Skin infections with bacteria (pyoderma) or yeast (*Malassezia dermatitis*) often are found in dogs secondary to other diseases such as seborrhea, endocrine diseases and allergic diseases. Many of these cases have abnormalities in skin barrier function or desquamation and even when the primary disease is controlled if this defect is not corrected the dog may still be prone to recurrent infections though episodes may be less severe or less frequent. In chronic or recurrent infections other factors may develop which are referred to as perpetuating factors. The most common bacteria to cause skin infections in dogs is *Staphylococcus pseudintermedius* which used to be called *Staph intermedius*. However in some cases other bacteria such as *Enterococcus*, *Corynebacteria*, *E. coli*, and *Pseudomonas* may be pathogenic. The diagnosis of a skin infection is simple if the lesions are recognized and sampled for cytology. Success treating skin infections requires appropriate antimicrobial therapy and this has been the main emphasis of veterinarians for many years. Topical therapy though considered helpful can actually be essential to successful therapy and in some cases with resistant bacteria such as methicillin resistant Staph (MRS) may become the main or sole method to eliminate the infection. In addition successful long term management will require that underlying primary diseases are identified and managed and predisposing factors are eliminated or controlled. Additionally any pathologic changes in the normal anatomy or physiology of the skin that occur because of the inflammation from the infection need to be reversed or controlled. If any part of these components are not addressed then more antimicrobial therapy will be required and success will be limited.

Pyoderma is a common skin disorder in small animal practice. Yet it remains a frustrating disorder as *Staphylococcus* tends to be an opportunist which takes advantage of compromised skin. Sorting out the diseases which predispose to pyoderma is a critical feature of infection management, yet many pyodermas become recurrent. We often consider underlying diseases but we may not consider features such as owner and patient compliance, suboptimal dosing, incorrect choice of antibiotic, and an overall reduction in the use of topical therapy. The age of methicillin resistance is now with us in veterinary medicine and we are struggling with how best to deal with this phenomenon which has plagued physicians for some time. The increase in prevalence of multi-drug resistant bacteria is sadly coupled with decreased antibiotic drug discovery and development, so veterinarians and physicians are coming back to old antibiotics for treatment of resistant bacteria as well as nonantibiotic topical therapy, which is particularly suited for dogs with pyoderma. It is important to realize that the best protection against spread of MRS in both humans and dogs is hygiene. Handwashing, the use of alcohol-based hand cleaners, and environmental disinfection do more to reduce the spread of infection than antibiotics can.
What Bugs Cause Pyoderma in Dogs?

The major canine skin pathogen is *S. pseudintermedius*; however, *S. schleiferi*, *S. aureus*, and *Pseudomonas aeruginosa* also can be identified from canine patients with pyoderma. For many years, the canine pathogen was referred to as *Staphylococcus intermedius*. This bacterium has undergone a reclassification, based on the use of newer molecular techniques to identify and characterize genetic diversity among *S. intermedius* isolates. It has been concluded that the bacteria isolated from dogs come from the *S. pseudintermedius* phyotype of the *S. intermedius* group. *S. pseudintermedius* binds preferentially to canine skin cells compared to human or feline skin cells, and this binding is enhanced when the corneocytes are derived from atopic dogs. While not considered as virulent as the human pathogen *S. aureus*, *S. pseudintermedius* shares many of its virulent characteristics, including enzyme and toxin production, ability to adhere to matrix adhesive proteins, and ability to form biofilms. Each of these features contributes to the ability of the bacterium to colonize and invade the skin. *S. schleiferi* was first identified from human clinical specimens in 1988. It has now been identified as the cause of pyoderma and otitis externa in dogs as well. *S. aureus*, the human pathogen, has been identified in a low percentage of dogs; this bacterium has received a great deal of attention because of the interest in methicillin resistance in humans and the possible zoonotic role that pets might play. Last, while not common, *Pseudomonas aeruginosa* can also be identified from the skin of dogs, particularly in lip fold pyodermas and post-grooming folliculitis.

**Treatment failure** differs from chronic recurrence in that clinical pyoderma does not fully resolve with therapy. In these cases, patients may not improve at all, partially respond but not fully resolve, or respond but relapse rapidly (<7 days) after finishing therapy. For chronic recurring pyoderma, veterinarians should 1) manage the current infection and 2) manage the underlying disease. In the case of treatment failure, veterinarians must determine the reason for failure and address this reason aggressively, until clinical resolution is achieved. Investigating underlying disease is still important. The top 5 reasons for treatment failure are 1) non-compliance, 2) wrong antibiotic, 3) wrong dose or duration, 4) antibiotic resistance, and 5) wasn't pyoderma.

**Reason #1. Poor Client Compliance: How Dermatologists Work to Overcome Poor Compliance**

According to the National Pharmaceutical Council, one-third of written prescriptions are never filled; and of the prescriptions filled, less than 50% are taken correctly. Veterinarians have the distinct advantage of dispense medication at the time of diagnosis, ensuring that the client at least has the antibiotic; however, we rely on the client to give the medication. Common reasons for non-compliance once out the door include difficulty giving pill, difficult schedule, and general forgetfulness. Typically owners are highly motivated during initial phases of treatment when the patient demonstrates active disease, but motivation wanes rapidly if there are adverse reactions, such as vomiting, or progressive difficulty giving medication. Motivation may also wane as the condition appears to resolve, resulting in early cessation of therapy prior to microbial resolution. Veterinarians should do everything reasonable to reduce barriers to full compliance. First, dispense full amount of antibiotic to complete the full course at the initial visit. Avoid writing prescriptions to be filled at the owner's discretion or dispensing fewer pills and asking owner to
return for refills. Use simples schedule; once is superior to twice or three times daily therapy. Cefpodoxime and Ormetoprim sulfadimethoxine are once daily choices appropriate for Staphylococcal pyoderma. Provide the easiest method to deliver the medication (i.e., suspension or injection if can't give pills). One of the best methods for overcoming non-compliance with oral medications is to remove the option of missed doses by administering the long acting injectable cephalosporin, cefovecin. With a single injection, the veterinarian effectively prescribes, dispenses and administers the appropriate antibiotic at the appropriate dose for the next 14 days, without requiring any effort by the owner.

Reason #2. Wrong Antibiotic: How Dermatologist Choose Antibiotics for Staphylococcal Pyoderma

The goal of therapy is resolution of clinical disease. Selection criteria for antibiotics is based on (1) Safety: minimize risk to patient, (2) Efficacy: which antibiotic has the highest probability of success, and 3) Cost. Safety first. Gentamicin maybe inexpensive and very effective against most *Staphylococcus*, but because of potential nephrotoxicity and costs associated with laboratory monitoring, aminoglycosides are rarely chosen to manage pyoderma except in unusual circumstances. Veterinarians should be familiar with common side-effects, adverse events, drug interactions, and other factors affecting safety of antibiotics they use.

Since most antibiotics routinely used for Staphylococcal pyoderma are safe, the main criterion for selection is efficacy. Efficacy is determined by spectrum of activity, achievable concentrations in target organ, and ease of use. With the exception of methicillin-resistant *Staphylococcus* sp, fewer than 5% of clinical veterinary *Staphylococcus* isolates demonstrated resistance against cephalosporins, amoxicillin/clavulanate, oxacillin, and fluoroquinolones; making them all good empirical choices with predictable susceptibility. Other antibiotics demonstrated variable resistance, clindamycin, Lincocin, erythromycin, doxycycline, potentiated sulfa, and chloramphenicol should be reserved for cases with culture and antimicrobial susceptibility profiles for each individual case, rather than as empirical first choice antibiotics. Bad choices based on predicted susceptibility include penicillin, ampicillin, amoxicillin, and tetracycline, all demonstrating resistance in as high as 83% of isolates. Most of the antibiotics listed above achieve good tissue concentrations in the skin and this is reflected in observed clinical efficacy. Most cephalosporins are eliminated by kidneys, with limited hepatic elimination.

Cephalosporins have "time-dependent" antimicrobial action; differences in efficacy duration of concentration above minimum inhibitory concentration (MIC). In general cephalosporins are eliminated by renal tubular secretion of the free-drug fraction; the higher the degree of protein binding, the less free-drug, the longer the half-life. The longer the half-life the longer the dosing interval and the longer the period of time active drug concentration exceeds the MIC of the target bacteria. In dogs, Cefadroxil has the lowest plasma protein binding (11.7%) and therefore the shortest half-life of 2 hours. Cephalexin is 14–26% protein bound with a half-life of 2.4–4.7 hours. Cefpodoxime is more highly protein bound 82–91%and has a half-life of 6–10 hours, permitting once daily dosing. The unbound (active) fraction of cefpodoxime in interstitial fluid remains above MIC90 for *E. coli* and *Staphylococcus* for 24 hours. Cefovecin has the highest level of protein binding at 98.5%, resulting in a half life of 133 hours, and a dosing interval of 14
days. Because dosing interval influence client compliance; all other factors being equal, ease of use is the final criteria for efficacy. Cost is a consideration, but should not the first criteria for antibiotic selection. Choosing based on cost can create a false economy, as an inexpensive but less effective antibiotic may require a longer duration, or extra costs of culture and a new course of antibiotics. Clients want resolution; always recommend a treatment course that has the highest probability of success at the least risk to the patient. Have alternatives ready, discuss the actual cost of the entire treatment course, not cost per pill. Do the savings justify trade-off in efficacy for client.

All factors considered, the cephalosporin class is safe, effective, encounters low levels of resistance, and have easy to administer options in oral and injectable form. Except for cases of methicillin-resistant *Staphylococcus*, cephalosporins are the first choice for managing canine Staphylococcal pyoderma.

**#3a. Wrong Dose: How Dermatologists Calculate Appropriate Dosing**

Calculating appropriate dosage depends on the class of antibiotics. Antibiotics can be classified as "time-dependent" or "dose-dependent". In "time-dependent" classes, the length of time the tissue level remains above MIC is most critical; spiking the dose up higher does not result in more rapid or more effective killing, just more expense and more risk of side-effects. Penicillins and Cephalosporins are "time-dependent." Half-life, dosing interval and period above MIC are most important. Therefore whenever possible select the cephalosporin with the longest half-life. When calculating the dosage from a range, always round up to the next most convenient dose rather than rounding down. For example, if the dosage range for cefpodoxime is 5.0–10.0 mg/kg, for a patient weighing 49 lbs (22.3kg) the lowest acceptable dose is 112mg; always round up to 150mg (one and one-half 100mg tablets) or 200mg (one 200mg tablet), never round down to 100mg.

The bactericidal effect of "dose-dependent" antibiotics is based on how high the concentration is above MIC and is less influenced by how long the drug remains above MIC. Fluoroquinolones and aminoglycosides are the classic "dose-dependent" antibiotics. Dosing around MIC or slightly above is a big mistake, not only does this reduce probability of success, but dosing in this range produces selective pressures that result in higher rates of mutation and rapid selection for resistant strains. Microbiologists refer to this as the "mutant selection window." Ideally fluoroquinolones are dosed at levels that exceed the "mutant prevention concentration," the effective level above selection for mutations and resistant strains. In general, for fluoroquinolones, push the dose as high as the patient and owner can tolerate and give it once a day.

**#3b. Wrong Duration: Why Dermatologist Treat for 30 Days**

Providing antibiotics for too short a duration is as undesirable as providing too low a dosage. Clients will always give antibiotics for less than or equal to the duration we prescribe. Clients may stop too soon because the medication is challenging to give, adverse side-effects, the infection cleared up too fast, the infection didn't clear up fast enough, or general poor
communication. Avoid giving clients one more reason to stop too soon—running out of medication. Always prescribe for as long as you intend the owner to give the medication.

How long should veterinarians treat canine Staphylococcal pyoderma? Deep pyoderma responds more slowly and requires longer periods to achieve clinical and microbiologic resolution, generally 6 weeks. During therapy the skin may appear normal long before the infection has resolved. Foci of *Staphylococcus* may be sequestered in a granuloma below the now normal appearing epidermis; stopping antibiotic too soon could result in rapid recurrence. The same is true with superficial pyoderma, but for slightly different reasons. Superficial pyoderma usually occurs from colonization of an abnormal epidermis than has been altered by underlying disease. Primary disease disrupts the normal epidermal barrier, exposing more binding sites for *Staphylococcus*, resulting in higher local colonization. Exposure of higher concentrations of bacterial antigens across the abnormal epidermal barrier promotes greater inflammatory response, further disruption, increased colonization and clinical pyoderma. Systemic and topical antibiotics rapidly reduce bacteria, but do not restore the disrupted epidermal barrier. Healing of the epidermis takes time. Until then affected areas are prone to recolonization by remaining *Staphylococcus*. Antimicrobial therapy should be continued beyond apparent clinical resolution, until the barrier function has been restored. In general the epidermis takes 21 days to turnover from the deepest basal layer to the superficial stratum corneum. If the underlying disease continues longer courses antimicrobial therapy may be indicated.

Another reason to treat beyond clinical resolution is that the skin will look better before the number of *Staphylococcus* is reduced to "normal" carriage levels. Somewhere between normal and severe pyoderma there is a level of colonization that is required to induce clinical signs of pyoderma; below that level the patient has higher than normal colonization but appears clinically normal. As pyoderma is treated, the number of bacteria falls rapidly and the skin begins to heal. If therapy is discontinued when the skin appears normal, but still is colonized greater than normal carriage rates, then recolonization is more rapid and the interval between clinical infections will be shorter. As a general rule, treat all pyoderma for 7-10 days beyond clinical resolution to allow for healing of the epidermal barrier and prevent rapid recolonization by remaining *Staphylococcus*.

#4. Antibiotic Resistance: What is the Deal with Methicillin-Resistant *Staphylococcus*?

Methicillin is a semi-synthetic penicillin introduced in 1959 in response to the rise of penicillin-resistant "super-bugs." Like cephalosporins, semi-synthetic penicillins are resistant to degradation by penicillinase enzymes. Methicillin-resistant *Staphylococcus* species (MRSS) alter the target of antibiotic action: penicillin-binding protein (PBP) in the cell wall. The altered PBP has low affinity for all Beta-Lactam antibiotics, rendering high level resistance to penicillins, augmented penicillins, cephalosporins, carbens, and cephems. In human medicine, Methicillin-resistant *Staphylococcus aureus* is the most common nosocomial infection worldwide, and a major cause of morbidity and mortality. Canine patients can be colonized by methicillin-resistant strains of *S. intermedius*, *S. aureus*, and *S. Schleiferi*. The prevalence of MRSS in veterinary patients is highly variable between geographic regions. In a retrospective survey of staphylococcal isolates at the University of Pennsylvania (2003-2004), 569 dogs/cats/birds/rabbits had positive culture for *Staphylococcus* sp. (336 *S. intermedius*, 122 *S.
A staggering 145 of 569 Staphylococcal infected patients carried MRSS (25.5%): 17% of S. intermedius, 40% of S. Schleiferi, 35% of S. aureus. Methicillin-resistance should be suspected in any patient with pyoderma, cytologic evidence of coccoid bacteria and poor response to appropriate therapy. Treatment failure without an obvious cause is an indication for culture and sensitivity.

#5. Not Pyoderma: Recognizing Diseases that Mimic Pyoderma

Occasionally, pyoderma does not respond to antibiotics because the skin condition wasn't really pyoderma to begin with. Several skin diseases mimic pyoderma, including demodicosis, dermatophytosis, Malassezia dermatitis, pemphigus foliaceus, erythema multiforme, actinic dermatosis, and epitheliotropic T-cell lymphoma. Whenever a case is not responding as expected, reassess diagnosis by repeating cytology. If no bacteria can be identified, then additional diagnostic tests are indicated: skin scrape, dermatophyte culture, and biopsy.

Dermatologist Secret Weapon Against Recurring Pyoderma: Frequent Bathing

Topical antimicrobial shampoo is not just for treating active pyoderma, but also aids in reducing recurrence. Frequent bathing accomplishes multiple, high value goals. Continued application of antimicrobial shampoo to the skin suppresses bacterial re-colonization prior to development of clinically significant infection. Additionally, emollients and other ingredients, such as phytosphingosine, can help normalize and restore a disrupted epidermal barrier. Finally, for dogs with atopic dermatitis, bathing assists removal of allergens and irritants from the skin. Humans inhale their allergens, but for dogs, evidence points towards absorption of allergens across the skin. Conditioners that contain emollients and antimicrobials are additionally beneficial. Clients are more likely to continue to use a product that is appealing to them; therefore, medicated shampoos with superior aesthetic characteristics improve client compliance. Proper instructions to clients are essential. Since 5 minutes contact time is necessary to maximize antiseptic benefit, many veterinarians request owners apply the shampoo for 10 minutes before rinsing. A different approach is to direct owners to apply shampoo to the problem areas first, move on to the rest of the body, and rinse problem areas last. Even the most impatient owner will achieve maximal contact time on areas of active infection. Without specific instruction owners will typically start on the dorsum, which is rarely the most affected area. After pyoderma is resolved, owners should continue to focus on previous areas of infection, as these are the most likely areas to recolonize.

Bacterial pyoderma in dogs is considered a secondary disease and when it recurs, we try to determine whether underlying causes exist. The major considerations for recurrent pyoderma include parasitic diseases such as demodicosis or scabies, allergic skin disease, endocrinopathies such as hypothyroidism, hyperadrenocorticism or diabetes mellitus, and disorders of keratinization. However, for some dogs we cannot find an underlying cause.

Malassezia pachydermatis (Pityrosporon canis) is a lipophilic yeast found on the skin and ear canal of normal dogs and many other species of animals, including birds. It is a normal resident and an opportunistic pathogen.
Factors that may lead to overgrowth of yeast and consequent dermatitis or otitis are not all clearly defined, but some correlations have been drawn from a series of retrospective studies. Malassezia is a common secondary infection, with or without concomitant bacterial overgrowth, in some dogs with allergies or keratinization defects. Malassezia produce factors that induce inflammation and even may induce allergic responses or increase allergic responses to other substances.

There is also some evidence that a hypersensitivity reaction to the yeast may exist in some dogs. Thus some animals may show extreme pruritus and other signs when relatively few organisms are detectable. Recent work has shown that atopic dogs with skin disease had an Ig-E mediated type I hypersensitivity reaction to intracellular protein extracts of M. pachydermatis, whereas normal, nonatopic dogs did not.

Certain breeds have been reported to be at-risk for developing clinical Malassezia dermatitis. These include the West Highland white terrier, Springer spaniel, German shepherd, cocker spaniel, silky terrier, Australian terrier, Maltese, Chihuahua, poodle, Shetland sheepdog, Lhaso apso, and dachshund. This may be due to deficient T-lymphocyte responses to the yeast. In addition, many of those same breeds are at risk for atopic dermatitis.

Clinical Signs

Malassezia dermatitis usually presents with pruritus and erythema of infected areas. There is a musty or yeasty odor and there may be visible greasy or hyperhidrotic skin changes. The skin often becomes lichenified in affected areas. Otitis externa and pododermatitis are the most common regional dermatoses. Typical clinical signs include persistent head shaking, excessive foot licking, or waxy paronychia. Exudate in the ears is often moist and brown in color. Other areas of involvement include lip, muzzle, axillae, periocular area, chin, inguinal area, antebrahial folds, hock and the skin over the ventral neck. Lesions may be focal, multifocal, or generalized. Lesions may be sharply demarcated with adjacent skin remaining non-inflamed and haired. Alopecic greasy lichenified lesions gradually expand peripherally to involve previously normal skin.

Diagnosis

Cytology is the best way to identify yeast overgrowth. The type of specimen to be obtained depends on the condition of the skin surface that is to be sampled. Skin cytology should be routine minimum data base in all dermatitis cases. Samples should be taken from skin folds, interdigital areas and ears of dogs with skin disease. Hair should be gently clipped out of the way, without disturbing the surface of the skin.

For greasy hyperkeratotic lesions, a clean glass slide may be pressed against the skin. This should leave an impression that resembles a fingerprint on clean glass. Alternatively, a cotton swab can be rubbed on the skin surface and rolled onto the slide. If this does not provide a smear of skin cells, then a technique employing adhesive tape or slides is needed. I recommend the use of double-sticky clear acetate tape or the purchase of Durotak® (Delasco - (800) 831-6273) slides with clear adhesive already applied to the surface. To use the tape, one can carefully apply
a strip of tape onto a clean glass slide, taking care to leave minimal fingerprint on the tape. This can then be pressed against the skin surface, without any rolling or shearing motion, for 10–15 seconds. When the slide is peeled away, one should be able to observe the imprint of the skin surface cells. The Durotak® slide is used in a similar fashion.

The slide with tape attached or Durotak® slide is then stained in a dip-in type cellular stain, as used for hematology. These are then carefully dried with a slide dryer or air blower and then examined microscopically.

The slide is first inspected under low power (40–100X) for the presence of a good cellular layer. Then 1000X–oil immersion, is used to inspect for micro-organisms. Several fields should be examined and the range of numbers of yeast and bacterial organisms should be recorded. In our practice, 0 - 1 yeast or coci are recorded on normal skin and above that, abnormal numbers seem to correlate roughly with the severity of the dermatitis. For ear swabs, >10 yeast/OPF is considered abnormal.

Alternatively, sterile swabs or contact plates can be submitted for culture, but unless culture colonies are quantified for you, you should be aware that Malassezia can be cultured from 50% of normal dogs.

**Therapy - Topical treatment** is best accomplished with either 4% chlorhexidine or with imidazole treatments ( clotrimazole, miconazole, ketoconazole or enilconazole). Local disease can be treated with sprays lotions or scrubs. Widespread disease with shampoos or rinses. Topical therapy is warranted in every case of Malassezia dermatitis. Topical products should initially be used two to three times weekly for generalized disease. Oral therapy (ketoconazole - Nizoral®, fluconazole or itraconazole - Sporanox®) is warranted in cases of widespread Malassezia dermatitis. I typically use Ketoconazole in all my cases at 5 to 10 mg/kg daily. Improvement (but not cure) should be noted in 2 weeks. Occasionally this is associated with gastrointestinal upset and in rare cases the dog will develop a toxic hepatopathy. Griseofulvin is not effective against Malassezia. Treatment should be administered until the clinical signs have abated and no yeasts are seen on examination.

A search for an underlying disease or predisposing factors should be undertaken. If an underlying disease is not found or if predisposing factors are not addressed, the Malassezia dermatitis is likely to recur.