**Killing bacteria without killing your patient:**
Common Sense Antibiotic Use in the Horse

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**Antibiotics overview:**
- Penicillins
- Cephalosporins
- Aminoglycosides: Gentamicin & Amikacin
- Potentiated Sulfas: SMZ/TMS
- Macrolides: Erythromycin, Azithromycin, Clarithromycin
- Flouroquinolones: Enrofloxacin
- Metronidazole
- Doxycycline
- Chloramphenicol

**Antibiotics:**
- Horses very different from dogs/cats
- Few oral options – lack of bioavailability and risk of inducing diarrhea
- Antibiotic induced colitis – severe and life threatening
  - *C. difficile* commonly implicated
  - Regional differences
  - Risk exists with ALL antibiotics
  - Potentiated by stress, travel, withholding feed, anesthesia/surgery
- Almost all antibiotics are used “Off Label” in horses

**Antibiotic selection:**
- Is it active against known or likely pathogens?
- Will it reach adequate levels in the affected tissue/system?
  - CSF
  - Abscesses
  - Bone
  - Uterus
  - Mammary
- Safety?
- Cost?
- Ease and route of administration?

**Penicillins**
- Bacteriocidal
- Spectrum:
  - Most gram + aerobes except only 50% coag + staphlococcus
  - Most anaerobes except *Bacteroides fragilis*
- Time dependent – must maintain tissue levels above MIC for as long as possible – frequent dosing necessary (BID-QID)
- No oral administration due to poor bioavailability.
- Renal excretion – reach high levels in urinary tract
Penicillins: PPG (Procaine Pen G)
- White milky, must be refrigerated
- Dose: 20,000-40,000 IU/kg IM q12 hrs.
- Shake well before drawing up
- IM ONLY! Serious reactions if accidental IV administration
  - Aspirate to check for blood
  - Can still see "procaine reactions" : hyperexcitable, seizures
  - True anaphylactic reaction – death!
  - Increased risk with repeated injections
- Muscle soreness and myositis at injection sites
- Inexpensive

Penicillins: K-Pen (Potassium pen G)
- Higher tissue levels than PPG, but requires more frequent dosing
- Dose: 22,000 IU/kg IV q4-6 hours. SLOW IV. Dilute.
- Refrigerate once re-constituted.
- Expensive, requires round the clock treatment (after hours)
- When giving (especially too fast): teeth grinding, grimacing, yawning, hyperactivity, mild agitation, colic, diarrhea or soft stools – all generally transient
- Prokinetic on large intestine

Cephalosporins
- Bacteriocidal
- Time dependent
- Broad spectrum of activity against gram +, Gram -, and anaerobes
- Generally tolerated well – no procaine reaction risk, less muscle soreness than PPG
- Cost is somewhat more than PPG, less than K-pen
- Antibiotic induced colitis severe in certain regions, patient populations
- High urinary tract levels due to renal excretion, enterohepatic cycle – liver disease
- Won’t reach CSF, placentitis, mastitis

Cephalosporins: Naxcel/Cetiflex
- Reconstitute powder and refrigerate up to 1 week, 8 weeks if frozen – amber liquid
- Dosing: 2.2-4.4 mg/kg q 12-24 hours – IV or IM
- Typical 1000# horse dose: 1-2 g IM q 12-24hrs (20-40cc)
- IM dosing maintains higher tissue levels longer than IV
- Foals: 5-10 mg/kg SQ q12 hours
- Cost?

Cephalosporins: Excede
- Single IM dose maintains tissue levels for 5 days, 2 doses 4-5 days apart
- No refrigeration required – milky white, thick
- Some soreness and swelling at injections sites – recommend using 16 ga needle, split dose between two sites
- 1000# horse dose – 15 cc IM
- Some unofficial reports of “sudden death” reactions from injections – may be true anaphylaxis to cephalosporins, or inadvertent arterial injection... not well documented.
- Diarrhea/colitis risk seems low?

Cephalosporins
- Oral use of Cefpodoxime and other cephalosporins in FOALS ONLY!
- Good oral option for gram + and anaerobic organisms vs SMZ.
Aminoglycosides
- Amikacin, Gentamicin used most frequently for systemic use in horses
- Vancomycin regionally or in uterus
- Bactericidal
- Concentration dependent – once daily dosing with a higher level is more effective and less toxic than lower doses more frequently
- Post-antibiotic killing effect
- Spectrum: Gram - aerobes, few gram + (staph: amikacin>gent), no anaerobes
- No oral absorption
- IV or IM use (IM injections cause soreness IV recommended)

Aminoglycosides: Gentamicin
- Dosing: 6.6 mg/kg IV SID – adult horses
- Foals: 11-15 mg/kg IV SID
- Average dose for 1000# horse = 30 cc/1 gram
- Relatively inexpensive, frequently used in adult horses in combination with penicillins
- Less activity against gram + such as coag + staph, staph aureus
- Increasing resistance
- More nephrotoxic than amikacin

Aminoglycosides: Amikacin
- More expensive than gentamicin
- Rarely used systemically in adult horses due to cost
- Often used systemically in foals
- Less nephrotoxic than gentamicin
- Dosing: 12 mg/kg IV q 24 hrs.
- Foals: 20-25 mg/kg IV q 24 hrs.
- More activity than gentamicin against staph aureus, etc.
- Commonly used intra-articularly (for infections or with joint injections prophylactically) and RLP (Regional Limb Perusions)

Potentiated Sulfas
- SMZ/TMS/TMPs
- Bactericidal – Antipprotozoal (EPM)
- Broad spectrum of gram + and Gram – bacteria
- No anaerobes
- Limited effectiveness against strep in vivo, despite in vitro susceptibility
- Excellent tissue penetration
- Time dependent – dose 2x daily!
- Dosing: 20-30 mg/kg PO q 12 hours
- IV use rare, but available – don’t combine with Alpha-2 drugs!

Sulfas
- Eliminated by renal and hepatic excretion
- Benefits:
  - One of few oral options for horses
  - Relatively inexpensive
  - Easy for owners to administer
  - Broad spectrum, good tissue penetration
- Downsides:
  - Increasing resistance in bacteria due to widespread use
  - May induce neutropenia with chronic use
  - Antibiotic induced colitis common in some regions – otherwise limited to no toxicity
Equisul – Liquid oral sulfa

- Comparison from sulfadiazine and sulfamethoxazole – sulfadiazine is more bioavailable and requires lower dosing.
- FDA approved
- Increased bioavailability
- Decreases risk of colitis?

Macrolide antibiotics

- Erythromycin, Azithromycin, Clarithromycin, Lincomycin, etc.
- ONLY USE IN FOALS! All cause severe life-threatening colitis in adult horses. Sometimes mares of foals being treated are affected.
  - Some use of low dose erythromycin to stimulate GI motility
  - Gram + bacteria
  - Most commonly used in foals to treat Rhodococcus pneumonia, Lawsonia intracellularis infections.
  - Often combined with rifampin

Macrolide antibiotics

- Benefits: Oral dosing, newer drugs can give once daily for 5 days, then every other day
- Toxicity/precautions: Can cause fatal hyperthermia, diarrhea
- Most macrolides are time dependent, but azithromycin has some concentration dependent post antibiotic killing effects (not as strong as aminoglycosides or fluoroquinolones)

Fluoroquinolones:

- Enrofloxacin most common (Baytril), marbofloxacin etc.
- Bactericidal
- Concentration dependent
- Excellent gram – aerobes, some gram + especially Staph aureas, MRSA
- Great for cellulitis, lymphangitis in horses
- Dosing: 5 mg/kg IV q 24 hrs
  - Dilute and give slowly, ideally with catheter in place – irritation to veins. Muscle pain and soreness IM.
  - 7.5 mg/kg PO q 24 hrs.

Enrofloxacin: Baytril

- Renal excretion – high levels in urinary tract
- Toxicity/precautions:
  - Arthropathy in developing foals and young horses
  - Try not to use in animals under 3 years old
  - If have to use, consider adequan IM q 4 days – may be protective
  - Reports of tendon weakening and achilles ruptures in humans – not proven reported in horses

Metronidazole

- Bactericidal, anti-protozoal
- Narrow therapeutic spectrum – anaerobes only, protozoan
- Often use in combination with other antibiotics
- Treatment of choice for C. difficile colitis, Bacteroides fragilis
- Dosing: 20-25 mg/kg PO q 8-12 hours (Concentration dependent)
### Metronidazole

**Benefits:**
- Oral dosing (can also give IV or intra rectally)
- Compatible with penicillins, aminoglycosides, macrolides
- Active against *bacteroides fragilis* and other anaerobes

**Downsides/toxicity:**
- Narrow spectrum of activity – rarely used alone
- Poor palatability – bitter – anorexia
- Very rarely neurotoxic
- Requires somewhat frequent dosing

### Tetracyclines: Doxycycline, Minocycline

- **Bacteriocidal**
- **Renal excretion**
- **Gram + bacteria**
- Excellent against intracellular bacteria, good bone penetration
  - Potomac horse fever (*Neorickettsia risticii*)
  - Anaplasma phagocytophilum
  - Lyme
  - Leptospirosis
  - Rhodococcus
  - *Lawsonia intracellularis*, Lyme disease

### Doxycycline

- Oral dosing
- Expensive
- Dosing: 10 mg/kg PO q 12 hours
- Concentration dependent at high doses, time dependent at low doses
- Also has some anti-inflammatory properties and anti-MMP (Matrix metalloproteinases) activity
  - Role in inflammatory airway disease? Laminitis?
  - Excreted in tears – can help tx corneal ulcers, uveitis
- Toxicity: High doses -> diarrhea, colitis
  - Limited nephrotoxicity

### Minocycline

- Similar profile to doxycycline
- May be more cost effective in some cases, although still expensive
- May have better absorption orally than doxycycline
- 4 mg/kg PO BID

### Chloramphenicol

- Bacteriostatic at q8, cidal at q6 hrs
- Broad spectrum – gram +, gram -, anaerobes
- Excellent tissue penetration – CSF, bone, joints, abscesses
- "Big gun" antibiotic – reserve for select cases
- Dosing: 50-60 mg/kg PO q6hrs
- Osteomyelitis, Pleuropneumonia are common indications

### Chloramphenicol

- Benefits:
  - Oral dosing – owner can dose at home
  - Big gun – very effective
- Precautions/toxicity:
  - Expensive (~$40-80/day) for adult horse
  - Risk of aplastic anemia in humans – must limit exposure
    - Always soak tabs, never crush or grind
    - Wear gloves, mask?
    - Consider compounded to reduce human exposure, cost but may have reduced bioavailability?
    - (tablets > paste > suspension)
  - Frequent dosing required
  - Bacteriostatic vs cidal?
Regional Limb Perfusion

- Place tourniquet and inject into local vasculature
- Tourniquet 15-30 minutes (new study 10-15 min)
- Low doses, reduces cost and systemic toxicity
- Achieves hugely high tissue levels, even in infected tissue
- Concentration dependent antibiotics used most commonly – amikacin, gentamicin
- Often used for joint and bone infections – every day or every other day for 3 treatments
- Relatively easy and inexpensive to perform

Penicillin CRI

- Maintains tissue levels above MIC continuously
- Due to time dependent nature of penicillins – may be useful in severe infections

Antibiotic induced colitis

- Often Salmonella, Clostridium, e. coli species
- Often idiopathic or unknown (colitis x)
- Kits to test for pathogenic clostridium spp. toxins
- Salmonella is HARD to culture, so a negative culture does not rule it out.

Risks for antibiotic induced colitis:

- Stress (recent training, travel, competition, weaning, etc)
- Withholding feed (colic, pre-op etc)
- Change in diet
- Multiple antibiotics and/or changing antibiotics
- High doses of antibiotics
- Surgery/anesthesia
- Regional
- Population dependent (ie Race horses in one area)
- Idiopathic

Reducing risk of antibiotic induced colitis

- No changes in diet
- Don’t withhold feed
- Probiotics/pre-biotics (Saccharomyces spp.)
- Appropriate doses – don’t under or over dose!
- Don’t change antibiotics frequently or mix incompatible antibiotics
Antibiotic combinations

- General Infections, severe wounds, synovial infections, pre-op colic surgery:
  - Penicillin + Gentamicin
  - Penicillin + Enrofloxacin

- Foal sepsis/PPF:
  - Penicillin + amikacin
  - Ceftiofur high dose +/- amikacin

- Foal sepsis/FPT:
  - Penicillin + amikacin

- Pneumonia/Pleural Pneumonia:
  - Penicillin, gentamicin, + metronidazole
  - Penicillin, enrofloxacin, + metronidazole
  - Ceftiofur + metronidazole
  - Chloramphenicol

- Osteomyelitis:
  - Penicillin + amikacin
  - Chloramphenicol
  - Cefazolin, amikacin RLP

- Tissue penetration (walled off abscesses, internal abscesses, etc)
  - Add rifampin to Pen/gent or Sulfas long term

- Foal umbilical infections:
  - Sulfas
  - Chloramphenicol

- Minor wounds:
  - Excede
  - Sulfas

References


Questions?

OThank you!