

# Antibiotics for Small Animals

## Barriers to Change

Presidential Advisory Council on Combating  
Antibiotic-Resistance Bacteria

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# Veterinary Medicine - One Health ?

## 1<sup>o</sup> General Practice

- small animal
- equine
- food animal (field services / corporate )
- poultry (field services / corporate)
- aquaculture (field services / corporate)

## 2<sup>o</sup> Specialty Private Practice

Procedure Based Service

## 3<sup>o</sup> Veterinary Practice / University Hospitals

# Small animal medicine – species?

- Canines
- Felines
- Pocket pets
  - Hamsters, mice, rats, hedgehogs, guinea pigs, ...
- Avians – pet / aviary
- Amphibians Reptiles Fishes

# Barriers to Change

## *Antibiotic Resistance in Small Animal Medicine*

- Inappropriate Abx use
  - Continuing education – pharmacokinetic review & C&S
  - Client compliance
  - Rising costs to consumers
  - Nosocomial risks
- Identify alternative prevention & adjunctive care
- Access – Watch – Reserve      WHO

# Small animal medicine – antibiotic choices?

- Penicillins such as penicillin and [amoxicillin](#)
  - Carbapenems, e.g., meropenem imipenem
- Cephalosporins such as [cephalexins](#) (Generations 1-2-3-4-5)
- Macrolides: erythromycin, clarithromycin, [azithromycin](#) and lincomycin
- Fluoroquinolones: [ciprofolxacin](#), [enrofloxacin](#), marbofloxacin, [pradofloxacin](#)
- Sulfonamides with trimethoprim **TMS**
- Tetracyclines such as tetracycline, minocycline, [doxycycline](#)
- Aminoglycosides such as [neomycin](#), [amikacin](#), [gentamicin](#), tobramycin
- **Chloramphenicol ?**
- Glycopeptide – vancomycin, **clindamycin**
- RESERVE: Fosfomicin, Colistin, Linezolid, Tigecycline

# Use of Antibiotics in Small Animal Medicine

- Concentration dependent (volume of distribution)
- Time dependent
- BASICS of infectious disease?
  - Host Status – Organism – Infective Dose
  - Appropriate Tx selection, correct dosing, compliance
- Drug selection
  - Organ system and data
  - Comorbidities
  - Guidelines of Probability vs C&S
- \* Use in small animal veterinary medicine
  - miniscule by scale of use

# Small animal clinical antibiotic use?

## Veterinary Bacterial Infections


- Pathogens – similar but generally host specific
- Any situation you would find in human medicine ...
- Treatment? [Review is needed for most veterinarians](#)
- Zoonosis and reverse zoonosis
- Nosocomial Infections
- **Resistance** issues

# Resistance is a daily consideration:

- E. coli
- MRSPi
- MRSA
- Klebsiella
- Mycobacteria
- Actinomyces
- Enterococcus
- Enterobacter
- Mixed Infections
- Saprophytes and Opportunity



# Resistance

- E. coli
  - MRSPi
  - MRSA
  - Klebsiella
  - Mycobacteria
  - Actinomyces
  - Enterococcus
  - Enterobacter
  - Mixed infections
- Veterinary approved products
  - Cost implications in selection
  - New antibiotics or routes of administration?
  - **Reduced fluoroquinolone sensitivity**
  - Reduced effectiveness of penicillin's, cephalosporins, TMS, (extended beta-lactamase)
  - Increased reliance on chloramphenicol, rifampin, aminoglycosides, multiple drugs, and perhaps, reserved drugs?
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# Antibiotic Resistance in Small Animal Clinical Practice

- Inappropriate use of antibiotics
  - Is there demonstrated occurrence in small animal clinical practice?
  - OTC availability
- Appropriate use of antibiotics
  - Still a selection pressure for resistance
- Mechanisms of bacterial resistance are multiple
- Transference between hosts and pathogens
  - Human MRSA and veterinary MRSPi
  - E. coli, Klebsiella, mycobacteria, Enterococcus, Enterobacter, Proteus
  - Contaminant to pathogen: Acinetobacter, Serratia, Citrobacter, Corynebacterial, ...

# Antibiotic Resistance in Small Animal Clinical Practice

- Role of client compliance
  - Human Patient Compliance at Univ of MO 1984
  - 1 week 87% compliance for QD,
    - 2 weeks 54% for QD
      - 2 weeks BID was 36%
      - 2 weeks TID was 27%
  - Veterinary client compliance?
  - Routes and options in administration formulations
    - Approved – Licensed Products
    - Compounding

# Resistance and Nosocomial Infections

- What is true in human medicine is true for veterinary medicine
  - Increases of patient mortality and morbidity
  - Suffer grieving and loss
  - Increased cost of hospital stays
  - Self propagation / transmission to community
  - *The EHA Consulting Group provides **litigation expertise** in the areas of infections contracted in the healthcare environment.*

# Nosocomial Infections

## Principles of Control

### Surveillance:

- Culture Monitoring
  - Talk with your lab / bulk rate ?
  - Sites to culture ...

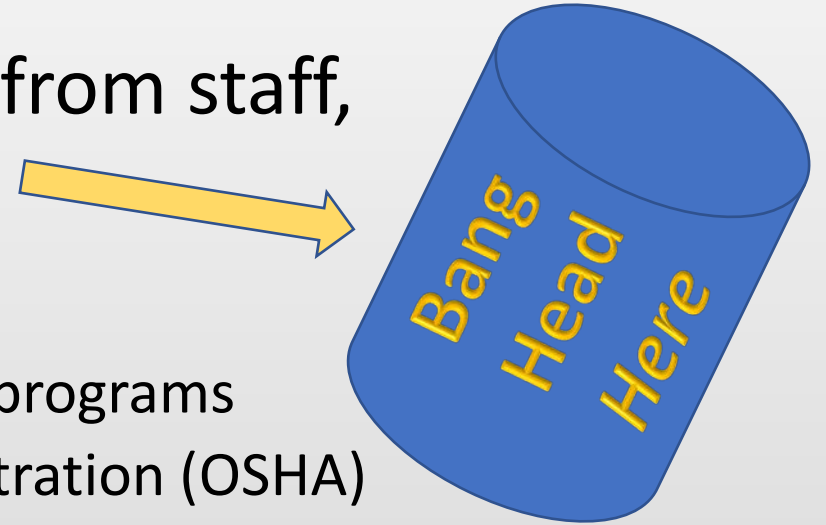
# Nosocomial / Resistant Infections

## Principles of Control - KNOWN CASE

- 1) Make last appointment of the day*
- 2) Ensure adequate cleaning of organic residues – UV?*
- 3) Appropriate disinfectants and dry times*
- 4) Cover all wounds*
- 5) Use shortest route to the destination*
- 6) Minimize number of involved staff*
- 7) Use Personal Protective Equipment (PPE)*
- 8) Isolation Wards and Boundary Isolation*

# Veterinary Nosocomial Infection Control

- It is necessary to get full support from staff, doctors and administration !
- Human Medical field
  - State and Federal regulations require IC programs
  - Occupational Safety and Health Administration (OSHA)
  - Minimum of \$5,000 per violation or more if injury has occurred
- Recruit enthusiastic staff “lead”
- Create a committee to meet routinely
- Convey the cost of action versus risk of inaction!



# Small Animal Veterinary Antibiotic Use

## Antibiotic Use Policies

- An active ongoing process of thought ... within a facility
- **Regulatory role versus strong suggestions?**
- To consider facility efforts and lack of metanalysis data:
  - Protocols for decreased contagion
  - When is prophylactic antimicrobial use reasonable?
  - Which antibiotics to match/choose to infectious situation?
  - Duration of use and dosing?
  - When is it not appropriate to prescribe antibiotics?
  - Compliance across doctors and service groups?
  - Cost effective UV room sanitization/sterilization in Vet Med?



# Summary – Enhancing Change

- Continuing education of veterinarians & hospital teams
- Prevent infection situations for patients and optimal host husbandry
- Culture and sensitivity testing as often as possible
- Proper use of antibiotics by clients (compliance)
- Concurrent therapies
  - Antiseptic wound care   HBOT if appropriate   Sanitation/hygiene   Affordable UV
- Nosocomial awareness / monitoring / protocols
- Sharing data – big reference Labs as Antech and IDEXX – lack microbiologist communication



Thank you!

Questions?

< 1950 – all *E.coli* sensitive to penicillin; sulfa resistance !

1981 JAVMA – *K. pneumoniae* UTI in Cornell VTH – SSI's

1999 Clinical Inf Dis – 64% of *Haemophilus* resistant ampicillin & b-lactamase resistance to cephalosporins

1999 The Record – aquaculture use of antimicrobials adds antimicrobials directly to the environment

2002 WSAVA – consensus of risk from livestock

- Prospective study at Tufts 12 of 83 hosp cases had HAI

2002 VCNA SAP – nosocomial infection review

2004 J Vet Intern Med - Isolation of Methicillin Resistant *Staphylococcus aureus* from the Environment in a Veterinary Teaching Hospital.

2005 US Gov USDA – 70,000 lbs quinolones used in US aquaculture is 0.4% of that used in animal production

2006 Current Microbiol – UV-B resistance of community bacteria.

- 2008 Infect Genet Evol - hospital acquired and community acquired MRSA infections now overlap showing mingling of Staph aureus genes in the organisms.
- 2008 Can J Vet Res - evidence of antimicrobial use in feeder /finishing pig units increases antimicrobial resistance to antibiotics
- 2009 JAVMA - 27% of cultured household members were MRSA positive; 8% of dogs in same households were positive for MRSA; wide overlap between people and dogs suggests risk of interspecies transmission
- 2009 Can Vet J - 11% of dogs and 15% of feline feces from private veterinary hospitals in Ontario contained E.coli with resistance to 2 or more antibiotics.
- 2010 Antimicrob Agents Chemother – human CTX-M and SHV genes for resistant ESBL E.coli from UTIs of dogs and cats in Pennsylvania.
- 2010 J Vet Intern Med - MSSA in people
- Arch Pediatr - In 1999, there were 5.1 cases of MRSA bacteremia per 1000 admissions of people to hospital. In 2010, there are 5.1 cases of ESBL bacteremia per 1000 admissions of neonates.
- Prediction – all of us will know at least one person to die of resistant bacterial infection in the next 10 years.

- [Acta Vet Hung.](#) 2017 Jun;65(2):173-184. doi: 10.1556/004.2017.018.
- **Species distribution, antibiotic resistance and virulence traits in canine and feline enterococci in Tunisia.**
- [Ben Said L](#)<sup>1</sup>, [Dziri R](#)<sup>1</sup>, [Sassi N](#)<sup>1</sup>, [Lozano C](#)<sup>2</sup>, [Ben Slama K](#)<sup>1</sup>, [Ouzari I](#)<sup>1</sup>, [Torres C](#)<sup>2,3</sup>, [Klibi N](#)<sup>1</sup>.
- [Author information](#)
- **Abstract**
- In order to investigate the possible role of dogs and cats in the carriage and potential dissemination of resistant enterococci, seventy faecal samples from dogs and cats were tested for enterococci. Fifty-eight enterococci were recovered. Isolates were identified as *Enterococcus faecium* (n = 31) and *E. faecalis* (n = 14) *E. durans* (n = 6), *E. casseliflavus* (n = 2), *E. hirae* and *E. gallinarum* (2 isolates each). Enterococcal isolates showed resistance to ciprofloxacin (n = 35), erythromycin (n = 31), tetracycline (n = 25), kanamycin (n = 15), streptomycin (n = 13), pristinamycin (n = 11), gentamicin (n = 10), chloramphenicol (n = 8), and linezolid (n = 6). The gene *erm(B)* was detected in 22 out of 31 erythromycin-resistant enterococci. All tetracycline-resistant enterococci carried *tet(M)* and/or *tet(L)* genes. The gene *aac(6')-Ie-aph(2'')-Ia* was identified in five of high-level gentamicin-resistant isolates, the genes *aph(3')-IIIa* and/or *aac(6')-Ie-aph(2'')-Ia* in eleven high-level kanamycin-resistant isolates and the gene *ant(6)-Ia* in eleven high-level streptomycin-resistant isolates. Only one strain harboured *cat(A)* gene, and five strains contained *vat(E)* or *vat(D)* genes. Virulence genes *gel(E)* (21 strains), *esp* (11 strains) and *cyIA/cyIB* (5 strains) were detected. High genetic diversity was demonstrated among *E. faecium* isolates by pulsed-field gel electrophoresis (PFGE). Dogs and cats can be carriers of antibiotic-resistant enterococci in their faeces that could shed into the household environment.

- [J Proteomics](#). 2015 Sep 8;127(Pt B):365-76. doi: 10.1016/j.jprot.2015.05.040. Epub 2015 Jun 9.
- **Mechanisms of antibiotic resistance to enrofloxacin in uropathogenic Escherichia coli in dog.**
- [Piras C](#)<sup>1</sup>, [Soggiu A](#)<sup>1</sup>, [Greco V](#)<sup>2</sup>, [Martino PA](#)<sup>1</sup>, [Del Chierico F](#)<sup>3</sup>, [Putignani L](#)<sup>4</sup>, [Urbani A](#)<sup>2</sup>, [Nally JE](#)<sup>5</sup>, [Bonizzi L](#)<sup>1</sup>, [Roncada P](#)<sup>6</sup>.
- [Author information](#)
- **Abstract**
- Escherichia coli (E. coli) urinary tract infections (UTIs) are becoming a serious problem both for pets and humans (zoonosis) due to the close contact and to the increasing resistance to antibiotics. This study has been performed in order to unravel the mechanism of induced enrofloxacin resistance in canine E. coli isolates that represent a good tool to study this pathology. The isolated E. coli has been induced with enrofloxacin and studied through 2D DIGE and shotgun MS. Discovered differentially expressed proteins are principally involved in antibiotic resistance and linked to oxidative stress response, to DNA protection and to membrane permeability. Moreover, since enrofloxacin is an inhibitor of DNA gyrase, the overexpression of DNA starvation/stationary phase protection protein (Dsp) could be a central point to discover the mechanism of this clone to counteract the effects of enrofloxacin. In parallel, the dramatic decrease of the synthesis of the outer membrane protein W, which represents one of the main gates for enrofloxacin entrance, could explain additional mechanism of E. coli defense against this antibiotic. All 2D DIGE and MS data have been deposited into the ProteomeXchange Consortium with identifier PXD002000 and DOI <http://dx.doi.org/10.6019/PXD002000>. This article is part of a Special Issue entitled: HUPO 2014.

- [Aust Vet J](#). 2008 Apr;86(4):147-52. doi: 10.1111/j.1751-0813.2008.00270.x.
- **Susceptibility of canine and feline Escherichia coli and canine Staphylococcus intermedius isolates to fluoroquinolones.**
- [Gottlieb S<sup>1</sup>](#), [Wigney DI](#), [Martin PA](#), [Norris JM](#), [Malik R](#), [Govendir M](#).
- [Author information](#)
- **Abstract**
- **OBJECTIVES AND DESIGN:**
- 1) A prospective study to determine in vitro concentrations for a range of fluoroquinolones, gentamicin and amoxicillin-clavulanate required to inhibit growth of recently collected, feline and canine Escherichia coli and canine Staphylococcus intermedius isolates. 2) A comparative retrospective study to compare the minimum inhibitory concentrations (MICs) of ciprofloxacin, enrofloxacin and amoxicillin-clavulanate for archived canine E coli and S intermedius isolates collected ten to twenty years earlier, with those for recently collected isolates.
- **PROCEDURE:**
- Susceptibility was assessed using disk diffusion, agar dilution susceptibility testing and Epsilon meter tests (E-tests) for both recently collected and archived isolates.
- **RESULTS:**
- All feline E coli isolates and recently collected canine S intermedius isolates were susceptible to all fluoroquinolones. There was a statistically significant increase in the MIC range of ciprofloxacin and enrofloxacin for recently collected E coli, and in the MIC range of amoxicillin-clavulanate for recently collected S intermedius isolates compared to archived isolates. Twelve of 59 recently collected canine E coli isolates were resistant to both ciprofloxacin and enrofloxacin. Resistant canine E coli isolates were associated with complicating host or infection site factors.
- **CONCLUSION:**
- This is the first report comparing the MICs for all veterinary fluoroquinolones currently available in Australia for a representative sample of canine and feline E coli and canine S intermedius isolates. Importantly, this study identified 12 of 59 canine E coli isolates resistant to fluoroquinolones and identified the development of low level resistance in canine E coli to ciprofloxacin and enrofloxacin and canine S intermedius to amoxicillin-clavulanate.

- [J Vet Pharmacol Ther.](#) 2014 Apr;37(2):201-4. doi: 10.1111/jvp.12069. Epub 2013 Jul 17.
- **Fluoroquinolone levels in healthy dog urine following a 20-mg/kg oral dose of enrofloxacin exceed mutant prevention concentration targets against Escherichia coli isolated from canine urinary tract infections.**
- [Daniels JB<sup>1</sup>](#), [Tracy G](#), [Irom SJ](#), [Lakritz J](#).
- [Author information](#)
- **Abstract**
- A 3-day course of oral enrofloxacin is effective for treating uncomplicated urinary tract infection (UTI) in dogs when administered 20 mg/kg Q24H. However, emergence of fluoroquinolone-resistant mutants of uropathogens is a concern. Urine concentrations of enrofloxacin and ciprofloxacin were measured in six healthy dogs following dose of enrofloxacin 20 mg/kg. Mutant prevention concentrations of Escherichia coli isolated from canine UTI were also determined against ciprofloxacin. Urine AUC(24)/MPC ratios considering ciprofloxacin concentrations ranged 3819-7767, indicating that selection of resistant E. coli mutants in dogs with uncomplicated UTIs is unlikely in the bladder given that an AUC(24)/MPC = 39 is considered to be protective against mutant selection for ciprofloxacin. However, additional studies are required to evaluate the effects of this enrofloxacin treatment protocol on bacteria that colonize anatomic sites where fluoroquinolones achieve lower concentrations compared to the urinary bladder.



- [J Vet Emerg Crit Care \(San Antonio\)](#). 2019 Apr 25. doi: 10.1111/vec.12842. [Epub ahead of print]
- **Antibiotic use in critical illness.**
- [Stewart SD](#)<sup>1</sup>, [Allen S](#)<sup>1</sup>.
- **OBJECTIVE:** To provide a review on the current use of antimicrobials with a discussion on the pharmacokinetic and pharmacodynamic profiles of antimicrobials in critically ill patients, the challenges of drug resistance, the use of diagnostic testing to direct therapy, and the selection of the most likely efficacious antimicrobial protocol.
- **ETIOLOGY:** Patients in the intensive care unit often possess profound pathophysiologic changes that can complicate antimicrobial therapy. Although many antimicrobials have known pharmacodynamic profiles, critical illness can cause wide variations in their pharmacokinetics. The two principal factors affecting pharmacokinetics are volume of distribution and drug clearance. Understanding the interplay between critical illness, drug pharmacokinetics, and antimicrobial characteristics (ie, time-dependent vs concentration-dependent) may improve antimicrobial efficacy and patient outcome.
- **DIAGNOSIS:** Utilizing bacterial culture and susceptibility can aid in identifying drug resistant infections, selecting the most appropriate antimicrobials, and hindering the future development of drug resistance.
- **THERAPY:** Having a basic knowledge of antimicrobial function and how to use diagnostics to direct therapeutic treatment is paramount in managing this patient population. Diagnostic testing is not always available at the time of initiation of antimicrobial therapy, so empiric selections are often necessary. These empiric choices should be made based on the location of the infection and the most likely infecting bacteria.
- *Studies have demonstrated the importance of moving away from a "one dose fits all" approach to antimicrobial therapy. Instead there has been a move toward an individualized approach that takes into consideration the pharmacokinetic and pharmacodynamic variabilities that can occur in critically ill patients.*