



## Antibiotic therapy: causes of resistance and strategies to manage resistant infections (Papich, MG).

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Drug-resistant bacteria have become an increasingly important problem for companion animal veterinarians. Treatment guidelines are established in textbooks and consensus documents available for treating routine infections in small animals. But these regimens and approved antibiotics for animals are designed for susceptible (wild-type) infections and are often not active against bacteria that carry resistance mechanisms. When the patient has an infection that is refractory to treatment, and/or caused by a resistant organism, other strategies and drugs may be necessary. As with many new treatments, there are few veterinary clinical studies to support a recommended use and dose and many of these details have been extrapolated from human medicine.

The gram-negative mostly likely to cause resistance problems are the Enterobacteriaceae and *Pseudomonas aeruginosa*. If the organism is *Pseudomonas aeruginosa*, *Enterobacter* species, *Klebsiella* species, *Escherichia coli*, or *Proteus* species, resistance against many common antibiotics is possible and a susceptibility test is advised using appropriate testing standards (eg, CLSI, 2013). Often, the drugs needed for these infections are fluoroquinolones, or injectable human antibiotics of the beta-lactam class, or aminoglycosides (eg, amikacin).

The gram-positive bacteria most likely to be associated with resistance in companion animals is *Staphylococcus*. *Staphylococcus* isolated from small animals is most likely to be *Staphylococcus pseudintermedius* rather than *Staphylococcus aureus*. When infection is caused by a typical wild-type strain, *Staphylococcus pseudintermedius* has a predictable susceptibility to  $\beta$ -lactamase resistant  $\beta$ -lactam antibiotics such as amoxicillin combined with a  $\beta$ -lactamase inhibitor or a cephalosporin. However, methicillin-resistant *Staphylococcus* species, especially *S. pseudintermedius* are being isolated with increased frequency from animals with skin and soft-tissue infections. If staphylococci are resistant to oxacillin or methicillin, they should be considered resistant to all other  $\beta$ -lactams, including cephalosporins and amoxicillin-clavulanate. Unfortunately, these bacteria often carry co-resistance to many other non- $\beta$ -lactam drugs, including lincosamides (clindamycin, lincomycin), fluoroquinolones, macrolides (erythromycin), tetracyclines, and trimethoprim-sulfonamides. The treatment of these *Staphylococcus* infections often requires chloramphenicol, aminoglycosides, tetracyclines, rifampin, and occasionally more expensive human-label medications.

How does resistance emerge? Antibiotic administration – if not active enough to eliminate resistant isolates – can *select* for these resistant strains, which then can multiply and flourish. This is often called *amplification*. There are examples of some drugs that can induce resistance mechanisms, but these are rare compared to selection and amplification of drug resistant strains. Inadequate antibiotic treatment consisting of doses too low, infrequent administration, or selection of a poorly active drug, is a common reason for emergence of drug resistance. Several studies have shown that resistant strains are more likely to be identified in a patient when the animal has previously been treated with antibiotics.

