Dr. Alexander Fleming (1928) initiated the ‘modern age of medicine’ with the discovery of penicillin.
Drs. Fleming, Florey & Chain (1945) were awarded the Nobel Prize in medicine.
They received no money for their amazing discovery.

**Beta-lactam antibiotics**
- Penicillin- Procaine penicillin G, Na or K penicillin
- Synthetic penicillins- ampicillin, amoxicillin, ticarcillin
- Cephalosporins-
  - First generation- cefazolin, cephalaxin
  - Third generation- ceftiofur, ceftazidime
  - Fourth generation- cefepime
    - all have extended gm (-) activity
    - increased resistance to B-lactamase org.
- Most infections in horses caused by B-hemolytic streptococcus spp. (uniformly susceptible to penicillins).
- Primary cephalosporin administered to horses is ceftiofur.
- Advantages include broad spectrum of activity and good safety profile.
- Several studies have evaluated concentrations (lungs, plasma) and safety of ceftiofur over wide range (1.1mg/kg to 11mg/kg) IM and IV.

**Ceftiofur**
- Approved for use in horses for respiratory tract infections (2.2 to 4.4 mg/kg Q24 IM).
- Higher doses recommended for treating gram - pathogens (Klebsiella, Salmonella, Enterobacter).
- Important to maintain concentrations above MIC with gm (-).
- Unlike other cephalosporins- it is extensively metabolized (desfuroylcetiofur DFC) primarily excreted in urine
- Protein bound DFC is reservoir for active drug at site of infection (reduced dosing interval)
- Protein binding extends effective half-life (t ½)
- Pharmacokinetic profile; IV vs. IM vs. SQ
- 99% protein bound (clinically significant)
- Binds to acute phase proteins (α1-anti-trypsin) which carries bound drug to sites of inflammation
- Time dependent antimicrobial
- Label dose is 2.2 to 4.4 mg/kg q 24h IM.
• Higher doses (5-10 mg/kg) q 12h IV or IM clinically successful in treating septicemic neonates.
• The IM route of administration + lack of “penicillin rxn’s” + broad spectrum of activity = excellent utility in treating polymicrobial infections (pleuropneumonia)

Excede
• Recent FDA approval (ceftiofur crystalline free acid)- sustained-release formulation of ceftiofur in United States
• Indicated for treatment of LRT disease caused by *Streptococcus zooepidemicus*.
• Produces 10 days of therapeutic ceftiofur blood concentrations with 2 IM injections (6.6mg/kg)
• Helps overcome irregular compliance increasing the likelihood of treatment success

Oral β-lactams?
• Very poor absorption and bioavailability
• 2 recent studies in foals; cephalexin and cephadroxil dosed at 30mg/kg PO q 12 hrs was effective

Trimethoprim-Sulfonamide (TMS)
• Considered bactericidal at high concentrations.
• Lipophylic and penetrates tissues well (including central nervous system).
• Broad-spectrum coverage (gm (+), (-) and some anaerobes.
• Interfere with synthesis of folic acid from PABA with sulfonamides competitively inhibiting PABA.
• Purulent fluids rich in protein and PABA, this will decrease TMS activity.
• Good activity against many *Streptococcus* organisms although some resistance noted despite susceptibility results.
• Potentiated sulfas Not recommended for initial treatment of *Streptococcus equi* infections; [Verheyen K, Newton J et al Equine Vet J. 2000; 32. 527-532].
• Excellent GI absorption although reduced substantially by feeding....(delay feeding).
• Lack of clinical activity against anaerobes.
Trimethoprim-Sulfonamide
• Oral formulation containing TMP with sulfadiazine in a 1:5 ratio commonly dosed at 20 to
  30mg/kg BID.
• In horses- rapid elimination of TMP leads to >persistence of sulfonamide and changes
  optimal ratio. Therefore, potentiated sulfonamides should be dosed BID.
  • t½ =sulfamethoxazole 3.5-5 hrs.
  • t½ =sulfadiazine 3-4 hrs.
  • t½ =trimethoprim 2-3 hrs.
• BID *per os* dosing is necessary to attain therapeutic plasma concentrations
  of trimethoprim (Dowling in Bertone,2004)

Macrolides
Erythromycin
• Macrolide; bacteriostatic except at high dosages they are -cidal.; good tissue distribution.
• Poor activity E.coli, Pseudomonas, Klebsiella & Salmonella.
• R. equi pneumonia- 25mg/kg q 6-8 hrs will achieve plasma conc. which exceed MIC.

Azithromycin
• Pharmacokinetic advance in macrolide arena.
• High oral bioavailability, large Vd (18.6L/kg) and peritoneal = synovial = serum conc.,
  T1/2 = 20hrs, conc. in bronchoalveolar cells 15- 170x [serum].
• Impression; fewer GI issues.
• Dose;10 mg/kg QD for 5 days then q 48hrs per os.
• Significant advantage over erythromycin.
• Bioavailability =56% in 6 healthy foals
• 10mg/kg QD PO for 5 days then reduced to every other day

Clarithromycin
• Oral bioavailability =57.3% +/- 12.0%
• 7.5 mg/kg BID PO provides serum, pulmonary epithelial lining and bronchalveolar cells of
  foals above MIC for R. equi isolates during entire 12 hr period
• Determined in 6 healthy foals
  (Womble, 2006)

Rifampin
• Bioavailability is 40 – 70%, lower bioavailability if fed with feed
• t½ =17 hrs. in foals, 6-8 hrs. in adults
• Dose 5mg/kg BID PO
• Emerging resistance especially if used as a monotherapy (Takai, 1997)
**Tetracyclines**
- Broad-spectrum bacteriostatic activity.
- Excellent tissue penetration (including CNS).
- High GI conc. which may cause diarrhea.
- Effective against several organisms (N. risticii) & Borrelia; oxytetracycline; 5-10mg/kg q 12-24 hrs iv

**Doxycycline**
- Semi-synthetic tetracycline.
- Very limited bioavailability (+/- 5%), t1/2 = 10-12 hrs.
- CNS penetration and good gm(+) activity.
- Dose; 10 mg/kg BID *per os*

**Minocycline**
- Semi-synthetic tetracycline.
- Good bioavailability (+/- 25%), t1/2 = 13 hrs.
- CNS penetration and good gm(+) activity.
- Dose; 4 mg/kg BID *per os*

**Chloramphenicol**
- Bacteriostatic (-cidal at high conc.)
- Broad spectrum activity; gm(-), (+) & anaerobes.
- Good intracellular penetration.
- Rapidly metabolized by the liver (short t1/2).
- Oral administration (very bitter).
- Minimize human exposure (animal toxicity rare).
- Dosage 25- 50 mg/kg q 4 to 6 hrs *per os*

**Fluoroquinolones**
- Very active against enteric gm(-) and many aerobic gm(+). No anaerobic activity.
- Enrofloxacin- good bioavailability and tissue penetration (higher conc. in resp. tract than serum).
- Arthropathies are concern in foals-not substantiated in adult horses.
- Injectable- 2.5 to 5mg/kg Q24, *per os* 7.5 to 10mg/kg Q24 is recommended.

**Aminoglycosides (General)**
- Widely used for treatment of gram (-) infections
- Concentration dependent antibiotics
- If a q24 h approach to dosing is employed, it should be augmented with another AB with gm(+) activity (ampicillin, ceftiofur).
- Serum aminoglycoside assays available at human & vet hospitals.
- Due to individual variability & alterations from disease states, therapeutic monitoring should be employed to optimize dose & interval.
**Amikacin**
- Concentration dependent aminoglycoside
- Once daily dosing is safer than more frequent administration while being as effective
- Dose 10mg/kg Q24 in adult horses
- Dose 25mg/kg in foals (Papich, 2005)

**Gentamicin sulfate**
- Rapid, bactericidal action indicated for acute gram (-) infection
- May be administered IM, SQ and IV.
- Synergistic with Beta lactam antibiotics (ampicillin, ceftiofur).
- Do Not administer to horses with compromised renal function
- Dose 6 to 8 mg/kg IM or IV Q24 in adult horses.

**Metronidazole**
- Nitroimidazole anti-infective- selectively taken up by anaerobes
- Effective vs. anaerobic (Clostridium spp) bacteria and protozoa (Giardia and Trichomonas spp.)
- Vd= 1-2 l/kg
- t½= 3-4 hrs.
- Concentration dependent antimicrobial
- Dose 15-20 mg/kg TID PO
- Widely used for colitis
- Resistance reported (rare) for C.difcile isolates
- Less information available for C.perfringens
- Neonates- 10mg/kg PO q 8-12 hours
- PK profile- Per Os > IV
- Pleuropneumonia PK; 15mg/kg initially followed by 7.5mg/kg PO q6h

**Polymyxin B**
- Cationic detergent AB (gram -) binds to cell membrane making it more permeable
- PMB was found to decrease in vivo endotoxin-induced TNF activity
- Compared with baseline values 5,000 U of PBM/kg should inhibit 75% of endotoxin induced TNF activity for 12 hours (Parviainen, 2001)