METHICILLIN-RESISTANT STAPHYLOCOCCAL INFECTIONS
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METHICILLIN-RESISTANT STAPHYLOCOCCUS

Methicillin-Resistant Staphylococcus Aureus (MRSA)
Until the last decade, methicillin-resistant staphylococcal (MRS) infections were uncommon in the general pet population. However, the numbers of dogs and cats infected with MRS infections has increased along with the increased prevalence of methicillin-resistant Staphylococcus aureus (MRSA) in humans. A 1-yr epidemiological study at The Ohio State University reported that nearly 7% of patients admitted were MRSA-positive, with several being apparently asymptomatic carriers. In both humans and animals, the prevalence of methicillin resistance varies geographically. The percentage of MRSA infections tend to be higher in communities with a large number of hospitals and other human health-care facilities. Preliminary results of investigations into risk factor for MRSA in dogs and cats show that pets are more likely to have MRSA vs. methicillin-sensitive Staphylococcus aureus (MSSA) when they are atopic, owned by healthcare workers, or live in families with a bird or a cat. The role of prior antimicrobial exposure is poorly determined. Plasmid-associated genes associated with virulence and resistance are more frequent in MRSA in human patients than when MRSA is isolated from dogs and cats. Genes coding for certain proteases, hemolysins, adhesion factors are absent in canine MRSA. Thus, MRSA does not appear to be as virulent in companion animals as it is in humans. Fortunately for our patients, no long-term difference in outcome was determined between patients with MRSA vs. MSSA. Survival rates for both types of infection are high.

Methicillin-Resistant Staphylococcus pseudintermedius (MRSP)
Prior to the designation of Staphylococcus intermedius as a separate species in 1976, all hemolytic coagulase-positive staphylococci were classified as Staphylococcus aureus. In 2005, Staphylococcus intermedius was subdivided into three separate species based on 16S rDNA sequencing; Staphylococcus pseudintermedius is the pathogen present on dogs. Pathogenicity and zoonotic potential differ substantially between MRSA and MRSP. Staphylococcus aureus appears to be host-adapted to humans, whereas Staphylococcus pseudintermedius is adapted to canines.

Methicillin-resistant Staphylococcus schleiferi (MRS)
Staphylococcus schleiferi is a relatively recently described pathogen in veterinary patients that occurs in two forms, a coagulase-positive type, Staphylococcus schleiferi subspecies coagulans, and a coagulase negative form, Staphylococcus schleiferi subspecies schleiferi. Not all diagnostic differentiate between Staphylococcus schleiferi subspecies coagulans and S. pseudintermedius; the coagulase-negative form is often lumped together with other coagulase-negative staphylococci. Staphylococcus schleiferi subspecies coagulans has been isolated from up to 4% of apparently healthy dogs and up to 2% of apparently healthy cats, although prevalence varies geographically.
Coagulase-Negative Staphylococci (CoNS)

Coagulase-negative staphylococci have traditionally been considered non-pathogenic. Most bacteria in this category are commensals, such as *Staphylococcus epidermidis* in humans. These organisms may be either methicillin-sensitive or methicillin-resistant. CoNS may play a role in certain infections, however, so are now considered an emerging threat. In humans, CoNS have been implicated in community-acquired infections. In veterinary medicine, *Staphylococcus schleiferi* subsp *schleiferi* is considered a newly emerging pathogen and has been associated with bacterial pyoderma and otitis. In horses, methicillin-resistant strains of *Staphylococcus saprophyticus*, *Staphylococcus vitulinis*, and *Staphylococcus haemolyticus* have been isolated from the nasopharynx of healthy horses in a Danish study; similar clones were isolated from human staff members and the environment. *Staphylococcus epidermidis* was identified as the agent of equine osteomyelitis and is associated with post-operative infection. As with other staphylococci species, outcomes do not differ between methicillin-sensitive and methicillin-resistant CoNS. When isolated from lesional skin, soft tissue, or bone, CoNS should be considered opportunistic pathogens and may be sole agents of infection. An increasing threat is the ability of CoNS organisms to transfer mobile genetic elements associated with resistance genes to more virulent species of staphylococci. CoNS were the first staphylococci to become resistant to glycopeptide antimicrobials and have the potential of transferring this resistance to other staphylococci.

BIOFILMS

A biofilm is a thin coating that consists of living organisms and their extracellular matrix products. This extracellular matrix consists of varying quantities of protein, DNA, and exopolysaccharide; the coating was developed to protect the bacteria within it from environmental fluctuations and toxins; the feature also protects bacteria from both the host’s immune system and from antimicrobial agents. Biofilms are formed by several classes of organisms, including gram-negative bacteria such as *Pseudomonas* and its relatives as well as some strains of *Staphylococcus*. Multiple types of biofilms can be produced by the same bacteria at different times, as environmental conditions and nutrient profiles change. Biofilms can form on environmental surfaces, air-water interfaces, skin and mucous membrane surfaces, intestines, the bladder wall, and surgical implants. Biofilms may be pathogenic or non-pathogenic. Bacterial pili and fimbriae assist in adhesion of the bacteria to surfaces in monolayer biofilms or to other bacteria in multilayer biofilms. A single biofilm may be associated with different types of bacteria: thus *Pseudomonas aeruginosa* may co-exist with *Acinetobacter baumanii* and/or *Stenotrophomonas maltophilia*.

MANAGEMENT AND TREATMENT OF RESISTANT INFECTIONS

Samples should be obtained for culture and sensitivity testing whenever a patient fails empirical therapy. Interpret sensitivity results carefully and cross-check dosage recommendations with clinical references. For example, doxycycline is not considered clinically effective against infection unless it is administered twice daily. Streptococci
and enterococci are likely to be resistant to fluoroquinolones in vivo, even if sensitive in vitro. Surrogates should not be used for interpretation of fluoroquinolone susceptibility: sensitivity to orbifloxacin does not infer sensitivity to enrofloxacin or marbofloxacin. Also, remember that ciprofloxacin does not achieve clinically effective plasma levels except at potentially toxic doses. Except for treatment of urinary tract infections, in which ciprofloxacin may accumulate, this drug is a poor choice; veterinary-labeled fluoroquinolones are significantly more bioavailable than ciprofloxacin.

Antimicrobial therapy should be based on culture/sensitivity results, with a treatment duration of 4 weeks or 2 weeks beyond resolution of clinical signs. Additional cultures may be required during or after the initial course of therapy as varying degrees of resistance may develop during treatment. Genetic transfer of resistance elements and mutations may also occur rapidly, particularly in *Pseudomonas* and its relatives. Topical therapy is an essential component of treatment; 2% chlorhexidine solution remains effective against MRS.

Drugs such as linezolid, vancomycin, and newer non-veterinary fluoroquinolones or aminoglycosides, considered “last-resort” antimicrobials in human infections, should be avoided. Unfortunately, inappropriate use of vancomycin is increasing in veterinary medicine. Appropriate use requires that the infection be susceptible to vancomycin, and resistant to all other drugs. The infection must be considered survivable, and vancomycin must be administered IV in a hospital setting.

Family members should practice careful hand hygiene. The home environment should be cleaned carefully, not only to prevent transmission to other individuals, but also to prevent recontamination of the infected patient. The pet’s bedding should be washed regularly, ideally daily. Beds that cannot be washed should be discarded. Because leather is porous, leather collars, leashes, and harnesses cannot be disinfected, so should be replaced with items that can be washed. Control of the underlying cause is critical to prevent recurrence in the patient and further spread in the environment. *Pseudomonas* and its relatives can persist in an aqueous environment, on hands, and on abiotic surfaces for long periods of time. Thorough cleaning is essential. Biofilms can protect the organism in faucets, drains, and surfaces, as well as in ears or skin folds. In general, in humans and dogs, transmission requires disruption of epidermal integrity. Immune-compromised or post-operative individuals and those with open skin lesions should take strong precautions; ideally, other family members should treat the patient. Although the risk of transmission of MRSA from dogs to humans is much greater than the risk of transmission of methicillin-resistant *Staphylococcus pseudintermedius* (MRSP) from dogs to humans, precautions should be taken for both species. Cases of MRSP in humans are extremely rare and are most commonly associated with bite wounds, immune-suppression, or surgery. Conversely, dogs have a greater chance of passing MRSP to another dog in the family than they do of transmitting MRSA.

Fact sheets on MRSA, MRS, and Multidrug-Resistant Organisms are available at the University of Minnesota website: www.cvm.umn.edu/cahfs/fact/
Selected References


Huber H et al., 2011. Prevalence and characteristics of methicillin-resistant coagulase-negative staphylococci from livestock, chicken carcasses, bulk tank milk, minced meat, and contact persons. BMC Veterinary Research 7: 6.


