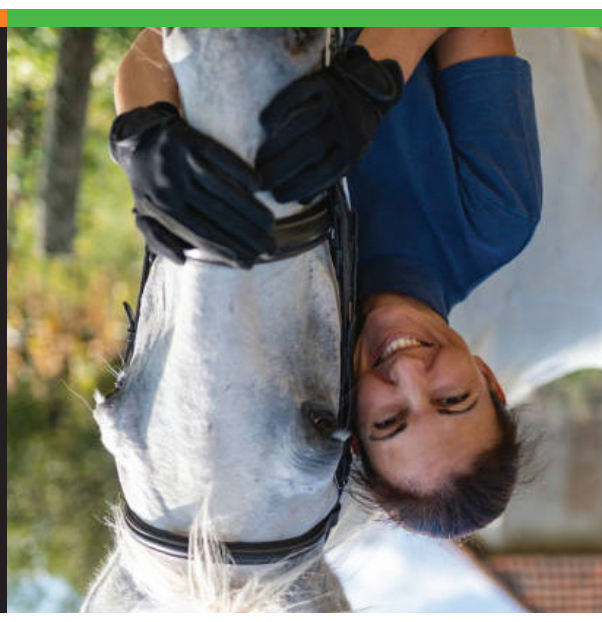
EQUINE VETERINARIANS AUSTRALIA
NCAS National Centre for Antimicrobial Stewardship
APCAH ASIA-PACIFIC CENTRE FOR ANIMAL HEALTH
THE UNIVERSITY OF MELBOURNE
AGRICULTURE VICTORIA



POCKET GUIDE FOR ANTIMICROBIAL USE IN HORSES

EVA & UNIVERSITY OF MELBOURNE

For more information and further resources visit
www.fvas.unimelb.edu.au/vetantibiotics

Version One.

Antibiotic Pharmacokinetics & Pharmacodynamics

Bacteriostatic

"ECSTaTiC for bacteriostatic"

Erythromycin (macrolides)
Clindamycin
Sulphonamides
Trimethoprim
Tetracyclines
Chloramphenicol

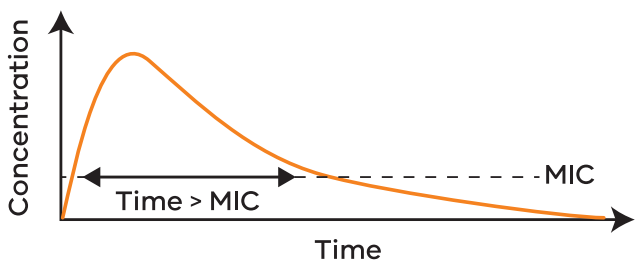
Bactericidal

"Very Proficient For Complete Cell Murder"

Vancomycin
Penicillin
Fluoroquinolones
Cephalosporins
Carbapenems
Metronidazole

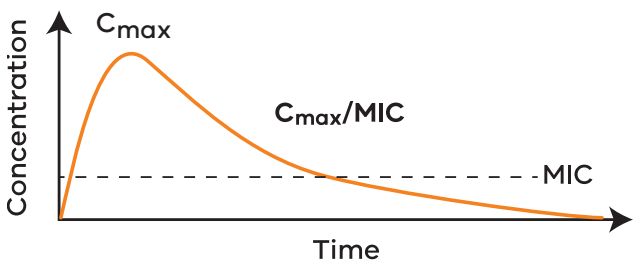
Time-Dependent

- Optimise killing by maximising **time above MIC.**
- **More frequent administration** or extended infusion increases efficacy by extending T>MIC.
- Goal **exceed MIC by 1-5 times for 50-80% of dosage interval.**
- E.g. penicillin, ceftiofur, TMS, tetracyclines chloramphenicol.



Concentration Dependent

- Optimise killing by maximising **peak concentration.**
- **Higher doses** at less frequent intervals increases efficacy by maximising C_{max}:MIC ratio.
- Goal **C_{max}:MIC >8.**
- E.g. aminoglycosides, fluoroquinolones, metronidazole.



Intrinsic resistance

All members of a bacterial genus or species have properties that make them naturally resistant to certain antimicrobials.

Acquired resistance

Previously susceptible bacteria acquire new genes or a mutation occurs conferring resistance.

Spectrum of Activity Against Common Bacteria

Refer to local antibiogram for susceptibility rates (if available).

Bug \ Drug	Procaine Penicillin	Ampicillin	Doxycycline	Oxytetracycline	Trimethoprim sulpha	Chloramphenicol*	Gentamicin	Metronidazole	Ceftiofur	Clarithromycin or Azithromycin + rifampin	Enrofloxacin	Amikacin
Beta-haemolytic streptococci	✔	+	±	±	±	+	IR		+		+	IR
Staphylococcus aureus ¥	±		±	±	±	+	±				+	±
Enterococcus faecalis ¥	+	✔	±	±	IR	±	IR		IR		±	IR
Enterococcus faecium ¥			±	±	IR	±	IR		IR		±	IR
Rhodococcus equi										✔		
Escherichia coli ¥	IR	±	±	±	±	±	✔		+		+	+
Klebsiella spp. ¥	IR	IR	±	±	±		✔		±		±	+
Enterobacter spp. ¥	IR	IR	±	±	±	±	±		±		+	+
Pseudomonas aeruginosa ¥	IR	IR	IR	IR	IR	IR	✔		IR		±	+
Actinobacillus equuli	±	±	✔	✔	✔	±	✔		+		+	+
Pasteurella spp.	✔	+	+	+	±	±	✔		+		+	+
Lawsonia intracellularis			✔	✔								
Bacteroides spp.	IR	IR	±	±		+	IR	+				IR
Clostridium spp.	✔	+	±	±			IR	+	±			IR

Traffic-light system is based on ASTAG antimicrobial importance rating system.

✔ Drug of choice.
\+ Good susceptibility.
± Variable susceptibility.
IR Intrinsically resistant.
* Chloramphenicol is prohibited for use in animals that may enter the food chain, which includes horses in some states. Check legislation in your jurisdiction.
¥ Susceptibility is poorly predictable, culture and susceptibility testing is strongly recommended.

Antibiotic use in **Horses**

NOT ALL BUGS NEED DRUGS

Stop, Think, Choose wisely

LOW IMPORTANCE

Ampicillin *
Doxycycline *
Oxytetracycline
Penicillin
Neomycin
Trimethoprim sulphonamides

* An antibiotic product is not registered for use in this species, check your legal obligations before using.

MEDIUM IMPORTANCE

Gentamicin §
Metronidazole §

§ Prohibited if food chain is a possible destination.

HIGHLY IMPORTANT ANTIMICROBIALS - AVOID

Amikacin
Imipenem
Ticarcillin-clavulanate
Vancomycin

HIGH IMPORTANCE

Ceftiofur #
Enrofloxacin * # §
Virginiamycin § ‡
‡ If no alternative, **PREVENTION FIRST,** treatment as last resort.
Clarithromycin or Azithromycin PLUS Rifampicin * †

Use only in an individual animal in exceptional circumstances, after culture and sensitivity testing, if there is no alternative.

†**ONLY use Rifampicin and macrolides in combination as above for *R.equi***

Antibiotic Pharmacotherapy by Class

* Many of the recommendations in this guide represent off-label use of antimicrobials. Compliance with the legal requirements of your jurisdiction is your responsibility.

** Exceptional circumstances defined as use in an individual animal based on culture and susceptiblity, where there is no effective alternate therapy and a reasonable chance of survival.

Drug Class	Importance Rating	Antibiotic	Route	Drug Dose	Adverse Reactions	Clinical Pearls
Beta-lactams	Low	Procaine penicillin	IM	22,000 IU/kg (22 mg/kg) q12h	Diarrhoea. Procaine reaction: Inadvertent intravascular administration of procaine resulting in CNS excitation and frantic, uncontrollable behaviour that generally resolves in minutes. Penicillin hypersensitivity reactions: urticaria, anaphylaxis, immune mediated haemolytic anaemia.	Drug of choice for streptococcal infections. Excellent anaerobic activity (except *Bacteroides* spp.). Often combined with gentamicin for broad spectrum coverage. Always draw back to check for blood before injecting and keep penicillin refrigerated to reduce risk of procaine reaction. Long acting penicillin formulations are not suitable for use in horses as they aren't long acting and don't reach therapeutic concentrations.
	Low	Benzylpenicillin	IV	22,000 IU/kg (13 mg/kg) q4-6h		
			IU	5 million IU for *Streptococcus zooepidemicus*	Secondary bacterial infection, fungal infection.	Uterine lavage and ecbolics are the primary focus of endometritis therapy. Uterine fluid/exudate may inactivate or dilute antibiotics. Inactivated in solutions with pH <5.5 or >8, do not mix with gentamicin, sulphonamides or sodium bicarbonate. Antibiotic use should be guided by culture, cytology and ultrasound findings.
	Low	Ampicillin sodium	IV/IM	20 mg/kg q6-8h	Ampicillin trihydrate irritant when injected IM.	Greater activity against gram-negative bacteria than penicillin.
	High	Ceftiofur	IM/IV	2.2-4.4 mg/kg q12-24h (Up to 10mg/kg IV q6h has been used in neonatal foals)	Diarrhoea, muscle soreness, hypersensitivity - urticaria, anaphylaxis.	**Reserve** for multi-drug resistant infections. Does not cross BBB. Ceftiofur is rapidly metabolised to desfuroylceftiofur to which most coagulase positive staphylococci are resistant (may appear susceptible *in vitro* but not *in vivo*).
Aminoglycosides	Medium	Gentamicin	IM/IV	6.6 - 9.7 mg/kg q24h (adults)	Nephrotoxic. Muscle soreness if given IM. Hypersensitivity reactions (rare).	Generally drug of choice for suspected or confirmed gram negative infections. No anaerobic activity. Streptococci & enterococci are intrinsically resistant. Inactivated by purulent material. Must penetrate bacteria to assert their effect, which is enhanced by drugs that interfere with cell wall synthesis – e.g. penicillin. Not effective clinically against *Salmonella* spp. but may appear susceptible *in vitro*. If kidney function is reduced, increase inter-dosing interval.
			IM/IV	8.8 - 12 mg/kg q24-36h (foals)		
			IU	1-2 g buffered with equal volume of 7.5% bicarbonate and diluted in 200ml saline.	Irritates endometrium or induce depigmentation of vulvar skin if not buffered. Secondary bacterial infection, fungal infection.	
	High	Amikacin	IV	10mg/kg q24h (adults)	Nephrotoxic.	Use severely restricted in human medicine. Not registered for use in animals and should not be used off-label except in exceptional circumstances**. **Reserve** for documented gentamicin resistant, amikacin susceptible infections where no alternative. No anaerobic activity. Streptococci & enterococci are intrinsically resistant. Inactivated by purulent material. Not effective clinically against *Salmonella* spp. but may appear susceptible *in vitro*. Can be used IA.
			IV	25 mg/kg q24h (foals)		
Tetracyclines	Low	Doxycycline	PO	10 mg/kg q12h	Diarrhoea. Bone/tooth discolouration. **DO NOT GIVE IV – FATAL.**	Excellent broad-spectrum activity, good anaerobic coverage but variable for *Bacteroides* and *Clostridium* spp. Drug of choice for *Lawsonia intracellularis* infection. Doxycycline bioavailability reduced by feeding; withhold feed before and shortly after dosing. Doxycycline can be used in horses with renal failure. Distributes well into pulmonary, peritoneal and synovial fluid and concentrates in urine.
	Low	Oxytetracycline	IV	6.6 mg/kg q12h	Hypotension & collapse if rapid IV administration of oxytetracycline. Renal tubular necrosis with high doses (i.e. for neonatal foals with contracted tendons). Bone/tooth discolouration. Colitis. Very irritant if extravascular or intramuscular.	Excellent broad-spectrum activity, good anaerobic coverage but variable for *Bacteroides* and *Clostridium* spp. Drug of choice for *Lawsonia intracellularis* infection. Distributes well into pulmonary, peritoneal and synovial fluid and concentrates in urine. High dose oxytetracycline causes tendon relaxation in foals with congenital contracted tendons (not acquired) and is most efficacious when given in the first 3 days of life (20 mg/kg IV). Care in foals that are, or may be, dehydrated due to renal effects; consider administration in 1L hartmans.
Sulphonamides	Low	Trimethoprim-sulphonamide	PO/ slow IV	30 mg/kg q12h	Diarrhoea. Thrombocytopaenia with prolonged use. Rapid IV administration can cause tremors and collapse. Concurrent detomidine can result in dysrhythmia, hypotension and death. Concurrent penicillin is antagonistic to sulphonamides. Irritant if given IU or IM.	Excellent broad-spectrum activity. Inactivated by purulent material. Undergoes urinary excretion therefore useful for urinary tract infections.
Macrolides	Low	Erythromycin	PO	25 mg/kg q6h	Severe colitis in adults, variable diarrhoea in foals. Altered thermoregulation in foals (hyperthermia), which seems more common with erythromycin.	Do not use in adults. Generally only used in foals with *Rhodococcus equi,* in combination with rifampin. Can be used in young foals with *Lawsonia intracellularis* infection but not first line choice.
		Clarithromycin	PO	7.5 mg/kg q12h		
		Azithromycin	PO	10 mg/kg q24h		
Ansamycin	High	Rifampin	PO	5 mg/kg q12h	Body fluids turn orange. Antagonistic to gentamicin.	Empiric use only for *Rhodococcus equi,* in combination with a macrolide. Otherwise only use in exceptional circumstances** based on culture and susceptibility and no effective alternative. Never use alone, resistance can develop within hours when used as monotherapy.
Fluoroquinolones	High	Enrofloxacin	PO/ slow IV	7.5 mg/kg q24h	OCD in young horses. DO NOT USE IM, IA, IU or as IVRP as causes necrosis and fibrosis. Oral paste has been associated with severe oral ulceration. Colitis. Fluoroquinolone have also induced tendonitis in juveniles.	Should be **reserved** for multi-drug resistant infections based on culture and susceptibility results and no effective lower importance rating option. Generally avoided in horses < 4 years of age and during pregnancy. Synergism with beta-lactams and aminoglycosides.
Nitroimidazoles	Medium	Metronidazole	PO	25 mg/kg q12h	Inappetence. Can cause neurological signs if underlying hepatic disease.	Excellent anaerobic activity. Use is generally combined with penicillin and gentamicin for broad spectrum coverage where anaerobes are suspected to be contributing (pleuropneumonia, peritonitis). Indicated in cases where *Bacteroides* spp. may be involved.
Phenicols	Low	Chloramphenicol	PO	50 mg/kg q12h	Wear gloves and mask when crushing tablets for horses as idiosyncratic aplastic anaemia (not dose related) can develop in **people** handling this drug. In horses, dose-related anaemia and pancytopenia may develop with prolonged treatment.	Broad spectrum. Prohibited for use in animals that may enter the food chain -which includes horses in some states. Check legislation in your jurisdiction. Do not give concurrently with penicillin, gentamicin, fluoroquinolones or macrolides. Hepatic clearance of phenytoin, phenobarbital, phenulbutazone and xylazine is decreased.
Polypeptides	High	Polymyxin B	slow IV	5000 U/kg q 8-12 hrs (anti-endotoxin dose)	Nephrotoxic.	Generally only used systemically to combat endotoxaemia. Care should be taken as endotoxic patients often have impaired renal perfusion.
Streptogrammins	High	Virginiamycin	PO	5g/100kg q24h	High importance antimicrobial - banned for Equine use in UK 2014.	Founderguard - reduces fermentative acidosis in the hindgut and may aid in the prevention of pasture-associated laminitis.
Other	Low	Sodium iodide	IV	20-40 mg/kg q24h	Iodinism.	Generally used for chronic fungal or bacterial infections where antimicrobial penetration may be poor.

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