Methicillin Resistant Staphylococcus

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Over the last several years there has been a worldwide increase in cases of multidrug and methicillin resistant *Staphylococcus pseudintermedius* (MRSP), *Staphylococcus schleiferi* (MRSS) and *S. aureus* (MRSA) infections. While MRSA is the dominant infection in people, it is MRSP and MRSS that is responsible for most of the drug resistant infections in veterinary patients. Some regions of North America are reporting that as many as 50% of skin infections treated are due to MRSP or MRSS. The escalating incidence of both MRSA and MRSP are causing some medical and public officials to call for regulation and restriction of the usage of certain antibiotics in veterinary medicine. Veterinarians must become even more judicious in the usage of antibiotics in the future, and should utilize basic and reasonable methods of reducing the spread of methicillin resistant Staphylococcus (MRS) within their practice and facilities.

Fortunately even though the incidence of MRS has clearly increased, the virulence of these bacteria has not seemed to worsen in our dermatology patients. Much of the pathology that Staphylococcus causes is due to the various toxins these bacteria can produce. The toxins that cause disease with sensational headlines such as "flesh eating" disease are still fortunately rare even in our referral dermatology practice. It is vital veterinarians remember this when they are making treatment recommendations.

Resistance to methicillin is due to a mecA gene, which is present in both S. pseudintermedius and S. aureus. The mecA gene encodes for production of an altered penicillin binding protein (PBP2a or PBP2') that has a low affinity for all beta-lactam antimicrobials such as the penicillins and cephalosporins. Therefore the bacteria are able to produce a normal cell wall despite the presence of these antibiotics.

Phylogenetic analysis of members of the Staphylococcus intermedius group (SIG) has revealed the existence of three closely related species (S. intermedius, S. pseudintermedius and S. delphini), and S. pseudintermedius turned out to be commonly misidentified as S. intermedius in the past

For many of the "milder" and superficial forms of pyoderma in the dog, I have become much more of an advocate of topical therapy. Three agents are commonly used by veterinary dermatologist. Numerous chlorhexidine shampoos, sprays, and leave on conditioners are now available, with strengths from 2%-4% and combined with either Tris-EDTA, or phytosphingosine, or formulated to "stick" to the epidermis and hair for as long as a week after bathing. If the skin is particularly greasy, then benzoyl peroxide is indicated. The clinician should utilize these products in all cases of pyoderma. Even dogs which are difficult to bathe can at least be sprayed with these products. Another topical product which is being used by some veterinary dermatologist is Vetericyn VF™ which is also available in a weaker OTC version of Vetericyn™ At 150 parts per million of Free Active Chlorine (FAC), Vetericyn VF™ is nearly double the potency of the consumer formula of Vetericyn (at 80 parts per million of FAC). At this time I still prefer the stronger chlorhexidine products. Mupirocin is a topical antibacterial agent that in humans is used both for the treatment of skin infections and for the suppression or elimination of nasal carriage of Staphylococcus aureus, including methicillin-resistant S. aureus. In veterinary patients it is ideal for the treatment of localized or focal lesions, and may be used when just a few lesions are present. Resistance to mupirocin is being documented in human medicine, and unfortunately sensitivity testing is not routinely available for our patients. Obviously not all clients are able to comply with a vigorous topical regiment, and not all patients will respond to topicals as the sole therapy, but with the rising rate of MRS we should be compelled to recommend more topical therapies.

When antibiotics are necessary, it is more imperative than ever to utilize proper doses and treatment duration. We are not doing our patients, clients or society any favors by utilizing inadequate doses in an attempt to save clients money. Remember the adage "Dead bugs don't mutate." Despite these recommendations, we continue to see patients with a pyoderma treated for less than the recommended three weeks for superficial infections and four weeks plus for the deeper infections. It has become imperative to educate owners if a positive response is not seen to an empirically chosen antibiotic, then a culture for sensitivity testing should be obtained before simply prolonging the use of an ineffective drug.

The other issue which many times is overlooked is investigation and treatment of the underlying cause of the pyoderma. Even with successful control of the active infection, if the underlying etiology is not identified and controlled, the patient is susceptible to further infections. The majority of the patients seen with recurring pyoderma suffer from an underlying allergy, or on occasion an endocrinopathy. There has been a true "paradigm shift" regarding our approach to the use of antibiotics. In previous years, it was "do everything reasonable" to avoid the chronic use of corticosteroids, but now we attempt everything reasonable to avoid the repeated use of antibiotics. Techniques such as "pulse dosing" of antibiotics to reduce recurrence of pyodermas are no longer utilized for our dermatology patients. There are some patients where the underlying cause of the pyoderma cannot be ascertained. Even more commonly we may know the patient is atopic but skin infections continue to recur despite our best attempts at treatment of the atopy. In such cases we have been quicker to recommend Staphage Lysate (SPL) ® injections. Staphage Lysate is useful for preventing new infections, not necessarily in treating an active infection. For a patient with recurring pyoderma, we will start SPL injections when we initiate antibiotic therapy, and then continue SPL injections on a weekly basis while monitoring for a relapse. It is still more effective

to identify and deal with the underlying allergy more directly such as allergy specific immunotherapy for the atopic patient, and diet restriction for the food allergic patient, but SPL does offer an additional option when control of the underlying allergy is not effective.

There are several studies to support the hypothesis that the frequent use of fluoroquinolone antibiotics has been one of the factors responsible for the rise in MRSP. Therefore they should be used for cases of pyoderma only when there are no other feasible or effective options. I still prefer the cephalosporins such as cephalexin or cefpodoxime as my first line of antibiotics, although clavulanic acid potentiated amoxicillin, Trimethoprim-potentiated sulfas, and clindamycin all remain appropriate first line empirical choices. I am now much quicker to recommend a culture if a patient is not responding to an empirically chosen antibiotic. Simply choosing a different antibiotic empirically risks wasting more time and money, especially since most MRS are resistant to many of the traditional empirically chosen antibiotics. For patients who do have a MRS infection, there still may be oral antibiotics to which the bacteria are sensitive. My preference in order that I will use is clindamycin, Trimethoprim/sulfa, doxycycline with chloramphenicol being a last resort. Injectable aminoglycosides are only used in the most serious and refractory cases. Rifampin is another potential therapy option, although most laboratories do not routinely screen for sensitivity to this drug. Potential side effects include hepatotoxicity, and the metabolites of this drug will always cause a red discoloration to the urine and tears. Previous recommendations were to use this drug in combination with other drugs such as clindamycin or cephalosporins to reduce the speed at which resistance might develop against Rifampin. There is no consensus amongst dermatologist, with some using it as a monotherapy. Rifampin does have the ability to penetrate into deep or scarred lesions, which is one of its indications for use.

Besides exposure to antibiotics, especially fluoroquinolones, the other notable risk factor for our patients acquiring a MRSP infection is veterinary visits which require hospitalization, especially surgery. Because of this, recommendations for prevention and control of bacterial resistance have been developed. Recommendations by the Canadian Committee on Antibiotic Resistance (2008) Infection Prevention and Control Best Practices for Small Animal Veterinary Clinics are available on the web at www.wormsandgermsblog.com and give more in-depth guidance for veterinary clinic and hospital policies. The highlights of these recommendations are as follows:

Summary of infection prevention and control best practices for small animal veterinary clinics

1. Infection prevention and control strategies are designed to protect patients, owners, veterinary personnel and the community. All veterinary personnel should play an active role in protecting every person and animal associated with the veterinary clinic.
2. Every veterinary clinic, regardless of type or size, should have a formal infection control program, a written infection control manual, and an infection control practitioner (ICP) to coordinate the program.
3. Some form of surveillance (either passive or active) should be practiced by all veterinary facilities. The keys to passive surveillance are to centralize the available data, and to have a designated ICP who compiles and evaluates the data on a regular basis.
4. Routine Practices that are critical to infectious disease prevention and control include:
    a. Hand hygiene, including:
        - Hand washing
        - Use of alcohol-based hand sanitizers
    b. Risk reduction strategies, particularly those related to:
        - Use of personal protective equipment (PPE)
        - Cleaning and disinfection
        - Laundry
        - Waste management
    c. Risk assessment of animals and personnel with regard to:
        - Disease transmission
        - Disease susceptibility
    d. Education
        - Veterinary personnel
        - Animal owners
        - Public
5. All surgical procedures cause breaks in the normal defensive barriers of the skin or mucous membranes, and therefore carry an inherent risk of surgical site infection (SSI). Good general infection control practices (e.g. hand hygiene, cleaning and disinfection) are important for prevention of SSIs, but there are also specific infection control measures pertaining to surgery that should be considered.

6. Every veterinary clinic should have an isolation area for caring for and housing animals with potentially contagious infectious diseases.
7. Proper wound care is critical to preventing transmission of bacteria, particularly multidrug-resistant pathogens, between animals, personnel and the environment.
8. Animals from shelters and similar facilities should be considered high risk from an infectious disease standpoint and managed appropriately to prevent transmission of disease.
9. Safety of personnel and animal owners should always be a priority. Personnel should take all necessary precautions to prevent animal-related injuries (e.g. bites, scratches), and all bite wounds should be taken seriously. Proper sharps handling practices should be emphasized to reduce the risk of needle-stick injuries.
10. Education of personnel and clients about zoonotic and infectious disease risks and prevention is crucial.