Prudent Antimicrobial Use in Dermatology

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Superficial Pyoderma

In dogs, superficial bacterial pyoderma is the most common form of pyoderma and a frequent reason for antimicrobial use in companion animals.[1] Superficial bacterial folliculitis, also known as superficial pyoderma, is a bacterial infection of the hair follicle.[2] The main pathogen causing superficial pyoderma in canines is *Staphylococcus pseudintermedius,* which is a commensal microbe of canine mucosa, skin and ears.[2] Several studies have isolated *S. pseudintermedius* from 46–92% of healthy dogs, with the highest prevalence at the perineum, followed by nasal and oral mucosa.[3] *S. pseudintermedius* has been documented as the predominant pathogen in up to 92% of canine pyoderma cases.[3] *S. pseudintermedius* is primarily identified in dogs, however, it has also been identified in other species, including cats, horses, and humans.[4] Other bacterial strains and species are also part of the normal microbiota and can become opportunistic pathogens. Bacteria may cause an infection secondary to epidermal barrier dysfunction in diseases such as atopic dermatitis, ectoparasitism, endocrine disease, local trauma or seborrhea.[2] This “opportunity” initiates the colonization of pathogenic *S. pseudintermedius*.

Superficial bacterial pyoderma will present with clinical signs such as papules, pustules, crusting, epidermal collarettes, and folliculitis (circular regions of alopecia).[2] However, none of these clinical signs are pathognomonic for a superficial pyoderma. Chronic or recurrent bacterial pyoderma can occur when the primary underlying cause of skin inflammation and barrier dysfunction is not identified or appropriately controlled. Other reasons for persistence of infection include inappropriate therapy, lack of diagnostics, a resistant bacterial population and client compliance.[5]

Diagnostic Testing

While the diagnosis of a superficial bacterial folliculitis is generally straightforward, simply observing folliculitis in a patient is not confirmatory for a bacterial infection.[5] Dermatophytes and demodex will also cause folliculitis as they invade the hair follicle. Certain immune mediated diseases, such as pemphigus foliaceus, will cause a pustular dermatitis. Cytology must be performed to confirm a diagnosis of bacterial pyoderma and other diagnostic tests, such as skin scrapings or fungal culture, should be used to rule out other causes of folliculitis.[2]

Bacterial culture and susceptibility for canine pyoderma is never contraindicated but is highly recommended in patients with chronic or recurrent pyoderma. Bacterial culture should be performed after cytology to verify that bacteria are, indeed, the reason for the skin lesions. Culture without cytology is rarely of use as most animal skin has commensal bacterial species that can grow on culture. Culture and susceptibility testing from pyoderma lesions can occur at any time, regardless of the use of topical or systemic antibiotics if bacteria continue to be found on cytology samples.[1] Caution should be taken when interpreting results based on where the culture sample was taken from and the likelihood of contamination. Ideally samples should be obtained from intact pustules, after gently removing the top with a sterile needle, under crusts, under the ring of an epidermal collarette or a region where bacteria was found on cytology. If systemic therapy is planned for the patient, results of the bacterial culture should guide this therapy.

Although bacterial culture of a superficial bacterial pyoderma is never contraindicated, there are five situations in which the likelihood of resistance is higher and bacterial culture should be pursued. [2]

1. A less than 50% reduction in lesions within 2 weeks of appropriate systemic antimicrobial therapy
2. Emergence of new lesions (papules, pustules, collarettes) 2 weeks or more after the initiation of therapy
3. Presence of residual lesions after 4-6 weeks of appropriate systemic antimicrobial therapy together with the presence of cocci on cytology
    a. A typical course of therapy is 21–28 days
4. Intracellular rod-shaped bacteria on cytology
5. There is a prior history of multidrug-resistant infection in the pet or in a pet from the same household as the affected individual

Methicillin Resistant *Staphylococcus pseudintermedius*

The emergence of Methicillin Resistant *Staphylococcus pseudintermedius* (MRSP) in dogs was first noted in 1999 from a dog in the US.[6] An altered penicillin-binding protein, encoded by the *mecA* gene, confers resistance to methicillin.[7] Oxacillin is also used as a marker for methicillin resistance by laboratories as it is equivalent to methicillin. Methicillin-resistant staphylococci are resistant to all β-lactam antibiotics and may be resistant to multiple other antimicrobials, making systemic therapy incredibly challenging for many cases.[8] In a study by Huerta *et al*, 78% of isolates of *S.pseuintermedius* were resistant to at least one antimicrobial agent, 32% were multi drug resistant and 10.4% were methicillin-resistant.[9]

Over the last number of years, the prevalence of methicillin-resistant isolates from Canadian dogs with pyoderma has ranged from 12.1% of all staphylococcal species in primary practice to 45% of coagulase-positive staphylococci in a referral practice.[10] Multiple previous studies have found that the use of antimicrobials in dogs increases the risk of resistant infections developing.[8-10] Commensal bacteria undergo selection pressure any time their host receives systemic antibiotics. Treatment can obliterate the susceptible commensal populations and allow re-colonization by a strain resistant to these drugs.[5] Over the last 2 decades, this lateral transmission has allowed this resistant bacteria to spread through canine populations.[8] The probability of isolating methicillin resistant *Staphylococcus* increases by a factor of four in dogs with recurrent pyoderma who have received systemic antibiotic treatment versus healthy dogs and those with first time pyoderma.[9] Another study also found that 0–4.5% of healthy dogs are colonized with MRSP as part of their normal flora.[11]

Unfortunately, even after successful treatment of pyoderma caused by resistant *Staphylococcus*, these organisms can continue to colonize dogs and cause future resistant infections.[10] Colonization with MRSP may persist after treatment of infection, therefore MRSP may be isolated from dogs in contact with MRSP-infected pets, dogs with superficial bacterial folliculitis that have previously had MRSP infections or are from households with other pets that have had MRSP infections. [10] In cases where topical treatment of pyoderma was pursued and the infection failed to resolve, it is acceptable to perform bacterial culture and susceptibility testing or to institute empirical systemic antibiotics. Dogs bred in urban habitats with a history of antibiotic therapy in the last year represent a significant risk of being an MRSP carrier.[9]

Treatment

As antimicrobial resistance is becoming widespread it is important to practice antimicrobial stewardship within the clinic. Efforts to combat antimicrobial resistance in all species are underway through the One Health initiative.

Three components for limiting antimicrobial resistance are preventing disease recurrence, reducing antimicrobial usage and improving antimicrobial drug use.[5] In companion animal practice, one of the most frequent opportunities to practice stewardship is in the management of canine pyoderma as, currently, pyoderma accounts for 30% of antimicrobial prescriptions. [1,12]

Historically canine and feline pyoderma has been treated using systemic antibiotics. This approach is no long reliable owing to the growing resistance amongst bacterial species. The most recent clinical consensus guidelines for the treatment of superficial pyoderma indicate that *"topical therapy should be used as the sole on-animal antibacterial treatment for surface and superficial infections whenever a pet and owner can be expected to be compliant"*.[8] Multiple factors can impact our therapy choices including resistance, severity and extent of skin lesions, concurrent disease, patient tolerance and owner ability to perform/give treatments. In veterinary medicine I find that we often "assume" that a client cannot do topical therapy and the perception that compliance will be poor exists. However, we should never assume this without having an honest conversation with our clients about what they can, and are willing, to do. When owners can perform and are committed to topical therapy, there are significant advantages such as decreased adverse effects, rapid lesion resolution, decreased chance of resistance and decreased costs.[1] If clients are able to bathe their pet, shampoo therapy not only provides antimicrobial activity but also serves to remove debris from the skin, remove microorganisms from the skin and hydrate the skin.[2] If clients are unable or resistant to shampoo therapy as part of the topical regimen, sprays, mousses, ointments or wipes are alternatives that can be recommended to treat infection. Resistance to topically applied antiseptics and antimicrobials is very uncommon and many agents will not only treat susceptible pyodermas but also those due to resistant species. The emergence of multidrug resistant bacterial strains with few to no options for systemic therapy has provided a new stimulus for topical therapy highlighting the importance of this approach. Chlorhexidine is an antiseptic used in many topical products for pyoderma treatment. Chlorhexidine penetrates and disrupts the bacterial cytoplasmic membrane resulting in leakage of cytoplasmic components as well as forming precipitates after entering the cytoplasm thereby killing the bacterium.[13] Many studies have shown chlorhexidine to be an effective antimicrobial. One such study found that 4% chlorhexidine digluconate products (shampoo and solution) were as effective as systemic therapy with amoxicillin–clavulanic acid in dogs with superficial pyoderma.[14] Also, no difference in efficacy was noted between MRSP and methicillin susceptible infections. [14] Benzoyl peroxide shampoos have been found to improve clinical signs associated with susceptible bacterial pyoderma within 3 weeks of therapy, however, these shampoos can be drying in some patients when used at increased frequency.[15]

Topical therapy is not dependent on the results of a bacterial culture and susceptibility. It is challenging to assess the validity of antimicrobial susceptibility tests for topical agents however, it is likely that high concentrations of topical agents are achieved at the site of application.[1] Good response to topical therapy alone was reported in 68% of dogs with MRSP pyoderma in one study and in 100% of cases with MRSP pyoderma treated topically in another case series.[16] For this reason, current guidelines also state that using topical anti-microbial agents with proven benefit in cases of resistant infections is the recommended treatment for surface and superficial pyoderma involving resistant infection; also for otitis and wounds.[8]

Systemic Therapy

Based on consensus guidelines, if topical therapy is not recommended for the treatment of bacterial pyoderma and systemic treatment is truly needed, antimicrobials are split into first tier, second tier and then higher tiers. First tier antibiotics are ones that most susceptible *Staphylococcus pseudintermedius* strains would be susceptible to. These include clindamycin, first generation cephalosporins, Amoxicillin-clvaulanate and trimethoprim-

potentiated sulfonamides. All other therapies are considered second tier or higher and should only be prescribed if a culture and susceptibility verifies the organism is susceptible to that specific antimicrobial. There is one class of antibiotics that is considered first or second tier, third generation cephalosporins (Cefovecin, cefpodoxime). There was insufficient evidence for the working group developing the guidelines to reach a consensus on categorization for these antimicrobials.[1] Cefovecin is more active against *E. coli*, *Klebsiella pneumoniae* and *Proteus* spp. compared with cefalexin and cefadroxil, and its *in vitro* activity against *E. coli* and *Proteus* spp. is comparable to cefpodoxime.[17] Pharmacokinetic data for cefovecin suggests that the concentration exceeds the MIC_{90} of *E. coli* for 2 days following injection and exceeds the MIC_{50} of *E. coli* for 6 days. This means the concentration can be sufficient to kill susceptible gram negative bacteria. This may lead to selection of resistant extended-spectrum β-lactamase (ESBL)-producing *E. coli* when cefovecin is used.[1] On the 8th February 2024 the World Health Organization published WHO Medically Important Antimicrobials List for Human Medicine.[18] Third generation cephalosporins are now classified as highest priority critically important antimicrobials for humans. This is an indication that we must be more prudent with the use of these antimicrobials. Guidelines for antimicrobial use in veterinary medicine can be found by accessing the CVMA Veterinary Guidelines for antimicrobial use on the Firstline App.

Oral Clindamycin is generally given twice daily due to time-dependent pharmacokinetics. However, one study found that once daily dosing was efficacious in treating canine pyoderma in the majority of doses at a dose of 11 mg/kg.[19]

Other Considerations when treating pyoderma

Transmission of *S.pseudintermedius* between humans and pets is low but can occur when living in the same house.[20,21] This highlights the need to treat pyoderma to avoid any risk of transmission. The risk of infection from *S.pseudintermedius* is low but infections due to this bacteria have been documented in humans.[22] Hygiene practices should be discussed with the owners, especially in households where a resistant bacterial infection has been documented.[23]

The most effective way to prevent pyoderma recurrence is by identifying and addressing the underlying cause of the skin disease. This can be challenging as many dermatologic diseases can lead to cutaneous inflammation and an abnormal skin barrier. Identifying this underlying disease via diagnostic testing, treatment and food trials, bloodwork etc is paramount to help reduce inflammation and prevent recurrence of the pyoderma.

Within the clinic, use of antiseptics with a spectrum of activity against Staphylococcus should be used to disinfect surfaces and hand washing should be instituted for all members of the healthcare team. Team members should be trained to identify potential resistant cases or risk factors for resistance such as individuals with multiple courses of antimicrobials. Many publications exist on hygiene within a veterinary clinic.[24]

Although recurrent MRSP infections are common, there are currently no controlled studies in dogs that would indicate potential effective methods of decolonization, nor the need for such procedures. Therefore, at this time, routine decolonization of carriage sites of dogs with recurrent MRSP infections is of questionable value and not recommended.[25]

As antimicrobial use has been identified as a risk factor for the emergence of MRSP, pulse therapy with systemic antibiotics is not advised and this approach should be replaced with intermittent shampoo baths or other topical approaches.[26]

Recheck

Most superficial bacterial pyodermas should be treated for 3-4 weeks, irrespective of whether topical or systemic therapy is prescribed. Patients should show improvement within 2 weeks of appropriate therapy with increased comfort and decreased clinical lesions. A recheck should be scheduled for 3-4 weeks after starting therapy so the patient can be re-evaluated by the clinician on the case. Cytology should also be performed to verify resolution of the pyoderma. Long-term management plans to address the underlying primary disease can also be assessed and modified pending the patient. If the pyoderma is vastly improved but not completely resolved, therapy should be continued until a minimum of 7 days past clinical resolution.[2,26]

Otitis

For otitis externa, topical treatment is recommended. Treatment should be selected based on cytology of the ear canals. For topical treatment a bacterial culture and susceptibility is not required. As previously mentioned, resistance to topically applied antimicrobials is possible but highly unlikely. A topical should be selected with a spectrum of activity that covers the type of microbe noted on cytology samples.

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