



# Multidrug-Resistant Bacteria in Man's Best Friends

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Pets—with dogs and cats being the most popular—have long been considered members of the family, living under the same roof and sharing the same cozy environment. They also take advantage of the latest medical technologies currently implemented in veterinary medicine. Infectious diseases are treated with the latest generation of antibiotics including critically important cephalosporins and fluoroquinolones, and in some cases with last-line antibiotics from human medicine.

The use of many different classes of antibiotics in animals has contributed to the selection of antibiotic-resistant microcosm within the normal flora of animals, and the establishment of healthcare-associated multidrug-resistant bacteria in veterinary settings. Some bacteria found in dogs and cats have become virtually resistant to all antibiotics used in veterinary medicine. Some have a zoonotic potential and behave as opportunistic pathogens causing different types of infections, while others only colonize healthy carriers, posing the risk that they silently spread their multi-drug bacteria in the household and further into the community.

## *Methicillin-resistant staphylococci*

*S. pseudintermedius* is a typical example of a bacterium from the normal flora of a dog, which has become resistant to almost all classes of antibiotics. Methicillin-resistant *S. pseudintermedius* (MRSP) emerged a decade ago and represents one of the most challenging bacteria in veterinary medicine. Some of the strains are only susceptible to antibiotics used as a last resort for the treatment of staphylococcal infections in humans e.g. linezolid and vancomycin (Table 1). Specific epidemic clones have been spreading worldwide with clonal complex CC71 being the most predominant, CC68 originated mostly through

North America and is now increasingly found in Europe, CC258 is localized in Europe and CC45 in Asia<sup>1</sup>. Dogs can be happy, healthy carriers of MRSP until they develop severe infections associated with skin diseases, or after a wound or surgery. The types of infections are multiple including pyoderma, otitis and sinusitis as well as post-surgical wound and bone infections.<sup>2</sup> Antimicrobial therapeutic options are very limited.

The close proximity of dogs and owners constitutes the ideal melting pot for the exchange of bacteria. Between four and thirteen percent of owners of pets with MRSP infections were also found to be nasal carriers of the bacteria,<sup>3</sup> increasing the risk of developing an MRSP infection. A first case of post-operative sinusitis in humans caused by MRSP and associated with dogs was reported in the U.S. in 2009 as “Beware of the pet dog: a case of *Staphylococcus intermedius* infection”. Cultures and bacterial fingerprinting analysis confirmed that the isolate from the patient's pet dog was identical to that of the patient.<sup>4</sup> The patient could only be successfully treated with a prolonged antibiotic therapy with vancomycin and linezolid.

One year later, a similar case of sinusitis was reported in Switzerland where the patient was infected with the same MRSP clone of sequence type ST71 that has been spreading in dogs throughout Europe.<sup>5</sup> Since then, several additional cases of human infections, almost all related to dog exposure, have confirmed the zoonotic potential of *S. pseudintermedius*.<sup>6</sup> Although less frequent than MRSP, methicillin-resistant *S. epidermidis*, *S. haemolyticus*, and *S. aureus* belonging to similar clonal lineages as those found in humans can also colonize and cause severe infections in companion animals also emphasizing transmission between humans and animals.<sup>7-10</sup> Similarly

**Table 1. Examples of multidrug resistance profiles in predominant lineages of bacteria from dogs and cats**

Bacteria	Sequence type	Classes of antibiotics with resistance
<i>Staphylococcus pseudintermedius</i>	ST71, ST68, ST45, ST238	Beta-lactams, trimethoprim, sulfonamides, fluoroquinolones, tetracyclines, macrolides, lincosamides, aminoglycosides, chloramphenicol
<i>Staphylococcus aureus</i>	ST22	Beta-lactams, trimethoprim, fluoroquinolones
	ST1	Beta-lactams, trimethoprim, tetracyclines, macrolides, lincosamides, aminoglycosides, streptomycin
	ST5	Beta-lactams, macrolides, lincosamides, aminoglycosides, chloramphenicol, fluoroquinolones, mupirocin
<i>Staphylococcus epidermidis</i>	ST2	Beta-lactams, aminoglycosides, macrolides, lincosamides, tetracyclines, trimethoprim, sulfonamides, fluoroquinolones
<i>Staphylococcus haemolyticus</i>	ST1	Beta-lactams, aminoglycosides, macrolides, lincosamides, tetracyclines, trimethoprim, sulfonamides, fluoroquinolones, chloramphenicol
<i>Acinetobacter baumannii</i>	ST1, ST2, ST10	Beta-lactams/beta-lactamase-inhibitors, 2 <sup>nd</sup> and 3 <sup>rd</sup> generation cephalosporins, aminoglycosides, fluoroquinolones, trimethoprim, sulfonamides, tetracyclines and tigecycline
<i>Klebsiella pneumoniae</i>	ST11, ST15, ST101	Beta-lactams including 3 <sup>rd</sup> generation cephalosporins, aminoglycosides, trimethoprim, sulfonamides, tetracyclines, fluoroquinolones, (carbapenem)
	ST274	Beta-lactams including 3 <sup>rd</sup> generation cephalosporins, aminoglycosides, trimethoprim, sulfonamides, tetracyclines, quinolones

to MRSP, they are also frequently resistant to several classes of antibiotics (Table 1).

#### Multidrug-resistant *Klebsiella pneumoniae* and *Acinetobacter baumannii*

*Klebsiella pneumoniae* and *Acinetobacter baumannii* are a major cause of severe healthcare-associated infections in human hospitals. Levels of antimicrobial resistance have been increasing throughout the past decade with some strains exhibiting resistance to all classes of antibiotics. They are also circulating in veterinary clinics and companion animals are not excluded from becoming infected with such multi-drug resistant bacteria. Dogs and cats may already be carriers of multidrug-resistant *K. pneumoniae* and *A. baumannii* or, like humans, they can contract them during hospitalization in a veterinary clinic which may act as a turntable for the spread of these multidrug-resistant life-threatening bacteria. Some multidrug-resistant *K. pneumoniae* and *A. baumannii* clones from

companion animals are similar to those found in humans and have also established themselves in the veterinary settings. Many have been found to be resistant to several antibiotics including critically important cephalosporins and fluoroquinolones with the exception of carbapenems, a class of antibiotics used as an absolute last resort in human medicine and not licensed for veterinary use (Table1). Despite this restriction, carbapenems are in some cases being used off-label for the treatment of urinary tract or post-operative infections in companion animals caused by multidrug-resistant *Enterobacteriaceae*, posing the risk of selecting carbapenem-resistant strains.<sup>11</sup> Such off-label veterinary use should be strongly discouraged, since acquired carbapenem resistance has already been reported among strains from dogs and cats mainly associated with plasmid and transposon-mediated *bla*<sub>OXA-48</sub> in *K. pneumoniae* and *bla*<sub>OXA-23</sub> in *A. baumannii*.<sup>12,13</sup> Uncontrolled use of carbapenems in companion animals may rapidly con-

tribute to an increase of existing carbapenem-resistant bacterial populations in animals. This could jeopardize one of the most critical antibiotics for human medicine since animal-to-human-transmission was demonstrated, placing pet owners at risk of also becoming colonized with life-threatening multidrug-resistant bacteria.

It is time to be cautious

Emergence of multidrug-resistant bacteria in animals has limited therapeutic options, leading to an increased risk that antibiotics used as a last resort in human medicine are also used in companion animals. In the absence of any other alternatives, these antibiotics can also be legally applied in the treatment of companion animals. However, use of these antibiotics should be strongly avoided and be kept only for the treatment of life-threatening bacterial infections in humans. For instance, selection of resistance to last-line antibiotics in *S. aureus*, *A. baumannii*, and *K. pneumoniae* may have dramatic consequences as these bacteria represent one of the most serious burdens to hospitals with often fatal consequences. In veterinary settings, it is also necessary to establish and maintain continuous and strict infection control strategies following guidelines for prudent use of antimicrobials, such as those recently released by the European Union.<sup>14</sup> We should all be aware that multidrug-resistant bacteria with zoonotic potential are spreading among cats and dogs. They may become a concern for every household and may represent a risk for both animal and human health. It is imperative to avoid close proximity and contact with animals under antimicrobial therapy or that have been recently hospitalized in a veterinary clinic, and strict hand hygiene remains one of the most important measures in preventing transmission. Nevertheless, the presence of multidrug-resistant bacteria in pets emphasizes that the cautious, prudent and prioritized use of antibiotics belongs to the global one-health concept in order to maintain effectiveness of all existing antimicrobials for all members of a family.

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