STAPHYLOCOCCAL PYODERMA: AN EMERGING CRISIS IN CANINE PRACTICE

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Staphylococcus pyoderma is the most common skin disease in dogs. The term pyoderma refers to any purulent skin disease. In veterinary medicine the term is most commonly used to refer to bacterial colonization or infection of the skin and/or hair follicle. Bacterial pyoderma is second only to flea allergy dermatitis as the most common dermatosis of dogs but this statistic is probably changing with the advent of newer flea-control products.

The skin of normal dogs is populated with small numbers of *Micrococcus*, alpha-hemolytic streptococci, *Propionibacterium acnes*, *Acinetobacter* and *Staphylococcus* spp. *S. intermedius* can frequently be isolated from the hair coat of normal dogs. It has been postulated that this might serve as the reservoir for infectious organisms of the skin. *S. intermedius* is involved in approximately 90% of canine bacterial pyodermas.

Approximately 80 percent of allergic dogs will have a secondary bacterial infection at the time of diagnosis. Canine pyoderma is caused almost exclusively by *Staphylococcus intermedius* (Scott *et al.,* 2001). However, the increasing prevalence of *Staphylococcus aureus* infections and the emergence of a new species of *Staphylococcus schleiferi* force the veterinary community to become more vigilant to prevent zoonosis.

Staphylococcus intermedius was first reported in 1976 (Hajek, 1976). It is almost exclusively pathogenic in dogs; however, it has been recovered from numerous species including humans and cats (Crossley and Archer, 1997 and Igimi *et al.,* 1994). The organism is a normal inhabitant of canine skin; however, in certain diseases, such as atopy, the epidermis demonstrates an increased binding affinity allowing more organisms to colonize the skin. The additional changes in sebaceous gland secretion, apocrine gland secretion, vasodilatation and subsequent skin temperature increases, all contribute to the development of secondary Staphylococcus intermedius pyoderma. The organism may modulate the immune system by acting as a super-antigen and can produce numerous toxins and readily demonstrates antibiotic resistance (Crossley and Archer, 1997). Documented cases of zoonosis are rare and limited to a couple of case reports (Tanner *et al.,* 2000).

Staphylococcus aureus is the main pathogen in humans but has been recovered from several species including dogs and cats (Crossley and Archer, 1997). *Staphylococcus aureus* is highly pathogenic and able to rapidly develop multiple antibiotic resistance through numerous mechanisms. Methicillin -resistant *Staphylococcus aureus* infections are the source of major crisis for the human medical community. Cases of reverse zoonosis are rare and often involve the pets of a health worker who was exposed to *Staphylococcus aureus* through the owner's direct contact with infected patients in medical facilities (Manian, 2003).

Staphylococcus schleiferi (coagulase negative) was first identified in 1988 and was named according to the German microbiologist Carl Heinz Schleiferi (Freney *et al.,* 1988). The first case information regarding *Staphylococcus schleiferi* infections in humans was reported in 1989 (Jean Pierre *et al.,* 1989). There growing evidence to suggest that Staphylococcus schleiferi is a pathogenic organism with a propensity for community based nosocomial infections. Humans demonstrated *Staphylo-coccus schleiferi* carriage in the preaxillary area. The first cases of *Staphylococcus schleiferi* skin infections were reported in the United States in canine patients in 2002 (Frank *et al.,* 2003). The organism demonstrated multiple antibacterial resistances including methicillin-resistance. Additional studies have isolated the organism in the ears of normal dogs as well as dogs with acute and chronic otitis. Documented cases of zoonosis and reverse zoonosis have not been reported; however, if both humans and dogs have the ability to serve as reservoir species for this opportunistic pathogen, then the implications for contagion, zoonosis and reverse zoonosis are considerable. *Staphylococcus schleiferi* is a unique species of *Staphylococcus* that exhibits pathogenicity, dual species carriage and the ability to cause serious infection in both humans and dogs.

Bacterial pyodermas are usually classified based on the depth of involvement from surface to cellulitis. A surface infection or colonization involves the stratum corneum. These include such diseases as intertrigo (skin-fold pyoderma) and pyotraumatic dermatitis ("hot spots"). Superficial pyoderma is the most common canine bacterial skin disease. The infection involves the epidermis below the stratum corneum and/or extends into the hair follicle. Impetigo, superficial folliculitis, and superficial spreading pyoderma are examples of this type of infection. A deep pyoderma occurs when the infection extends through the epidermis or hair follicle and involves a pyogenic inflammation of the dermis or subcutis. Often times there are evidence of rupture of the hair follicle. In addition to *Staphylococcus*, gram-negative bacteria such as *Proteus, Pseudomonas,* or *Escheria coli* can often be cultured. If an antibiotic is chosen that is effective against the *S. intermedius,* in most cases the other organisms are also eradicated.

Recurrent pyoderma is defined as a bacterial infection of the skin that responds entirely to appropriate systemic and/or topical therapy but recurs within a short period of cessation of therapy, usually within a month.

The presence of bacterial pyoderma is always secondary to an underlying cause. It is the obligation of the veterinarian to try to determine the precipitating cause and to treat or eliminate it in an effort to prevent re-infections. Unfortunately, sometimes we are just not clever enough to determine that cause.

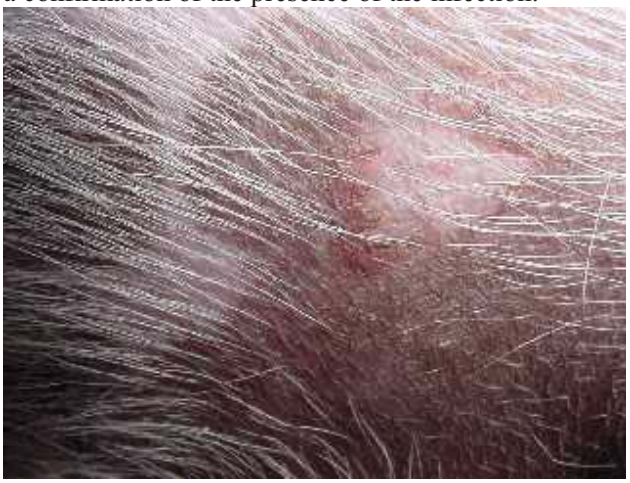
Almost every dermatologic disease of the dog can have bacterial pyoderma as a component. Allergic or pruritic diseases such as flea allergy dermatitis, food allergy, or atopic dermatitis are often complicated by secondary *Staphylococcal* infections. Diseases of cornification such as congenital or idiopathic "seborrhea", icthyosis, and sebaceous adenitis alter the normal surface microenvironment and allow the overgrowth of bacteria. Endocrine disorders including hypothyroidism, hyperadr-enocorticism (either iatrogenic or naturally-occurring), and abnormalities of the sex hormones cause changes in the cornified layer and will often be complicated by secondary bacterial pyoderma. Genodermatoses that cause cutaneous anatomic abnormalities such as color dilution alopecia, black hair follicular dysplasia, and follicular dysplasia often require long term therapy with antibiotics as a part of their management. Parasitic diseases of the dog including demodicosis, scabies, and *Cheyletiella* infestations and other infectious diseases of the skin such as dermatophytosis, deep fungal infections, and *Malassezia* dermatitis very often have colonization or infection with *S. intermedius* as a component.

Staphylococcus intermedius skin infection (pyoderma) may be perpetuated in some dogs by a hypersensitivity reaction to staphylococcal organisms. Dogs with idiopathic superficial or deep recurrent staphylococcal skin infections may thus have quantitative differences in serum antistaphylococcal IgE antibodies compared with healthy dogs. To test this hypothesis, antistaphylococcal IgG and IgE antibodies were measured by ELISA in groups of dogs with idiopathic recurrent pyoderma, recurrent pyoderma secondary to atopic disease, non-recurrent pyoderma, and in healthy dogs. All groups of dogs with prior staphylococcal skin infection had significantly higher mean serum antistaphylococcal IgG levels than healthy dogs ($P < 0.05$). Dogs with recurrent deep pyoderma had the highest mean levels of antistaphylococcal IgG. Dogs with idiopathic recurrent superficial pyoderma and those with recurrent pyoderma secondary to atopy had significantly ($P < 0.05$) higher mean levels of serum antistaphylococcal IgE than other groups tested. It is concluded from these findings that S. intermedius can behave as an allergen in some dogs and elicit an IgE response. These results support the concept that bacterial hypersensitivity may be responsible for initiating or perpetuating skin lesions in these animals.

In some dogs we feel that immunologic incompetence is the reason that there is a pyoderma or recurrent pyoderma. There are only crude tests available to veterinarians to use to access the immune system of the dog. Serum immunoglobulin quantitation and the total lymphocyte count are the only tests that available to private practitioners. Theoretically, an absolute neutrophilia with a lymphocyte count of at least 1000 cells/µl should be seen in immunologically normal dogs with bacterial pyoderma. Identification and quantification of subsets of lymphocytes using markers (CD3+, CD4+, CD8+, etc), neutrophil function tests, and in vitro lymphocyte blastogenesis are tests performed in some universities and in research situations. Very young or very old dogs, animals with a neoplastic disease, or those who are receiving immunosuppressive drug therapy (especially prednisone) are susceptible to bacterial skin infections secondary to immunoincompetence.

Bacterial pyoderma can be diagnosed in several ways. During the examination,

characteristic clinical lesions can be seen which are highly suggestive of a diagnosis. Erythema, alopecia, pustules, papules, crusts, and epidermal collarettes (raised borders of detaching stratum corneum present at the margins of circular areas of inflammation) are commonly seen on the skin of after a clinical cure has been seen or 2 weeks ning tract. The identification of large cocci, usually in pairs, is highly suggestive of pyoderma caused by *S. intermedius*. The presence of rods is indicative of a mixed infection (with gram-negative organisms). Many times these bacteria will be seen within the cytoplasm of a neutrophil showing that they are not just contaminants. A skin biopsy is another valuable tool for the diagnosis of pyoderma. Many veterinarians use the dog's response to the use of oral antibiotics as a confirmation of the presence of the infection.



Probable-staph-pyoderma

Treating Pyoderma

The depth of the infection can have a negative impact on successful drug therapy. Oral, systemic, antibiotics are the first choice for the treatment of canine bacterial pyoderma. The choice of an appropriate antibiotic can be made empirically or based on results of a culture and susceptibility test. A culture and susceptibility test is usually recommended in those cases of bacterial pyoderma that have made no clinical improvement after 2 weeks of treatment with an antibiotic that is usually effective against *Staphylococcal* infections. A culture and susceptibility is helpful if there is deep pyoderma, for infections caused by gram-negative organisms, or if the animal has been treated previously with several different antibiotics. It is important that the veterinarian prescribe an appropriate dose of an antibiotic for an appropriate period of time (minimum of 3 weeks; may need to extend for up to 8 weeks for deep infections). In every case, oral antibiotic therapy should be continued for at least 1 week after a clinical cure has been seen or 2 weeks after the discontinuation of oral prednisone.

The susceptibility of an organism to a drug is described in terms of the minimum inhibitory concentration (MIC) of drug. Drug efficacy is dependent upon drug concentrations reaching the MIC at the site of infection and will be enhanced if concentrations at the site are several magnitudes above the MIC. However, the concern for drug safety prevents indiscriminate increases in dosage to increase the drug plasma concentration. The breakpoint MIC of a drug is the highest concentration that can be safely attained in blood using the recommended (labeled) dosing regimen. Organisms are considered susceptible to a drug if the MIC is below the breakpoint MIC. Organisms characterized by intermediate susceptibility are inhibited at concentrations that approach breakpoint. The MIC for a resistant organism surpasses the breakpoint MIC of the drug, and for that drug the risk of toxicity outweighs the potential benefits of therapy.

The 3 essential components of successful treatment of secondary bacterial pyoderma in dogs include the proper selection of antibiotic, treatment with appropriate dose and duration of antibiotic therapy, and the identification and control of all underlying dermatoses (allergies, endocrinopathies, autoimmune diseases, keratinization defects etc.). Bacterial pyoderma is a common cause of pruritus. For this reason, it is important to determine the cause of a patient's pruritus (pyoderma, yeast dermatitis, allergies) rather than treating the itch with steroids. Topical therapy is also of great benefit to help mechanically remove organisms as well as providing a non-antibiotic method of killing the organisms. Shampoos containing chlorhexadine or benzyl peroxide are highly effective at reducing the superficial colonization of *Staphylococcus*. The overwhelming majority of first time bacterial pyodermas in dogs are caused by *Staphylococcus intermedius*. This organism has demonstrated consistent sensitivity patterns making empiric antibiotic selection possible. Amoxicillin with clavulanic acid and cephalexin are commonly used antibiotics that demonstrate good efficacy (Carlotti and Ovaert, 1988). Clindamycin, potentiated sulfur drugs, and erythromycin also demonstrate consistency good efficacy. The

antibiotic selected should be used for a minimum of 21 days to eliminate the infection and allow the normal antimicrobial function of the skin to return to a more normal and effective function. If inappropriately low doses of antibiotic are used or if the duration of therapy is too short, the populations of *Staphylococci* are altered so that antibacterial resistant strains are selected leading to chronic/recurrent infections making additional treatment even more difficult. For recurrent, resistant *Staphylococcus* cases, fluoroquinolones are often selected for their perceived increased potency; however, resistance may develop especially with inappropriately low doses or short duration. Unfortunately, the cost of fluoroquinolone therapy when dosed appropriately is very high. If the patient is on seemingly appropriate doses of antibiotic for an appropriate duration (minimum of 21 days) without clinical improvement in the papular crusting alopecic lesions, a resistant Staphylococcus infection should be suspected. The percentage of excellent responses to therapy, duration of therapy, and percentage of relapses after a 3-month post treatment follow-up period following treatment with tylosin compare favorably with results reported with other antibiotics commonly recommended for the treatment of staphylococcal pyoderma in dogs (Cannon, RW, 1976; Angarano and MacDonald, 1989; Guaguere and Marc, 1989; Paradis *et al.,* 1990; Scott *et al.,* 1993; Frank and Kunkle, 1993 and Prost and Arti, 1993). This is a constant problem when dealing with manufacturers' recommendations and the actual duration of treatment needed to eliminate staphylococcal infection in the skin of dogs (Scott *et al.,* 2001; Scott *et al.,* 1994; Paradis *et al.,* 1990 and Scott *et al.,* 1993). Other dermatoses that can mimic pyoderma include Demodicosis, Dermatophytosis, Scabies and Pemphigus. Once these differentials have been eliminated, the skin lesions should be cultured and antibiotic sensitivity profile performed to help guide antimicrobial selection.

Secondary bacterial infections are associated with abnormal function of the skin's natural antimicrobial defenses (sebum, pH, epidermal turnover, etc.) caused by the underlying skin disease. Allergies (environmental allergies, food allergy, and flea allergy) and endocrinopathies (hypothyroidism and Cushing's disease) are the most common primary diseases associated with secondary bacterial pyoderma. Other possible underlying dermatoses include autoimmune skin disease and keratinization defects. Aggressive diagnostic workups should be used to explore the endocrine status and identify any allergic disease. When the underlying dermatoses are successfully controlled, the normal structures of the skin return to the natural antimicrobial functionality and the recurrent nature of the infection is eliminated. If the primary underlying dermatoses cannot be identified or controlled, the patient will likely continue to develop secondary bacterial infections and likely establish multi drug resistant Staphylococcus pyoderma.

For recurrent skin infections, extended regimens of antibiotic therapy can be tried. These are to be used once the pyoderma has been brought under control. They do raise the potential of inducing or selecting resistant strains of bacteria. There is no "best" regimen to use. Some dermatologists recommend the use of an appropriate antibiotic for one week followed by one week without the drug. Eventually the length of time without antibiotics may be extended. Other veterinarians have recommended using antibiotics for 2 to 4 days per week at the full dose or even every other day. A third protocol involves a maintenance recommendation of once daily dosing. If this is successful then the dose of the antibiotic can be lowered. As a general rule, though, for the use of oral antibiotics to prevent recurrent pyoderma, the dose of drug should not be lowered or the interval without antibiotics should not be extended until you have waited for twice the length of time expected for the pyoderma to recur (i.e. if the animal can go for no more than 2 weeks without antibiotics before recurrence, wait a minimum of 4 weeks using a once daily dose before any further adjustments).

Topical antibacterial therapy is an integral part of the initial treatment of a bacterial pyoderma and is also useful in preventing reoccurrence of the condition. The owner is usually instructed to shampoo the dog as often as the dog needs it and as often as they are able. Shampoos containing benzoyl peroxide, chlorhexadine, triclosan, or ethyl lactate are generally prescribed and owners are advised to let the shampoo contact the dog for a minimum of 10 minutes before rinsing. Use of a final leave-on rinse after bathing will assure that the active ingredient remains in contact with the skin and haircoat. Antibiotic creams or ointments are useful for spot treatment. Mupirocin is an excellent topical antibiotic. Vets should try to avoid using products that contain corticosteroids.

Immunomodulatory therapy using products such as Staphage Lysate, Immunoregulin (*Propionibacterium acnes* bacterin), or Levamisol may alter lymphocyte and phagocyte immune

function by modifying the intracellular cyclic nucleotides of leukocytes. Cimetidine has also been proposed as an immunomodulatory drug because lymphocytes have H2 receptors that theoretically act to modulate cytokine production.

The zoonotic potential of *Staphylococcus intermedius, Staphylococcus aureus* and *Staphylococcus schleiferi* is becoming increasingly concerning. All three species have the potential to cause disease in both dogs and humans. This is propelling the veterinary community into a situation that is very similar to our human physician counterparts in their attempts to control *Staphylococcus aureus* and its multidrug resistant strains. The days of indiscriminate use of antibiotics in veterinary dermatology are rapidly coming to an end. It is simply a matter of time before sufficient cases of zoonotic infections are documented and publicized causing a fundamental and drastic reform in the veterinary profession. Soon, the most common skin disease in dogs may be regarded as a zoonotic infection with significant human health implications. This will impact almost every aspect of pet ownership and veterinary care; antibiotic use, isolation of infected patients, canine hospital visitation, guide dog access to public facilities, and owner liability for contagious zoonotic infections.

Key Features of Canine Pyoderma

- Pyoderma is the most common skin disease in dogs.
- Assume everything has pyoderma until you rule it out.
- Use the highest antibiotics dose possible to avoid resistance.
- Always treat for a minimum of 21 days.
- Secondary pyoderma can and usually does complicate every other primary skin disorder.
- Find and control the primary/underlying disease.
- Allergies and endocrinopathies are the most common primary/underlying diseases.

Monitor for resistant infection, especially if the infection is not improving.

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