MANAGING WOUNDS INFECTED WITH METHICILLIN RESISTANT STAPH

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Coagulase-positive *Staphylococcus intermedius* is the most common resident organism of dog skin; however, carriage of methicillin-resistant *Staphylococcus intermedius* (MRSI) in healthy dogs and dogs with pyoderma is uncommon. Methicillin resistance in *Staphylococcus* is conferred by an acquired penicillin-binding protein that is coded by the gene *mecA*, which confers resistance to all beta-lactam antimicrobials and their derivatives. Recently, MRSI isolates were determined to actually be a closely related species – *S. pseudintermedius*. Behaviors of the two organisms and another coagulase-positive species *S. schleiferi* are similar; therefore, for this review they will be grouped under the name MRSP.

Methicillin-resistant *Staphylococcus* infections have been reported in dogs with a variety of conditions, including pyoderma, pododermatitis, and chronic otitis. MRSP infections have also been documented in the genitourinary and respiratory tracts and the peritoneal cavity. In one review of acral lick granulomas by Shumaker *et al* (J Vet Derm, 2008), multiple antimicrobial resistance was noted in deep tissue cultures from 48% of dogs; 26% of these had methicillin-resistant staphylococcal species.

Methicillin resistance is thought to occur because of excessive or inappropriate use of antimicrobials in humans and animals. Antimicrobial resistance should be suspected in patients that have recurrent or nonresponsive wounds. Diagnosis of MRSP is based on deep tissue cultures obtained by aspirate or punch biopsy after aseptic skin preparation. Definitive diagnosis of these species requires DNA sequencing. Animals with MRSP should be evaluated for underlying disease (e.g. hyperadrenocorticism, allergies, hypothyroidism, diabetes mellitus) that could predispose them to infection or interfere with wound healing.

Methicillin-resistant *Staphylococcus* bacteria have several characteristics that increase their virulence. Many strains have a capsule, or “slime layer”, that inhibits chemotaxis and phagocytosis by leukocytes and enhances adherence of the bacteria to implants. Peptidoglycans within MRSP stabilize bacterial cell walls, which increases their tolerance to high heat, desiccation, and hyperosmotic environments. These peptidoglycans also enhance adherence to mucosal surfaces and protect them from host defenses. MRSP contain endotoxins that are associated with erythrocyte hemolysis and may cause gastrointestinal disease or toxic shock.

In general, animals with wound infections are treated similarly, regardless of the underlying cause. Supportive care (fluids, nutritional supplementation, pain management, oncotic support) are administered as needed. Perfusion to wounds is improved by maintaining normotension and normovolemia and by avoiding hypothermia, which increases vasoconstriction. Wound healing and clearance of infection are inhibited by necrotic tissue and foreign debris; thus, wounds should be debrided surgically, chemically, or mechanically as needed. Implants or sutures may need to be removed if they serve as a nidus for infection. Drainage is critical for reducing pressure on wounds by seromas and hematomas. Penrose and continuous suction drains may be sufficient in some animals; however, open wound management is preferable in most patients. Open wound management provides access for daily debridement, either with the bandage changing or wound cleansing process or by sharp dissection, and permits thorough topical application of antimicrobials. Because of the risk for disease spread, affected patients should be handled similar to animals with contagious systemic illness.

If possible, affected patients should be isolated from other animals. Any supplies and tools (e.g. stethoscopes, thermometers, writing utensils, leashes) used during patient handling should be restricted to the affected individual during its stay and then disinfected before using on other patients. Staff should take barrier precautions – e.g. wear gloves and gowns- when changing bandages and cleaning wounds. Eye or face protection and masks are worn during wound cleansing.

Hand hygiene is the most important step to reducing spread of the bacteria. Before and after handling the patient, personnel should use an alcohol based hand sanitizer. Tables and floors can be decontaminated with an appropriate disinfectant. MRSP is sensitive to many common detergents and disinfectant cleaners as long as an appropriate contact time is used. Efficacious contact times vary between disinfectants and some may require 10 minutes of contact before wipe down to ensure bacterial kill.

Systemic antimicrobial treatment should always be based on results of culture and susceptibility testing. If a methicillin-resistant bacteria is identified, an extended susceptibility panel should be requested to determine what drugs will be most effective. Toxicity, side effects, method of deliver, potential for future resistance, and expense of those drugs should then be taken into consideration. Microbiology laboratory personnel can be contacted to determine the most common sensitivity pattern of local strains while results are pending. In our hospital, MRSP is usually susceptible to chloramphenicol (100%) or amikacin (97%). Unlike *S. aureus*, MRSP may be susceptible to potentiated sulfonamides since they lack the plasmids that mediate resistance in those organisms.

Some strains of MRSP may display *in vitro* susceptibility that does not correlate with *in vivo* response. When selecting a drug dose, clinicians should consider whether the antimicrobial effect is dose or time dependent. For instance, the killing mechanism of fluoroquinolones is dependent on the amount of time the plasma drug concentration is above minimum inhibitory concentration ("dose dependent"). Therefore, clinicians should choose a dose that will produce peak plasma concentrations 8 to 10 times above the MIC for that organism. Systemic antimicrobials should be administered at least 1 week beyond remission of clinical disease (usually a minimum of 21 days). Repeated antimicrobial exposure at subtherapeutic concentrations or inappropriately short duration may select for resistance. Deep tissue cultures should be repeated during antibiotic therapy if healing is not progressing as expected.

Local wound management consists of wound cleansing, debridement as needed, application of topical therapy, and bandaging to protect the wound, limit environmental contamination, and facilitate healing. Local therapy is particularly critical when wounds are not amenable to systemic therapy, and may be used as a sole therapy when disease is limited to local, superficial infection.

Wound cleansing can be performed with compressed oxygen portable wound cleansing systems (JetOx). Because minimal amounts of fluid are used with the system, the patient stays dry and warm; additionally, lavage with this technique seems to cause less discomfort in patients. After the wound is cleaned and debrided, it is covered with a solution, cream or ointment that reduces bacterial growth. Options include antiseptics (chlorhexidine, povidone iodine, acetic acid), antimicrobials (fusidic acid, mupirocin, tea tree oil, silver), and hyperosmotic agents (honey, sugar, dextrans, hypertonic saline). In one paper of animals with MRSP infections (Loeffler et al, 2007), topical antimicrobial therapy alone was successful in 6/11 dogs. In those animals, most of the infections were superficial. Treatments included fusidic acid cream or otic preparation, benzoyl peroxide, mupirocin ointment, 2% chlorhexidine shampoo for skin, and ear cleansing with 0.1% chlorhexidine/Tris EDTA. The remaining animals were treated with a combination of topicals and systemic antimicrobials (clindamycin, apramycin, rifampicin).

Topical treatments are held in place with a primary bandage layer. Agents that potentiate effusion (sugar, honey, silver sulfadiazine) should be covered with a highly absorbent pad. For mild to moderately effusive wounds, silver/dextran impregnated foam provides an effective primary layer that is absorbent while retaining a

moist environment. Primary and secondary layers can be secured with a tie over bandage to improve skin mobilization. The entire wound area and associated dressings can be covered with iodine impregnated adhesive drape to maintain a moist environment while protecting the wound and containing any drainage.

Healthy dogs and people can serve as carriers for MRSP. In one reported outbreak of surgical wound infections in pets (van Duirken et al, 2008), MRSP carriage was detected in a surgeon, two surgical nurses, and staff members' dogs that were frequent visitors to the clinic. Colonized personnel were likely the source of the wound infections. Transmission of MRSI (reclassified as *S. pseudintermedius*, in recent studies) from dogs with deep pyoderma has been documented in 46% of their owners (Guardabassi et al, 2004). Infections within humans, however, are rare, although horizontal transference of antibiotic resistance to *S. aureus* could be a potential risk in MRSP -colonized humans.

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