DERMATOLOGY CLINIC FOR ANIMALS

Kimberly S. Coyner DVM, Diplomate American College of Veterinary Dermatology

Las Vegas Animal Emergency Clinic
5231 W. Charleston Blvd.
Las Vegas, NV 89146
Phone: (702) 821-1002 Fax: (702) 821-1007

Two Locations:

Animal Emergency Center
3340 E. Patrick Lane
Las Vegas, NV 89120
Phone: (702) 434 - 1002 Fax: (702) 434 - 1058

Visit us on the Web at www.dermvetvegas.com

Dermatology Discourse

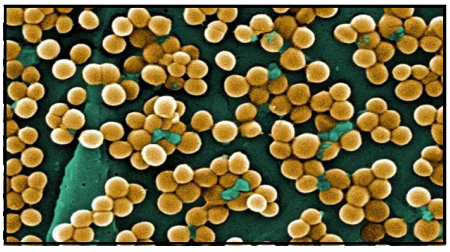
Methicillin-Resistant Staphylococcal Infections

What is Methicillin Resistance?

Methicillin is a beta-lactam antibiotic introduced in the 1950s; it is relatively resistant to beta-lactamase and so was used for the treatment of penicillin-resistant staphylococci. However bacterial resistance to methicillin emerged soon after its introduction. Methicillin-resistance is mediated by bacterial production of an altered penicillin binding protein (PBP2a), which does not allow microbial binding of beta-lactam antibiotics. Therefore MRSA isolates are resistant to all beta-lactam antibiotics (penicillins and cephalosporins) and are also frequently resistant to other antibiotic classes as well. The protein PBP2a is encoded by the mecA gene that resides on a mobile genetic element called the staphylococcal chromosomal cassette (SCC mec); the mobility of this genetic element allows it to be horizontally transmitted to other staphylococcal bacteria, conferring resistance easily. The laboratory diagnosis of a methicillin-resistant bacteria is actually done by testing for bacterial resistance against oxacillin, which is a similar antibiotic but is more stable for testing purposes.

Methicillin-Resistant Staphylococcus aureus (MRSA)

Staphylococcus aureus is often commensal in humans, and is carried in the nasal passages of 29-38% of humans. The prevalence of human MRSA colonization in the United State is estimated to be only 0.84%; however 30-40% of clinical *S. aureus* isolated from humans are methicillin-resistant and MRSA is now the most common nosocomial pathogen in the world. Risk factors that increase transmission of community acquired MRSA include crowded living conditions and shared bathing facilities. Risk factors for increased transmission of hospital acquired MRSA include previous antimicrobial therapy, immunosuppressive disease, invasive medical instrumentation, surgery and hospitalization. MRSA colonization occurs in 14.5% of household contacts of human MRSA patients. MRSA colonization may be an occupational risk for veterinary professionals: at a recent international veterinary conference, MRSA was cultured from 6.5% (27/417) of attending veterinarians and veterinary technicians; large animal practitioners were at greater risk of colonization (15.6%) compared to small animal practitioners (4.4%).



The prevalence of *S. aureus* colonization in dogs is low, and when present, usually originated from an in-contact human. *S. aureus* has been described as both commensal and pathogenic species in cats. As in humans, colonized animals usually show no adverse effects unless risk factors allow for development of clinical infection, including surgery, trauma, skin wounds, and immunosuppression. Methicillin-resistance in staphylococci isolated from domestic animals has been documented since the 1970s. In animals, MRSA is most frequently cultured from wounds, abscesses, otitis and chronic pyodermas. In a retrospective study from Antech Diagnostics, the overall percentage of *S. aureus* cultured from clinical infections in animals has remained unchanged from 2004 (3-5%) however the percentage of methicillin-resistant strains has increased from 19% in 2005 to 42% in 2007. Since animals contract MRSA from humans, this rise is not due to an increasing antibiotic resistance in animals, but rather from an increase in human MRSA.

Although pets that are colonized or infected with MRSA most likely contracted the bacteria from people, pets do have the capability to be carriers of MRSA and subsequently pass it back to in-contact humans. Most animals that are exposed to MRSA do not develop clinical disease, most eliminate the organism and an unknown number become colonized. Colonization involves survival of MRSA on the body without any adverse effect. If conditions permit, colonized pets may be at an increased risk for subsequent development of actual MRSA infection, and they can also serve as reservoirs of infection for other animals or for humans. In a retrospective study of 749 isolates of staphylococcal bacteria obtained from cultures of animals referred to the University of Pennsylvania School of Veterinary Medicine for workup of chronic refractory bacterial infections, 139 isolates were determined to be *S. aureus*, of which 39 were methicillin-resistant, a number likely reflective of chronicity of infection and prior use of multiple antibiotics. In a more recent prospective study from Penn, *S. aureus* was isolated from 6 of 59 dogs with inflammatory skin disease (only 1 of these was methicillin-resistant) and from 6 of 50 normal dogs (none of these was methicillin-resistant). In a similar study in cats, *S. aureus* was isolated from 14 of 48 cats with inflammatory skin disease (1 of these was methicillin-resistant) and from 10 of 50 normal cats (2 of these were methicillin-resistant). Optimal sites for MRSA screening in small animals have not been identified, but most references site the use of nasal, rectal and perineal swabs for bacterial culture.

Methicillin-Resistance in other Staphyloccal species

While *Staphylococcus aureus* is not considered to be normal flora on dogs, companion animals do normally carry other species of staphylococcal bacteria that can become pathogenic, *Staphylococcus intermedius* (now known to be *S. pseudointermedius*) and *Staphylococcus schleiferi*. In recent years, methicillin-resistant *S. intermedius* (MRSI) has emerged as a clinically important pathogen causing infections in dogs and cats, and like MRSA, methicillin-resistance in *S. intermedius* is mediated by penicillin-binding protein 2a (PBP2a), which is encoded by the mecA gene. Sequencing of the mecA gene in MRSI strains has revealed a high degree of similarity to the mecA gene of *S. aureus*, suggesting that the *S. intermedius* strains became methicillin-resistant via horizontal transfer of the *S. aureus* mecA gene. In addition to beta-lactam antibiotic resistance, most MRSI strains are also resistant to other classes of antibiotics. *S. intermedius* is not considered to be a human pathogen, but has occasionally been reported to cause severe infections in people, and humans may be colonized by the same strain of *S. intermedius* that infect their pets. Perhaps of more concern than direct zoonosis of MRSI is the potential for horizontal transmission of the mecA gene from animal-derived MRSI to susceptible *S. aureus* strains on people; in such cases pets could serve as reservoirs for spread of methicillin-resistance in humans, but further

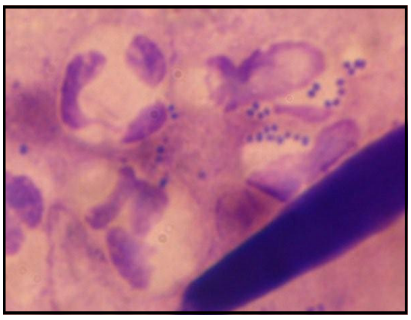
studies are required. In the previously described study of 749 isolates of staphylococcal bacteria obtained from cultures of animals referred to the University of Pennsylvania School of Veterinary Medicine for workup of chronic refractory bacterial infections, 462 isolates were determined to be *S. intermedius* of which 57 were methicillin-resistant. In a more recent prospective study from Penn which compared staphyloccal organisms isolated from 59 dogs with inflammatory skin disease vs. 50 normal dogs, *S. intermedius* was isolated from 52 dogs with skin disease (4 of these were methicillin-resistant) and from 34 of normal dogs (1 was methicillin-resistant). In a similar study in cats, *S. intermedius* was isolated from 11 of 48 cats with inflammatory skin disease (none were methicillin-resistant) and from 11 of 50 healthy cats (2 were methicillin-resistant).

Staphylococcus schleiferi ssp. *coagulans* is a relatively newly described staphylococcal pathogen in dogs; *S. schleiferi* ssp. *schleiferi* is a coagulase-negative variant that is also commonly pathogenic in humans. In dogs, *S. schleiferi* infection appears to be associated with prior antibiotic use, suggesting an opportunistic role when the normal bacterial flora are inhibited. In a retrospective study from University of Pennsylvania School of Veterinary Medicine, more than 200 isolates of *S. schleiferi* were collected from canine infections since 2002: 50 of these were determined to be *S. schleiferi* ssp. *coagulans,* and 150 were ssp. *schleiferi.* 50% of the *S.schleiferi* ssp. *schleiferi* strains were found to be methicillin-resistant. Of 749 isolates of staphylococcal bacteria obtained from cultures of animals referred to Penn for workup of chronic refractory bacterial infections, 148 isolates were determined to be *S. schleiferi*, of which 49 were methicillin-resistant.. In a more recent prospective study of staphyloccal carriage from 59 dogs with inflammatory skin disease vs. 50 normal dogs, *S. schleiferi* ssp. *coagulans* was isolated from 6 dogs with skin disease (1 was methicillin-resistant), and from 2 healthy dogs (1 was methicillin-resistant). *S. schleiferi* ssp. *schleiferi* was isolated from 6 dogs with skin disease (1 was methicillin-resistant) and from none of the normal dogs. *S. schleiferi* is rarely cultured from cats.

Management of MRSA Infections in Pets

Owners of pets with MRSA should be advised of the potential for zoonotic transmission; although the risk of disease is probably low for immunocompetent people, reports of community acquired MRSA in immunocompetent people are on the rise. Additionally, the concern for transmission is greater if the pet is exposed to immunosuppressed persons or when household members are in contact with higher risk people (ie. healthcare workers). Involvement of physicians is prudent, because veterinarians should not make specific recommendations for the prevention or diagnosis of disease in humans.

Treatment of MRSA in pets depends on whether actual infection is present vs. colonization. Clinical infection with MRSA almost always requires treatment; small superficial infections may be treated topically with topical medications such as silver sulfadiazine or mupirocin. If topical therapy alone is chosen, the animal must be closely monitored for progression of disease. In most cases, systemic antibiotic therapy is required to treat MRSA infections in pets. Because of the variability of MRSA isolates, antibiotic choice should be based on in vitro antibiotic susceptibility testing. MRSA infections should never be treated with beta-lactam antibiotics (penicillins and cephalosporins), even if in vitro testing implies susceptibility. According to Antech Diagnostics, antibiotics which may be effective include chloramphenicol (95% sensitive), potentiated sulfonamides (65-75% sensitive), clindamycin (<40% sensitive, only use if sensitivity to erythromycin is also indicated), or fluoroquinolones (25% sensitive). For superficial pyoderma, antibiotics are required for 3 weeks minimum; for deep pyoderma and chronic otitis cases, antibiotics may be needed for 4-8 weeks or longer. The use of vancomycin or linezolid for treatment of MRSA in animals is very controversial, as these drugs are often the last resort in human medicine. Pets treated for MRSA in a hospital environment must be treated as infectious, and isolated from the general hospital population. Gloves and gowns or dedicated labcoats should be used when handling the animals or any in contact items such as bowls or bandages. Pens and stethoscopes must also be dedicated to the patient. Disposable thermometer covers should be used or digital thermometers discarded after the animal is discharged. Following discharge, all cage items and medical equipment used on MRSA-infected animals must be aggressively disinfected with appropriately diluted disinfectants allowed to contact surfaces for 5-10 minutes (after removal of any organic debris that could potentially inactivate disinfectants). Treatment of methicillin-resistant *S. intermedius* and *S. schleiferi* infections is the same as for MRSA; although these staphylococcal species may not be as directly zoonotic as MRSA, preventative measures should still be taken to avoid propagation of the causative mecA gene. Additionally, animals infected with MRSI or MRSS can act as foci for nosocomial infection of other animals in the veterinary hospital, especially animals that are immunosuppressed or that have indwelling intravenous or urinary catheters.



Although dogs that are only colonized with MRSA may spontaneously eliminate the colonization with time, these pets are a potential source of infection to humans and other pets in the household. Management recommendations for MRSA-colonized pets are unclear, but most references recommend hygiene (washing hands frequently after touching the pet, not allowing the pet to lick or sniff at people, frequent washing/disinfection of pet bedding and housing surfaces), barrier precautions (dedicated outer wear to handle the pet +/- wearing gloves and gowns), and isolation of colonized or infected pets from immunocompromised people and pets. In most cases, use of systemic antibiotics is not recommended to eliminate colonization; topical antimicrobial shampoos and conditioners may be helpful but have not been specifically studied in animals. Topical use of mupirocin in the nasal cavity is unlikely to be successful as monotherapy in MRSA colonized pets, as studies have shown identical MRSA carriage from the nares, mouth, anus, groin and head. Useful recommendations for MRSA infection management in people can be found at www.cdc.gov. Additionally, the British Small Animal Veterinary Association has posted helpful online guidelines for MRSA management in veterinary hospitals at www.mrsainanimals.com/BSAVA.html.

References:

Abraham JL, Morris DO, Griffeth GC et al. Surveillance of healthy cats and cats with inflammatory skin disease for colonization of the skin by methicillin-resistant coagulase-positive staphylococci and *Staphylococcus schlieferi* ssp. *schlieferi.* Vet Derm 2007; 18: 252-259.

Antech Diagnostics Newsletter: Methicillin-Resistant *Staphylococcus aureus* (MRSA) Revisited. April 2008.

Griffeth GC, Morris DO et al. Screening for skin carriage of methicillin-resistant coagulase positive staphylococci and *Staphylococcus schleiferi* in dogs with healthy and inflamed skin. Vet Derm 2008; 19: 142-149.

Hanselman et al. Methicillin-resistant Staphylococcus aureus (MRSA) colonization in veterinary personnel. Emerg Infect Dis 2006; 12:1933-38.

Morris DO. Methicillin Resistance in Staphylococci: Implications for Veterinary Dermatology. In: 23 rd Proceedings of the North American Veterinary Dermatology Forum. Denver, CO. April 9-12, 2008.

Morris DO, Rook KA, Shofer FS and Rankin SC. Screening of *Staphylococcus aureus, Staphylococcus intermedius,* and *Staphylococcus schleiferi* isolates obtained from small companion animals for antimicrobial resistance: a retrospective review of 749 isolates (2003-04). Vet Derm 2006; 17:332-337.

Weese JS. Methicillin-Resistant *Staphylococcus aureus*: An emerging pathogen in small animals. JAAHA 2005;41: 150-157.