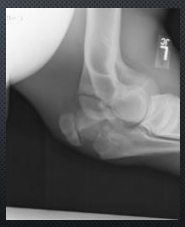



Region 3 Tibia


Smith Clin Tech Eq Prac 2006 v5 p154-60

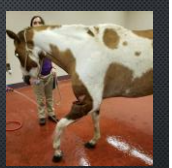
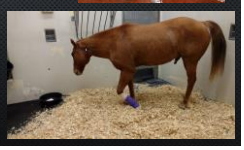
Region 3b: Ulna

- Ulnar fracture causes loss of triceps function
  - Classical dropped elbow stance with carpal flexion
- Single caudal splint from the ground to the point of the elbow
  - Locks elbow in extension & allows weight bearing



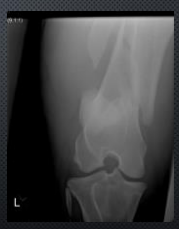
Region 3b: Ulna/Radial Nerve Paralysis



Region 4: Humerus & Femur

- Cannot be adequately stabilized externally
  - Distal humeral fracture may benefit from a caudal full limb splint to lock the carpus in extension
- Surrounded by adequate musculature to protect the fracture



Ideal Transportation Equipment

- Spacious, well lit interior (horse access from **all** **sides**)
  - Moveable stanchions for support
  - Well ventilated, +/- a fan or AC unit & heater
- Loading ramp & non-slip flooring throughout
  - Preferably side and rear loading
- Strong frame to support a winch & harness/sling
- Well stocked & easily accessible medical supplies
- Video camera access to the driver
- Available inflatable air mattress & loading sled

Emergency Trailer
3 different options

http://www.kimzeymetalproducts.com/

http://www.horsechannel.com

http://www.extension.org/

Loading the Horse

- Get the trailer as close as possible
  - Consider raising the nose of the trailer to lower the rear
- Slowly lead the horse into the trailer
  - Front of the trailer has smoothest ride
- Secure a rump bar, a chest bar,& a stall partition
  - All must be strong enough to allow the horse to lean on

Transporting the Horse

- Prior recommendation to face the horse:
  - Forward if a rear fracture & backward if front fracture
    - Thought to relieve stress on the horse during braking
    - May not be practical or possible
  - Adequate support bars & careful driving are more important

Transporting the Horse

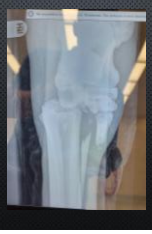
- I don't recommend a handler riding in the trailer
  - If separation is possible & safe, it may be useful to calm the horse & administer treatments
- Keep the horse untied to allow use of the head for balance
- Travel with reasonable speed and careful driving
  - Speed is not essential if limb is appropriately stabilized
- Support harness is helpful if equipped and tolerated

Unloading the Horse

- Go slow & allow the horse time to decide how to move
- Should unload using sound limbs first
  - Back the horse off if front fracture
  - Walk the horse off if rear fracture
    - Preferably through the side loading door
- Adjust trailer nose height or unload onto a platform level with trailer floor
- Mild sedation may be useful during unloading
  - A nervous horse may jump out

Questions?

You never know when you'll be called to help a horse.
New KSU grad, small animal interest/practice, 4 months post graduation


EQUINE PROCEEDINGS

June 4–6, 2023

Common Equine Toxins

Scott Fritz, DVM, DABVT, Kansas State University

KANSAS STATE UNIVERSITY | College of Veterinary Medicine

Equine Toxicology

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This presentation is case based, utilizing real cases to review the topics below. In lieu of a traditional proceedings document, bulleted "take-home" points are provided. Practitioners are encouraged to work with their diagnostic laboratory to select proper samples and testing strategy as the test offerings are dynamic in many instances. The common saying "Treat the patient not the poison" is the best advice that can be given for clinical cases. Post-mortem diagnosis can be difficult, frustrating, and expensive and an open line of communication between owners, veterinarians, and the diagnostic laboratory helps tremendously.

Fescue/Ergot

- Largely reproductive issue in horses – pregnant mares should not see fescue within 6 weeks of parturition
- High-dose exposure can result in the distal gangrene and hyperthermia observed in other species
- Fescue infected with novel endophytes can be used for forage – testing still warranted
- Detecting the alkaloids in urine can be useful but half-life is short
- This is a management disease

Pyrrolizidine Alkaloids

- Fresh plants largely unpalatable, dried plants in hay are the usual culprit
- Manifested after weeks to months of exposure
- Difficult to distinguish from aflatoxicosis histologically
- Analytical techniques exist but not routinely offered at most D-labs

Taxus sp.

- Causes a conduction issue, histologic lesions rare and non-specific
- Dried clippings most commonly blamed
- Finding leaves in stomach is nearly definitive, horses chew the leaves so this can be difficult
- Preventing exposure is essential, owner education important
- Testing not routinely offered

Acer Rubrum

- Generally associated with wilted or dried leaves either after a storm or in the fall
- Hemolytic anemia with leaves in GI tract
- Don't house horses near Red Maple trees, try to keep leaves out of hay

Juglans nigra

- Multiple limbs affected
- Edema, hyperthermia, lameness
- Laminitis in severe cases
- Resolution following bedding removal
- Toxic principle unknown – testing unavailable
- Maybe PCR to detect black walnut in shavings

Berteroa incana

- Clinically indistinguishable from Black Walnut
- Plants unpalatable, usually present in the hay
- Common weed in hay fields especially from Northern US
- Prognosis generally good if coffin bone is not rotated
- Toxic principle unknown – testing unavailable

Fumonisin

- Most common mycotoxin detected in grains
- Usually associated with cooler growing seasons and wet harvest conditions
- Equine Leukoencephalomalacia aka. Moldy Corn Poisoning
- Don't feed horses moldy feed
- Many D-labs offer feed testing

Aflatoxin

- Generally associated with hot and dry conditions
- Black light shows kojic acid not aflatoxin
- Targets the liver, histologically similar to pyrrolizidine alkaloid toxicosis
- Photosensitivity can be secondary issue
- Many D-labs measure aflatoxin in feedstuffs, tissue methods less common

Slaframine

- Mycotoxin from "Black Patch" disease of red clover
- Similar structure to acetylcholine
- Profuse salivation that resolves after limiting exposure
- Analytical techniques not routinely offered

Blister beetles

- Toxic principle is cantharidin, testing available for feed and urine/serum
- Desiccant, blistering and sloughing of GI and urinary mucosa
- Beetles crimped in alfalfa hay from southern US
- Buy first cutting hay to avoid swarming later in summer

BGA

- Warm, stagnant, nutrient-rich surface water
- Hepatotoxic and neurotoxic varieties
- Subject to winds, downwind side of water has the most algae
- Blooms occur rapidly
- Water testing to ID algae or quantify toxins available at many D-labs
- Tissue methods lacking

Botulism

- Typically due do ingestion of preformed toxin in contaminated feeds
- Multiple recent recalls of alfalfa products
- Flaccid paralysis, especially the tongue
- Diagnosis is complicated by lack of approved labs
- NVSL mouse bioassay is gold standard but lacks specificity

Selenium

- Substantially different clinical syndromes depending upon chronicity
- Acute toxicosis is similar to cardiovascular collapse and shock, almost always from injections
- Chronic toxicosis is more common and results from excessive dietary consumption
- Hoof and hair lesions predominate in chronic cases
- Diagnosis readily achieved by analyzing various tissues for selenium status, whole blood most practical

Fluoride

- Rare but still occurs
- Bone and teeth problems – weight loss and lameness
- Diagnosis achieved by measuring feed, water, and bone fluoride concentrations

Ionophores

- Horses are 10x more sensitive than cattle to monensin
- Cardiovascular disease predominates
- Horses can succumb much more rapidly than cattle

- Tissue concentrations prove exposure and when combined with histologic lesions a diagnosis is made

EQUINE
PROCEEDINGS

June 4–6, 2023

High-Impact Equine Diseases in the U.S. National Veterinary Accreditation Program Module 31

Andy Hawkins, DVM, Epidemiologist, Kansas
USDA-APHIS-Veterinary Services
Field Operations District 4

KANSAS STATE UNIVERSITY | College of Veterinary Medicine

National Veterinary Accreditation Program

Module 31: High-Impact Equine Diseases in the U.S.

USDA APHIS | NVAP Training Modules for Accreditation Renewal
https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/nvap/ct_aast

EQUINE PROCEEDINGS

June 4–6, 2023

Respiratory Disease of Foals - I & II

Katherine Delph Miller, DVM, MS, DACVIM-LAIM, Kansas State University

KANSAS STATE UNIVERSITY | College of Veterinary Medicine

Respiratory disease of foals

Katherine Delph Miller, DVM, MS, DACVIM-LA
Kansas State University
85th Annual Conference for Veterinarians
June 5, 2023

1

Objectives

- Know differentials for foal pneumonia
- Rank differentials based on respiratory diagnostic work-up
- Institute a treatment plan for neonatal foal pneumonia versus older foal/weanling with either suspected *Streptococcus zooepidemicus* or *R equi* pneumonia
- Implement preventative strategies for *R equi* endemic farms

2

Differentials for foal pneumonia

< 1 month

- Hematogenous infection from sepsis
  - Gram negative
    - ***E. coli***
    - *Klebsiella* spp
    - *Actinobacillus* spp
    - Other gram negative aerobes
  - Gram positive also
    - *Enterococcus* spp
    - *Streptococcus* spp
    - *Staphylococcus* spp
- Aspiration
  - Milk
  - Meconium

> 1 month

- Inhalation
  - *Streptococcus equi* subsp. *zooepidemicus*
    - Sole or mixed infection
  - *Rhodococcus equi*

3

Diagnostic work-up for foal pneumonia

- Physical exam
- Blood work
  - Hematology, serum biochemistry, serum amyloid A
- Respiratory function testing
  - Pulse oximetry
  - Arterial blood gas
- Diagnostic imaging
- Organism identification

4

Respiratory exam of the foal

Normal

- Slight abdominal component to breathing due to compliance of ribs
- Regular respiratory pattern in standing foal but erratic pattern in sleeping foal can be normal
- Lung sounds are easier to hear in neonate than adult
  - Often only subtle lung sounds are present even with severe pathology so thoracic auscultation can be unreliable

Abnormal

- Marked abdominal component
- Paradoxic movement of ribs and abdomen
- Increased nostril flare
- Periods of apnea
- Older foals
  - Cough, nasal discharge, depression, fever

Newborn (1 day old)	7 days old	30 days old
60-80 brpm	40-50 brpm	<40 brpm

Bernard and Barr. Equine Pediatric Medicine 2nd Ed 2018

5

Pulse oximetry

- Non-invasive
- S_aO_2 >92% in foals

6

Arterial blood gas

- Define severity of disease by assessing level of hypoxemia
- Assess response to therapy
- Goal P_aO_2 80-120 mm Hg using O_2 if needed
- Struggling and position of foal affect results
- Dorsal metatarsal artery, brachial artery, facial or transverse facial artery

7

Thoracic ultrasonography

- Loss of normal reverberation artifact pattern
  - "comet tails," thickening of pleural surface, peripheral consolidation
- Pleural effusion
- Peripheral pulmonary abscess
- Pneumothorax
- Rib fractures
- Hemothorax

8

Thoracic radiography

- Right and Left lateral radiographs
- Evaluate type, severity, and location of pulmonary disease
- Interstitial, alveolar, or bronchiolar pattern
- Severity of alveolar pattern and number of cavitary lesions associated with decreased survival Giguere and Roberts. Vet Radiol Ultrasound 2012

Diffuse infiltrates	Atelectasis Interstitial pneumonia Bacterial pneumonia Viral pneumonia Fungal pneumonia Pulmonary edema Hyaline membrane disease
Cranioventral infiltrates	Aspiration pneumonia
Caudodorsal infiltrates	In-utero acquired pneumonia Hemorrhage
Focal areas of opacity	Abscess formation

9

Organism identification

- Blood culture
- Transtracheal aspirate
  - Cytology
  - Culture
  - PCR

10

Learning Points

- Thoracic imaging is helpful for ranking differentials for foal pneumonia
- Can perform TTW if needed when more stable
- *Streptococcus zooepidemicus* is high differential for foals similar to adults
- Mixed infection is possible
- Can use inhaled (MDI or nebulized) medications on foals

11

Rhodococcus pneumonia

- *Rhodococcus equi*
- *Rhodococcus hoagii*
- *Prescotella equi*

12

R equi

- Gram positive intracellular bacteria
- Found in environment and manure of healthy herbivores
- Environmental concentration increases
  - Replicates in horse manure
  - Infected foals shed larger amounts of virulent *R equi*
- Aerosolization
  - High foal density
  - Hot dry weather
- Virulent and avirulent strains
  - Virulence-associated protein A (VapA)
    - Required for intracellular survival and replication inside macrophages

13

R equi pathogenesis

- Airborne virulent organism
  - First 2 weeks of life
- After inhalation
  - → infects alveolar macrophages and replicates inside cell → macrophage necrosis occurs
  - → continuous macrophage death and reinfection of new macrophages → characteristic abscess formation
- Slow growing → clinical signs develops weeks to months after infection

14

Clinical signs: Pulmonary form

- Fever, anorexia, lethargy
- Tachypnea, increased respiratory effort, nostril flare
- Cough and nasal discharge

- Uncomplicated pneumonia survival rate: >90%
- Severe pneumonia have high mortality: 19%

15

Clinical signs: Extrapulmonary disorders

- Abdominal
  - Most common, can cause severe disease and high mortality
  - Granulomatous enterocolitis or enterotyphlocolitis
  - Abdominal lymphadenitis
  - Abdominal abscess
  - Septic peritonitis
- Polysynovitis
  - Immune-mediated or possibly septic
  - Septic arthritis or osteomyelitis
- Uveitis
- IMHA, IMTP
- Mediastinal lymphadenopathy
- Pericarditis
- Granulomatous meningitis

16

Diagnosis of Rhodococcus pneumonia

- EARLY DIAGNOSIS
- Cannot differentiate based solely on CS
- Presumptive
  - Signalment, farm history
  - Thoracic US and radiographs
  - Blood work
- Definitive
  - Culture and PCR

17

Imaging for Rhodococcus pneumonia

- Radiographs
  - Multifocal nodular interstitial pattern
- Ultrasonography
  - Superficial abscess or consolidation
- Common but not pathognomonic
- Thoracic abscesses on radiographs
  - 71% sensitivity and 85% specificity for Rhodococcus pneumonia Leclere et al Vet J 2011

18

Blood work for Rhodococcus pneumonia

- Leukocytosis
- Mature neutrophilia
- Monocytosis
- Hyperfibrinogenemia
- Hyperglobulinemia
- Elevated SAA not a predictor for R equi
  - Useful for monitoring progression and response to treatment Passamonti et al Vet J 2015

19

Fecal testing for R equi

- PCR for VapA in feces
- Present in normal and subclinical foals Shaw et al J Vet Intern Med 2015

20

R equi pneumonia diagnosis

- Foals 2-6 months of age
  - Clinical signs of pneumonia
  - WBC > 20,000/ul
  - Hyperfibrinogemia >700 mg/dl
  - Likely infected with *R equi*
  - Specificity of 85% Giguere et al J Am Vet Med Assoc 2003

21

Treatment for Rhodococcus pneumonia

- Treat foals with clinical signs of disease
- Challenge to decide when/if to treat subclinical foals
  - Adverse effects of medications
  - Risk of antimicrobial resistance developing

22

Antimicrobials

- Wide variety active *in vitro* but only a few effective *in vivo* due to intracellular location
- Macrolide and rifampin
  - Standard of care

23

Macrolide and rifampin

- Clarithromycin or azithromycin
  - C: 7.5 mg/kg PO q12h
  - A: 10 mg/kg PO q24h for 5 days, then q48h
- R: 5 mg/kg PO q12h or 10 mg/kg PO q24h

24

Macrolide and rifampin

- Duration: 4-8 weeks, depends on disease presentation
- Combination therapy still superior than monotherapy
- Rifampin decreases oral absorption of clarithromycin
  - Not clinically significant
  - Concentration in PELF and pulmonary macrophages above MIC for *R equi* still

Sanz VCNA EQ 2023
Peters et al Drug Metab Dispos 2011
Berlin et al Equine Vet J 2017
Berlin et al Mol Pharmacol 2016
Burton et al Antimicrobial Agents Chemother 2015

25

Other macrolides

- Tulathromycin
  - IM once weekly 2.5 mg/kg
  - Not effective when used alone
  - Similar when combined with oral rifampin to A-R combination
    - Mild to moderate to severe pneumonia

Sanz VCNA EQ 2023
Venner et al Vet Rec 2013
Rutenberg et al J Vet Intern Med 2017
Goebel et al EVE 2022

26

Other macrolides

- Gamithromycin
  - IM once weekly 6 mg/kg
  - Noninferior to A-R combination
  - 60% developed significant adverse effects
    - Colic requiring analgesics
    - Marked lameness
    - Local pain for 5 days when administered SQ
  - IV administration had less adverse effects but not recommended without additional research

Sanz VCNA EQ 2023
Berlin et al Mol Pharmacol 2016
Hildebrand et al J Vet Intern Med 2015
Hildebrand et al Pferdeheilkunde 2015

27

Other antimicrobials

- Gentamicin
  - Highly active in *in vitro* intracellular bactericidal assay
  - Failed to reach mutant prevention concentrations in BAL cells and PELF
- IV liposomal gentamicin
  - Effective in experimental infection
  - Nephrotoxicity in 50% of treated foals
- Gallium maltolate
  - Not recommended because clinical efficacy not demonstrated

Sanz VCNA EQ 2023
Giguere et al Vet Microbiol 2015
Berghaus et al Vet Microbiol 2013
Cohen et al J Vet Intern Med 2016
Giguere and Cohen EVE 2018

28

Learning Points

- Clinical signs solely does not differentiate R equi from other causes of pneumonia
- Definitive diagnosis is useful even on *R equi* endemic farms
  - Mixed infection
  - AMR strains
- Standard treatment is combination of macrolide and rifampin
- If AMR strain, treat based on C&S

29

Preventative screening for Rhodococcus pneumonia

- Screening protocols on endemic farms
  - Aim to reduce mortality
  - Risks
    - Adverse effects of antimicrobials
    - Development of antimicrobial resistance
- US screening Slovis et al AAEP 2005; McCranken and Slovis AAEP 2009
  - Incidence of disease on farms using US screening: 29% to 64%
  - Incidence of disease on farms not using US screening: 5% to 20 %
- Many foals with small pulmonary lesions recover without treatment
  - Median abscess score ≤ 6-10 cm

30

Antimicrobial resistance

- Increased concentration of AMR strains on farms that prophylactically treated based on US screening programs
  - In soil and from clinically affected foal samples
- Resistance reports
  - Before 2010: 0.7% to 3.7% in KY and TX
  - Between 2007 and 2017 in KY
    - 13% resistance for rifampin
    - 16% resistance for macrolides

Sanz VCNA EQ 2023
Huber et al J Am Vet Med Assoc 2021
Giguere et al J Am Vet Med Assoc 2010
Huber et al Antimicrobial Agents Chemother 2019

31

Clinical implications of AMR strains

- Macrolide resistance in R equi
  - Caused by erm(46), erythromycin-resistant methylase gene
  - Identified only in R equi to date
  - Resistance to all macrolides, lincosamides, and streptogramin B
  - Could transfer horizontally to other bacterium
- Foal survival
  - Resistant strains have lower survival
  - Only 25% survived to discharge when infected with resistant strain
    - 69% survival rate when infected with nonresistant strain

Sanz VCNA EQ 2023
Huber et al Antimicrobial Agents Chemother 2019
Asoh et al J Clin Microbiol 2003
Guiguere et al Microbio Spectr 2017
Alvaerz-Narvaez et al Appl Environ Microbiol 2020

32

Screen and treat protocols

- Identify clinical versus subclinical foals
  - PE
  - US
  - Blood work
- Individualized protocol for each endemic farm
- Goal
  - Decrease the incidence and severity of clinical pneumonia
    - Minimize use of antimicrobials each year
    - Decrease development of AMR strains

33

Hyperimmune plasma for Rhodococcus pneumonia

- No commercially available vaccine
- *R equi*-specific HIP on endemic farms for prophylaxis
  - Early literature: mixed results
  - Newer data: clinical benefits
  - Reduced severity of pneumonia in experimental challenge Sanz et al Vet Rec 2016
- Mechanism for protection
  - *R equi*-specific antibodies Kahn et al PLoS One 2021
  - Other proteins, complement, instrumental for *R equi* opsonization Cywes-Bentley et al PLoS Pathog 2018

34

Re-HIP

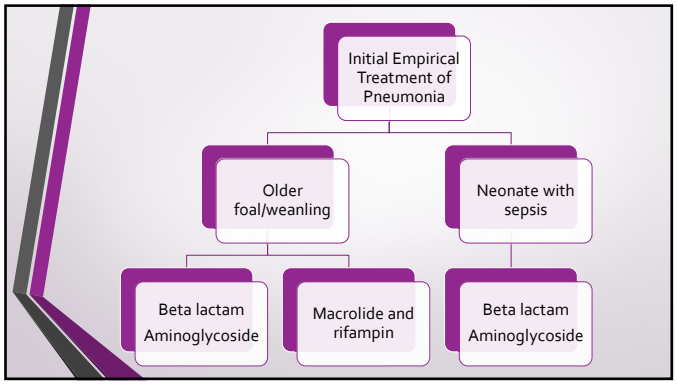
- Volume administered
  - 2 L shortly after birth Kahn et al J Equine Vet Sci 2019
    - 2.4 times less likely to develop clinical pneumonia compared to 1 L
    - Also lower proportion developing subclinical pneumonia via US (12% vs 32%)
    - Safe for administration Flores-Ahlschwede et al Equine Vet J 2021
- Shed less virulent R equi in manure after exp infection Sanz et al Vet Rec 2019
  - More research on environmental contamination in clinical infections
- Novel PNAG HIP investigated compared to Re-HIP Kahn et al J Vet Intern Med 2021
  - β-1 →6-poly-*N*-acetyl glucosamine
  - Not superior to Re-HIP protecting against natural pneumonia development

35

Learning Points

- EARLY diagnosis and treatment implementation in clinical cases of *R equi*
- Ultrasonographic lesions of *R equi* without clinical signs does not indicate antimicrobial therapy is needed
- Screening and treatment protocols should be individualized to *R equi* endemic farms
- *R equi* AMR has clinical and public health significance
- Re-HIP administration IV shortly after birth is useful for decreasing disease severity

36



37

Acute Respiratory Distress Syndrome

- Syndrome of respiratory failure associated with noncardiogenic pulmonary edema, decreased pulmonary compliance, and ventilation-perfusion mismatch → hypoxemia
- Not primary disease syndrome
  - Always secondary to other disease processes
  - Possible risk factors
    - Viral or bacterial pneumonia
    - Pneumocystis carinii
    - Toxins
    - Allergic response
    - Heat stroke
    - Nonpulmonary sepsis

38

Pathogenesis of ARDS

- Inciting agent initiates damage to alveolar and terminal airway cells → pulmonary congestion and interstitial edema, and flooding with inflammatory cells, fibrin, and cellular debris
- Damaged type I pneumocytes are replaced by type II pneumocytes → diffuse pulmonary fibrosis and scarring of the interlobular septa and pleura

39

Clinical signs of ARDS

- Acute onset respiratory distress
- Tachypnea
- Nostril flare
- Increased respiratory effort
- Possibly febrile

40

Diagnosis of ARDS

- Auscultation abnormalities
- Profound hypoxemia
- Thoracic radiographs
  - Bronchointerstitial pulmonary pattern of varying severity
- Thoracic ultrasonography
  - Diffuse coalescing comet tails radiating from lung surface
- Can try to identify causative agent

41

Treatment of ARDS

- Oxygen administration
  - Bilateral nasal cannulas
  - Intratracheal catheter
- Corticosteroids
  - Hydrocortisone
    - 1-4 mg/kg per day IV divided into 4-6 doses reported for CIRCI
  - Dexamethasone
  - Methylprednisolone sodium succinate
- Antimicrobials
- +/- bronchodilators
- IV fluid therapy
- Nutritional support

- Prognosis is very guarded
  - Development of hypercapnia and respiratory acidosis: poorer prognosis

42

Parasitic pneumonitis

- Lungworms: *Dictyocaulus arnfieldi*
- **Round worms: *Parascaris equorum***

43

Clinical signs of parasitic pneumonitis

- Chronic cough
- Mucoid to mucopurulent nasal discharge
- Respiratory distress
- Poor body condition
- Possibly colic
- History: often poor response to antimicrobial therapy for suspected bronchopneumonia

44

Diagnosis of parasitic pneumonitis

- Inflammatory leukogram: mature neutrophilia, hyperfibrinogenemia, hyperglobulinemia
- Possible mild to moderate elevation in hepatic enzymes
- Thoracic radiographs: moderate to severe bronchointerstitial pattern
- TBA cytology
  - Abundant eosinophils (5-50%, normal <2%)
  - Concurrent neutrophilic inflammation
  - +/- organisms visualized → culture
- Fecal likely negative during prepatent period
- Response to therapy

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Treatment of parasitic pneumonitis

- Anthelmintic therapy
  - Fenbendazole 10 mg/kg PO daily
    - Resistance of migrating larvae at lower doses
    - Ivermectin resistance noted
      - Concerns of ascarid impaction
- Based on severity of CS and concerns of secondary infection
  - Oxygen supplementation
  - Antimicrobials
  - Aerosolized corticosteroids

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Idiopathic or transient tachypnea of foals

- Reported in Clydesdale, TB, Arabians
- May develop signs a few days after normal birth
  - Persist for several weeks
- Dysfunction of thermoregulatory center
  - → elevated temperature and tachypnea/panting
  - Warm, humid environmental conditions
- R/O other causes of tachypnea
- Treatment
  - Cooling measures
  - Typically temperature doesn't respond to antipyretics
  - Antimicrobial therapy until infectious process ruled out

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Learning Points

- Remember other less common or additional differentials for foal pneumonia
- "Typical" cases may require additional therapeutics based on additional diagnoses

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