What is pruritus? Pruritus is a medical term derived from the Latin prurire meaning itch. 340 years ago Samuel Hafenreffer defined pruritus as “an unpleasant sensation provoking the desire to scratch.” If you feel an itchy sensation, you scratch near it in order to change your perception of that sensation. This is distinctly different from pain – which is an unpleasant sensation provoking the desire to move in the opposite direction and say ouch. There are many clinical diseases that are associated with pruritus; however, many are uncommon and rare for even dermatologists to encounter. When entering an exam room for a 15-20 minute appointment with a patient presented for pruritus it is important to have a coherent, consistent approach to diagnosis and management.

Top 5 essential reasons dogs itch
(1) Atopic Dermatitis
(2) Adverse Food Reaction
(3) Parasite hypersensitivity (Fleas, Sarcoptes, Cheyletiella, or Otodectes)
(4) Malassezia dermatitis
(5) Staphylococcal pyoderma
To make it even easier, (4) Malassezia dermatitis and (5) Staphylococcal pyoderma are almost always complications of (1 – 3) Atopy, Food allergy, or Parasite hypersensitivity.

First Visit
Talk about the 5 major causes for itch, but really focus on parasites, bacteria, and yeast. If the patient has any of these three cause, effective management will have the biggest impact on the patient's quality of life. Indeed, managing only yeast and bacteria can cause a reduction in pruritus as much as 60-70% within two weeks. Granted the bacterial or yeast infections may be secondary to Atopic Dermatitis or Food Allergy, but it really doesn’t matter how good you are at managing Atopic Dermatitis or Food Allergy if you under treat infections. Therefore evaluating for infection and parasites is critical on the first visit, while you lay the ground work for diagnosis and management of primary allergic diseases.

History: None of the top 5 causes for pruritus can be definitively ruled in or out by history, but they can be ordered differently based on history. Age of onset can be useful. Patients less than one year are most likely parasite hypersensitivity or demodicosis, but can rarely have atopy or food. Between 1 and 4 years of age, anything is possible, but atopy is most common. Over 6 years of age, food allergy becomes more likely than atopy. Over 8 years of age start thinking about endocrinopathy with secondary yeast/bacterial overgrowth. Patients with definite seasonality are usually atopy or flea allergy dermatitis. Year round pruritus does not eliminate atopy or flea allergy, but add food allergy. Ask about recent additions to the household, high risk parasite environment, if other animals or people in the house are itching.

Breed: Not particularly useful, but can lead you astray, convincing you that commonly atopic breed, such as French Bulldog or West Highland White Terrier is atopic, when it really just has sarcoptes. Breed predisposition lists are over long, change based on breed popularity, geography, and time. Any dog can be atopic, food allergic, acquire parasites, or become overgrown by Malassezia and/or Staphylococcus. Ignore breed and approach all itchy dogs the same.

Physical Examination: Atopy and food allergy can look identical in the exam room. Resist the temptation to rule in or rule out either based on body distribution sites. Flea allergy tends to affect the back half of the dog worse, with classic signs of alopecia, erythema, papular dermatitis at dorsal tail head, also check the umbilicus; many dogs with flea hypersensitivity have lesions here as well. Sarcoptes is most commonly associated with the pinna, elbows, flank; but not always. Never rule out Sarcoptes based on PE, any dog that itches can be a sarcoptes dog. Cheyletiella usually has heavy dry scale on the dorsum. Check for a pinnal-pedal reflex by rapidly scratching the leading edge of the pinna. If the ipsilateral leg starts stratching, then positive. Positive in majority of sarcoptes dogs, while negative with most other pruritic diseases. A rough tool, but if positive a parasite treatment trial is always indicated. Don’t rule out Sarcoptes based on negative pinnal-pedal reflex.
**Diagnostic testing:** Every patient gets cytology, skin scraping, and a parasite treatment trial.

Perform cytology for bacteria and yeast. Major cause of pruritus complicates diagnosis of allergic disease. May be primary cause of pruritus in patients with hypothyroidism, etc. Skin scrape for *Sarcoptes, Cheyletiella, Demodex*. Negative scraping does not rule out either; however, if you get lucky and find mites then no need to keep going with other diagnostic testing. Parasite treatment trial is an essential part of logical diagnostic plan for pruritus. Author prefers selamectin: every 2 weeks for 3 treatments. Alternatives include Milbemycin at 2mg/kg once weekly for 4 weeks or Ivermectin 300mcg/kg once weekly for 4 weeks. Since any breed can be ivermectin sensitive, always titrate up to full dose. Lime sulfur dip is an excellent and safe miticide, that also happens to help with dermatophytosis, but kinda smelly.

Additional Diagnostics Based on Suspicion
- Dermatophyte Culture: Hey, not a top 5 cause in my clinic, but in your region it may be a common enough diagnosis that you want to perform a screening culture for all patients presenting for pruritus. In many regions of the country this is considered an essential test as part of the “minimum dermatology database.”
- 8-week elimination diet trial followed by challenge feeding may be appropriate on the first visit, if not at least discuss the methodology with owners, so they are prepared if bacteria/yeast/pruritus continues to relapse.
- Antifungal treatment trial. Usually yeast and bacteria are easily found on cytology, however, in some practices yeast is tricky to find consistently. First, work on improving your cytology technique; however, if there is significant odor and no evidence of bacteria on cytology, then you may consider treating for yeast empirically. Recommend Ketoconazole or Fluconazole 5mg/kg once daily for 30 days. Combine with Weekly antiseptic shampoo: Chlorhexidine, Ketoconazole, Miconazole, Benzoyl Peroxide.
- Biopsy is diagnostic test of choice for any pruritic patient that just doesn’t look right. If you have a patient with any sort of unusual appearing lesions associated with pruritus biopsy early. Consider biopsy on later visits, if the patient is not responding or skin disease is progressing in spite of therapy.

**Two or Four Week Recheck**
At Two weeks verify that the bacterial and yeast infection are resolved or resolving. If not responding to therapy and cytologic evidence for bacteria is present, then perform a bacterial culture and sensitivity to screen for methicillin-resistant *Staphylococcus* species. Verify parasite prevention is being used properly. Reinforce good behavior in the owner and encourage them to keep going. If at 4 weeks, bacteria, yeast, and parasites are fully resolved, whatever itch is left over is due to food allergy or atopic dermatitis. Approach the owner about performing an elimination diet trial while continuing topical antiseptic shampoo therapy AND parasite prevention.

**8-week elimination diet trial**
Key components of an effective diet trial is (1) avoidance of any possible trigger for 8-weeks and (2) provocative challenge feeding at the end of the trial. There is no magical property to novel proteins or hydrolyzed diets that reduce itch. These diets are simply providing nutrition while the owner avoids all previously fed proteins. If your patient is allergic to chicken there is no value to the owner feeding a 99% chicken free diet. Additionally the diagnostic value is not in evaluating how much better the patient gets while on the new diet, but rather do they get worse when challenged with the original diet at the end of 8-weeks. Fewer than half of patients with food allergies show any improvement during the first 4 weeks on the new diet, and 20% may still have some level of pruritus as late as 8-weeks. However, when you challenge a patient to the allergen after an 8-week break, they will show relapse of more intense clinical signs. If the patient flares up, congratulations you have diagnosed food allergy, return to test diet. If the patient does not flare up, congratulations you have ruled out food allergy. Clearly this is a simplified discussion of food trials and more detailed discussion is appropriate, please consult texts or other lectures for nuanced approach to diet testing.

**Visit after 8-week diet trial**
If you have ruled out food, eliminated parasites, and managed secondary bacteria and yeast infections, then whatever itch is left over is likely due to Atopic Dermatitis. At this stage continue parasite prevention, antiseptic topical therapy, and focus your attention on both short and long term maintenance for Atopic Disease. This may include corticosteroids for temporary relief of inhumane levels of itch, antihistamines, omega III fatty acids, topical emollient therapy, topical antipruritic therapy, cyclosporine, oclacitinib, or allergen specific immunotherapy. Regardless of your preferred approach, I promise you that this atopic patient will be easier to manage now than patient with atopy AND concurrent food allergy, fleas, bacteria and yeast.
ATOPIC DERMATITIS: CURRENT CONCEPTS AND THERAPY

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INTRODUCTION
Each year Veterinary Pet Insurance publishes a list of top 10 claims for veterinary patients. For dogs, the number one claim is Allergic Dermatitis second is Otitis Externa, and third is Bacterial Skin Infection. To a dermatologist, these 3 things are all clinical manifestation of the same underlying process: Atopic Dermatitis. This is an exciting time to be a veterinarian because our understanding of the most common disease we see and manage is changing. New information is emerging that has dramatically changed our understanding of the physiology of itch and the genetic and environmental factors that result in the disease we recognize as Atopic Dermatitis. Curiously our new understanding of this important disease is very different from what we learned in school as short as 5-10-15 years ago.

What I Learned in School
The traditional understanding I was taught in school was that Atopy was similar to hayfever in people. It was triggered by abnormal immune response to inhalant allergens such as pollens, molds, house dust, house dust mites, etc; except that dogs itched and people sneezed. The whole process was dependent on inhalated allergens binding to IgE on the surface of mast cells in the skin. When the antigen bound to the IgE the mast cells degranulated releasing histamines and other inflammatory mediators that trigger swelling, erythema, and pruritus. Scratching further damaged the skin resulting in secondary bacterial infections. Since Mast Cells were found in high concentrations on the face, pinna, and paws; itch was frequently localized to these areas, except in severe cases when itch was more generalized. This all made perfect sense. Except that we now know it isn’t true (or at least most of it isn’t)

What we know now
First, while the antigens are similar to those that cause allergic disease in human, the route of exposure is not inhaled, it is across this skin. This makes much more sense, but took some time and a few very cool studies to prove definitively. In both humans with atopic dermatitis (eczema) and canine patients there is a series of genetic and environmental factors that result in disruption of the epidermal barrier function. The stratum corneum and other parts of the epidermis in atopic humans is fundamentally different from that of non-atopic humans. There are proven defects in the key protein (filaggrin), the key lips (cerumides), as well as disruptions in normal keratinocyte tight junctions, maturation, differentiation, transit, and exfoliation. All of this results in a leaky barrier. This leaky epidermal barrier allows for increased transepidermal water loss, penetration of antigens deeper into the lower layers of epidermis, and increased colonization by Staphylococcus. Environmental factors such as house dust mite proteases and exfoliative exotoxins produced by Staphylococcus further the breakdown of cerumides and worsening of the epidermal barrier defect. Cool, huh?

Second, while IgE and Mast cells do play a role in inflammation in the skin, they are not as important as T-lymphocytes to the immunologic dysfunction of atopic disease. Both atopic and non-atopic dogs have two populations of T-lymphocytes (Th1 and Th2) These two population produce different cytokines in response to antigenic stimulation. Th1 cells produce cytokines we associate with good anti-viral response (Interferons), good antibacterial, antifungal, wound healing, and neutrophil/macrophage responses (IL-1, TNF-alpha) and, finally Th1 cells promote solid IgG production by B-cells. Th2 cells produce cytokines we associate with good parasite response that recruit eosinophils, upregulate mast cells, histamine release, and promote IgE production. Guess what, atopic dogs have an imbalance in Th1 and Th2, tilting dramatically towards an excess Th2 response and upregulation of eosinophils, mast cells, and IgE production.

Third, while histamine can cause vascular dilation, swelling, and erythema, it is only a mild player in pruritus in the skin. We know this intuitively because our entire careers anti-histamines have disappointed us case after case with a frustrating inability to modulate pruritus. Research into the neurologic origins of pruritus revealed a new player called IL-31. IL-31 is a cytokine that is produced by Th2 cells in the epidermis after exposure to antigenic stimulation. IL-31 and other Th2 cytokines bind directly to unmyelinated peripheral nerves and triggers a sensation in the brain that says – scratch here. This action is mediated by a Jak-Stat pathway and is the most direct neuronal mediator of pruritus. If you inject canine Il-31 into a normal dog they will exhibit classic pruritus seen with naturally occurring atopic dermatitis. If you take a dog with naturally occurring atopic dermatitis and administer a Jak-Stat inhibitor (oclacitinib) to the dog, they stop scratching Pfizer Animal Health
(now Zoetis) developed an experimental Jak-Stat inhibitor (oclacitinib) that blocks the action of IL-31 into their new drug Apoquel.

Finally, Staphylococcus and Malassezia are not mere nuisances and flare factors that trouble allergic dogs. We now know that Staphylococcus and Malassezia contribute to the progression of atopic disease; the bacteria and yeast are inseparable from atopy. Early allergic skin and the genetic epidermal defect results in increased colonization by bacteria and yeast. The exotoxins from the organisms further lipid breakdown worsening the defect. The antigens from bacteria and yeast further stimulate the T-lymphocytes, activating danger signals within the epidermis, so that when environmental antigens from pollens, molds, housedust, housedust mites, etc are introduced the co-stimulation results in recognition of these harmless proteins as enemies by the lymphocytes. Then future exposures result in an aberrant and exaggerated immune response to ragweed, birch, housedust mite, etc. The result is the rolling progression of worsening skin disease from a normal appearing puppy to a slightly itchy young adult with mild recurrent bacterial folliculitis, to year-round pruritus, dermatitis, and relapsing yeast and bacterial infections we recognize as Atopic Dermatitis.

**Translate new findings into therapy for our patients**

1. Increased focus on the epidermal barrier defect. Topical emollients and essential oils applied early on and consistently can help reduce progression of atopy in young dogs, and help repair the thickened damaged skin of older atopic patients.
2. Early recognition and aggressive intervention, management, and prevention of superficial bacterial and yeast skin infections.
3. It is not possible to over bathe allergic dogs. All of our new shampoos and conditioners are detergent free and unlikely to dry the skin. Rather, the new products all have ingredients like phytosphingosine (a procerumide) and cerumides to repair the epidermal barrier. Additionally chlorhexidine reduces both yeast and bacteria both during active infections and as a preventative between infections. Minimum of once weekly chlorhexidine will reduce the frequency and severity of future skin infections
4. Push to desensitize (immunotherapy injections) earlier in disease. I’d much rather allergy test and start immunotherapy at 1-2 years of age than 3-4 years of age. If you know what direction this is going with a young patient, start immunotherapy NOW. Antigen specific immunotherapy promotes T-regulatory lymphocytes that restore Th1 and Th2 imbalance.
5. Direct intervention of neuronal mechanism of pruritus with Apoquel can provide rapid relief from itch while managing the causes of itch. This reduces our reliance on prednisone and other glucocorticoids for symptomatic relief. Think of Apoquel as a steroid alternative that is safe for both short and long term use.
6. Atopica (cyclosporine) is predominately a T-lymphocyte modulator and is still a very safe and effective therapy with a 15 years of experience and knowledge behind it.
FOOD TRAILS AND TRIBULATIONS: CLIENT COMMUNICATION ESSENTIALS

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In a recent survey of veterinarians in my area, discussing food trials with clients ranked somewhere between having root canal and getting a poke in the eye with a sharp stick. Why is this? Because, in spite of constant flogging by dermatologists about the importance of performing a food trial on every patient with pruritus, pyoderma, or otitis; in real world practice, food trials are frustrating, difficult, and frequently met with substantial resistance by otherwise perfectly rationale pet owners.

Successful performance of a food trial is even more difficult than convincing owners to agree to do it. The most common reason for failure is continued exposure to other ingredients in addition to the test diet. In spite of frequent failure and frustration elimination diet trials are still a very important diagnostic test for evaluation of patients with pruritus, dermatitis, and otitis. This presentation is designed to improve understanding of the mechanisms of a food trial, improve diagnostic value, and provide client communication tips to improve compliance and completion.

WHAT IS FOOD ALLERGY?
In spite of much study and discussion, we still don't have a solid understanding of all the mechanisms of adverse food reactions; indeed most dermatologists can't even agree what to call this condition. Adverse food reaction (AFR): any clinical abnormality associated with ingestion of a food item. This is an umbrella term that encompasses all food related syndromes, including cutaneous, respiratory, gastrointestinal neurologic, or hematologic disease. Food allergy: True hypersensitivity reaction involving a demonstrable immunologic reaction to a dietary protein. Food intolerance: Abnormal physiologic responses to food, food additives, or food contamination. Mechanisms may be metabolic, toxic, idiosyncratic or pharmacologic. If you eat bad fish and vomit that is a food intolerance not food allergy. Food-related dermatitis: any cutaneous manifestation of disease resulting from diet. The other term sometimes used is Cutaneous Adverse Food Reaction. FRD or CAFR may be either an allergy or intolerance, but definitely involves the skin or ears. For the rest of this presentation when I say food allergy, I mean food-related dermatitis

Food Allergy can be acquired and expressed at any age. 30% of dogs diagnosed AFR manifest prior to one year of age. On the other end of the spectrum dogs that never itched prior to 14 years of age have developed AFR. Sensitization takes 2 months or longer to develop. >50% of dogs are fed offending protein for 2 years before onset of clinical signs. The most antigens are large molecular weight proteins that are common ingredients in commercially available diets. Typical protein size is 10-60 kDaltons. Chicken is the most common food allergen followed by beef. Other proven allergens include lamb, pork, dairy, horse meat, egg, wheat, oat, fish, corn, and corn starch. More recently rice, potato, venison, and duck can be added to that list. Even tiny amounts of protein can trigger profound clinical reactions. In one laboratory population of known food allergic dogs some dogs would flare in clinical signs when given a montain of rice, or CAFR.

HOW COMMON IS FOOD ALLERGY?
You might find less agreement on this than on how to define food allergy. One study at a private referral dermatology practice identified food allergy in 7.6% of all dogs, and 32.7% of dogs presenting for allergic skin disease. Establishing true incidence in the general dog population is difficult, but you are safe to tell clients with confidence that 10 to 15% of dogs that see veterinarians for itch have food as their trigger.

WHEN TO SUSPECT FOOD ALLERGY?
Any patient with otitis, pruritus, dermatitis, or recurrent pyoderma or Malassezia dermatitis
Clinical signs are indistinguishable from atopy. Regional or generalized pruritus. Ears and Rears is the classic mantra, but is not sufficient to rule in or rule out food vs any other cause for itch. In a study of 51 dogs, regional involvement occurred in ears (80%), paws (61%), inguinal region (53%), and axilla, anterior foreleg, muzzle, and periorbital skin in (31-37%). In 24% of patients, only ears were involved with no other skin lesions. Primary lesions may include erythema, papules, erosions, ulceration. Less common primary lesions: urticaria, angioedema, perianal fistula, onychomadesis. Secondary lesions included excoriation, alopecia, or scales, crusts, hyperpigmentation, lichenification, and pustular eruptions associated with secondary bacterial or yeast
infection. In cats, the two most common presentation of food allergy are (1) intense head and neck pruritus, and (2) “psychogenic alopecia” aka excessive grooming because they itch. Differential diagnoses: atopic dermatitis, flea bite hypersensitivity, contact reactions, sarcoptes, cheyletiella, lice, pyoderma, Malassezia dermatitis, demodicosis, and dermatophytosis.

No, really, when should I suspect food allergy?
When should I really push hard for a food trial? Although you cannot diagnose food allergy based on history and physical exam findings there are certain clues that can raise your index of suspicion.

- **Non-seasonal pruritus.**
- **Concurrent gastro-intestinal signs.**
- **Any observation that exposure or change in diet worsened pruritus or GI signs.**

**WHAT ARE THE KEY COMPONENTS TO A DIAGNOSTIC FOOD TRIAL?**

Food trials are multistep processes. Communicating to the owner the necessity of a diagnostic food trial and what to expect. You must convince the owners that they want their dog to be food allergies, you must convince the owners that they want the trial to succeed. Useful phrase: “If I could choose between food allergy or environmental allergy, I’d pick food every time! You can control what Bandit eats, you can’t control pollen.”

**Establishing a baseline:** In order to take some of the guess work out of observations, have the owners establish a baseline of current level of itch and give them a diary to keep. “On a scale of 1 to 10, 10 being the worst itch you have every seen, where is she today.” Ideally establish this baseline after infections have been resolved. Encourage the owners to pay attention to other signs besides itching: redness and swelling of the ears, odor, head-shaking, rolling/rubbing, improvement from generalized itch to only itching paws. Clearly subjective and influenced by owners desire or refusal to believe the food could be a component, but better than no scale at all. Have owners score their pets once weekly. 8-12 week period of avoidance. Useful phrases: “Nothing else passes the patients lips except for the test diet.” “There is nothing magical about Rabbit that takes away itch. This new diet isn’t what makes your dog better. It is avoidance of the offending protein. This diet is simply providing nutrition while we eliminate the offending proteins from the body. Since we don’t know which protein could be making Fifi itch, we must avoid all of them.” Manage Expectations: We do not expect complete resolution of symptoms. Indeed there may be no change for 4-6 weeks. “Don’t give up yet, you have already come this far, lets keep going. Less than 25% of known food allergic dogs were better by 4 weeks.” Emphasize to owners that even partial response is still a response, as patient may have other conditions contributing to itch (atopy, fleas, pyoderma, etc)

**Provocative challenge:** The single most important part of a diagnostic food trial is provocative challenge. Perhaps any improvement noted during the avoidance portion of trial was due to other medications, elimination of infection, elimination of parasites, or seasonal change in exposure to environmental allergens. How do we know it was the food and not something else? – Challenge feed! We must know through observation, if reintroduction of original diet (plus treats, heartworm medication, supplements, or flavored toys) produces the previously observed symptoms. This is also important in apparent failure to reduce symptoms during avoidance. I have had owners tell me their dog isn’t any better, well except for the redness, the infections, the odor from the ears, and the constant scratching and head shaking, but he still licks his front paws! “That food didn’t do a thing.” Sometimes the changes may be subtle or the owner’s memory is faulty, but with challenge the owner may notice a return to high level signs. Don’t just switch back 100%. We don’t want the poor dog to burst into flames! For 5 days, mix the test diet with the original diet in a 3:1 ratio. In other words, however much they put in the bowl, make it ¾ test diet and ¼ original diet, plus whatever regular treat they liked to give. Monitor closely for any change from most recent “itch scale” observation. If the dog flares, don’t continue to challenge and return to test diet exclusively. This flare in signs should not last long since challenged with a small amount after 8-12 weeks of avoidance. Anticipate 5-15 days before return to baseline. If the dog has not flared after 5 days, probably not food allergy and you have completed a successful diagnostic test.

Congratulations. Good work. Time to focus on other causes for itch. Some owners will refuse to challenge feed if their dog is close to 100% normal. I consider the provocative challenge to be THE diagnostic test, all the rest is just to get us ready for the challenge. Let me give you an example. 1.5 year old Labrador with otitis, facial and pedal pruritus of 4 months duration starting in May. You perform a food trial and in 8-12 weeks the dog is normal. Owner never challenges and keeps feeding the test diet. Now it is March and the dog starts itching again, but they also started going to the dog park 2-3 weeks ago where he maybe scavenging dropped treats. Does this dog have food allergy or seasonal atopy? You have no idea. Had the owner performed the provocative food trial in December when he was normal and there were no trees pollinating, both you and the owner wouldn’t be trying to make a guess at the cause of the itch in March. Discuss with owners the need to be sure of diagnosis. However, if owners absolutely refuse, that is fine as long as the test diet is nutritionally
complete and the owner understands that we still aren’t certain of the final diagnosis. Have owners observe carefully following any future unintentional dietary indiscretions. In animals with severe clinical signs of food allergy, such as seizure disorder, onychomadesis, or perianal fistula, a challenge may not be in the patients best interests. Resolution of signs when return to test diet. Personally, I am content with the diagnosis of food allergy with flare in clinical signs after provocative challenge. Other dermatologists consider a second resolution of signs without any other therapeutic change to be the most critical step in confirmation of the diagnosis. There is no doubt this would be a useful data point, as would a second flare following a second challenge, but I feel I need to stop somewhere.

**Individual ingredient challenge**

So far we have only provide that food does trigger clinical signs. We haven’t proved what protein is the trigger. In one study of known food allergic dogs challenged with individual ingredients, 40% reacted to only one protein, 40% reacted to two proteins, 10% to three proteins, 10% to five allergens (apparently none reacted to 4). Since the only effective treatment for food allergies is avoidance of offending proteins, the owners must choose between continuing to feed the test diet forever or attempting to determine what one or two proteins they need to avoid and simply avoiding those. For owners interested in making that determination, instruct them on how to perform individual ingredient challenges. Have a 2 week wash out to re-establish baseline.

Challenge with pure ingredient, such as ground beef, chicken breast, or canned corn, etc. Give only 1 tablespoon or less of the pure ingredient with each meal since more may precipitate a greater reaction. Continue for 5 days. Watch carefully for flare as described above. If flare stop challenge and have minimum of 2 week wash out before continuing to next ingredient list. If no flare, still return to only test diet (i.e. don’t continue to give beef on the side). A 2-5 day washout before next ingredient.

**WHAT DIET SHOULD I USE FOR FOOD TRIALS?**

You basically have 3 choices: (1) Home-cooked novel single protein, single carbohydrate, single oil diet, (2) Commercial novel protein diet, or (3) Commercial hydrolyzed protein diet. Home-cooked is considered the optimal method for eliminating all potential dietary allergens. Commercial diets may be processed in same factory as other “flavors” and chicken residue from one diet may end up in test diet. Other dermatologists worry about reactions to 4th, 5th, or 10th ingredients even in limited antigen diets and prefer to stick to one protein and one carbohydrate only. Some dogs only respond to home-cooked and never improve with multiple attempts at commercial diet trials or react when challenged with any commercial diets. Patients often respond faster to home-cooked diets: 4-6 weeks vs 8-12 weeks. Unfortunately home-cooked diet trials are labor intensive and may not be nutritionally complete for long term feeding. Pet may also lose substantial weight with home-cooked diet and the high fiber content may result in impressive increase in bowel movements.

Recipes for home-cooked diet: Generally 1:1, 2:1, or 3:1 protein to carbohydrate plus a tablespoon of oil. Throw it together in a crockpot or pressure cooker and make a nice stew. Good Protein Choices may include, Pinto beans (most common), Kangaroo, Ostrich, Rabbit. Not as useful or to avoid entirely Pheasant, Duck, Turkey, Egg, Fish, Buffalo, Venison, Elk, Lamb. All have been observed to trigger reactions in known food allergic dogs. There may be cross reactivity with other animal muscle proteins common across species. These proteins may be fine for maintenance diet, but not for test diets. Carbohydrate choices that I like yams, pumpkin, quinoa. More marginal choice due to inclusion in many diets: Potato or Sweet Potato. I don’t like to use any grain, including rice. Oil choices that I prefer are Walnut oil, Sunflower seed, olive; avoid corn oil. For long term feeding of home-cooked diets, I recommend consulting with nutritionist to provide balanced supplementation with calcium, minerals, vitamins, and other essential nutrients. Another option is to use Balance It Original Blends. This blend provides all the carbohydrate, vitamins, minerals, trace elements and nutrients EXCEPT the protein. You chose the protein, choose the blend, plug in the patient characteristics and the website provides the number of ounces of protein + cups of Blend. Cook with oil and dogs go love it.

While not statistically as efficacious as home-cooked diets, commercial diets are preferred by clients due to convenience. Conceptually the idea of a novel-protein diet is you can’t be allergic to a protein you have never been exposed to before. Realistically there may be cross-reactivity between different meat sources. Recent work has demonstrated that beef allergic dogs may also react to exposure to other source muscle proteins as well. In a study of 40 known food allergic dogs, exposed to three European diets containing either chicken, venison, or catfish, 62% reacted to one or more of the diets, but only 5% reacted to all three. No single diet is effective at diagnosing 100% of food allergic dogs, multiple diet trials may be necessary to fully evaluate the subset of dogs that might cross react with one of the novel proteins. I recommend sticking to protein sources that are absent from puppy foods and that are not closely related to beef, chicken, or fish. That pretty much leaves Rabbit and Kangaroo at this point in time. Other novel protein diets may be perfectly acceptable as
maintenance diets if no reaction on challenge to a known food allergic dog; however, when performing a diet trial to determine if a dog has food allergy, you want the diet to be as close to perfect as possible. Conceptually the idea behind hydrolyzed-protein diets is that in order to be a decent stimulator of the immune system the protein needs to be of a certain molecular weight (15-60 kDaltons). So if the protein molecule is cleaved to a smaller size, then the immune system won’t recognize it, and it won’t stimulate an adverse reaction. Great theory, unfortunately some dogs still react. In a study of 19 dogs with confirmed AFR on home or novel protein diets, 1 of 19 relapsed when fed hydrolyzed diet DVM Exclude. In 14 known corn allergic dogs, fed Purina CNM HA (hydrolyzed soy with corn starch), 3 dogs and worsening of clinical signs.

ISN’T THERE AN EASIER WAY?
There have been several valiant attempts to make testing for food allergies a more client-friendly experience: serologic testing, intradermal testing, and even endoscopic stomach lining testing (they drip the extract onto the lining. Sadly none have produced acceptable validated results to justify use.

Intradermal allergy testing Basically injecting specific food protein extracts into the skin and observing for hive formation (allergen-specific triggered degranulation of mast-cells). Sadly mast cells may have nothing to do with manifestations of AFR. One study showed very poor correlation with specific proteins that triggered reaction when fed to patient in provocative challenge setting. In other words what they reacted to or didn’t react to on the skin test had very little to do with what made them itchy (or didn’t make them itchy) when fed. Sensitivity 10% Specificity 96% Positive predictive value 60% Negative predictive value 62%. In fact a higher percentage of dogs with negative skin tests improved on diet trials than dogs that had positive reactions (17% vs 10%).

Serologic Testing measures food allergen-specific IgE by ELISA. Unfortunately, IgE may not be involved in the pathogenesis of AFR and has demonstrated poor correlation to specific protein proven by provocative challenge. Sensitivity of only 14%, Specificity of 87%, Positive predictive value 40%, Negative predictive value of 61%.

Patch Testing, similar to what is done to identify contact allergies, is showing some promise. In these tests a suspension of pulverized dog food or individual ingredient is suspended in a neutral lanolin base, placed into Finn chambers, and taped onto shaved area of skin for 48 hours. At the end of the period, the test apparatus is removed and lesions are scored based on erythema and skin turgor under each test ingredient. At this time the apparatus and methodology is too cumbersome for routine use in primary care practice. My hope is that a simple apparatus could be use to determine if a food trial is necessary. A simple yes/no test that if negative there is no indication to pursue food allergy (high negative predictive value), whereas if positive proceed with elimination diet trial. Until that time – keep talking to clients, focus on what doesn’t pass the dog’s lips during the diet trial, and carefully explain the purpose, process, and diagnostic challenge at the end.

Suggested Reading

• Any lecture by Craig Griffin, DVM, DACVD on the topic of food allergy or diet trials.
• Rosser E “Diagnosis of food allergy in dogs.” JAVMA (1994)
• White SD “Food allergy in dogs” Compendium for Continuing Education (1998)
ACRAL LICK DERMATITIS: THREE PRONG APPROACH FOR BETTER OUTCOME

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INTRODUCTION
Acral lick dermatitis (ALD) is among the top 10 most common dermatologic diseases of dogs. ALD is frustrating, expensive, miserable for the patient, responds poorly to therapy, and reoccurs frequently. Therapeutic success rates range from 20-65%, including unusual treatments, like intraliesional Cobra venom. In spite of this, there is remarkably little clinical research performed to improve understanding of the pathogenesis of ALD.

CLINICAL PRESENTATION
ALD is characterized by self-traumatizing licking that results in progressive development of well-circumscribed, firm, proliferative, erosive/ulcerative, alopecic plaques or nodules on the lower portion of the limb. While appearance and size can be quite variable, the consistent feature recognized by veterinarians and owners is excessive licking. Lesions are usually found on the dorsal aspect of the carpus, occasionally extending down the metacarpus, or up to the elbow. Less commonly the lateral tarsus or metatarsus is involved. A recent survey, demonstrated front limb only involvement in 21 of 31 dogs (68%), front and hind limb involvement in an additional 6 of 31 (19%), and hind limb only involvement in only 4 of 31 (13%). Lesions are often painful with patients resisting manipulation or palpation; some dogs demonstrate lameness or decreased activity. Any breed can be affected, but there is a predisposition for large breed dogs with short coats: Doberman Pinscher, Great Dane, Labrador Retriever, Boxer, and Weimaraner. Other frequently mentioned breeds are German Shepherd, Golden Retriever, and Irish Setter. A common theme is relatively short hair on the dorsal aspect of the limbs. Median age of onset is 4 years (range 1 – 12 years).

CAUSE
Etiology of ALD is complex and multifactorial. To simplify understanding, all causes and contributing factors can be divided into three categories: (1) predisposing, (2) primary, and (3) perpetuating factors.

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<thead>
<tr>
<th>Predisposing</th>
<th>Primary</th>
<th>Perpetuating</th>
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<tr>
<td>Large Breed Dog</td>
<td>Food Allergy</td>
<td>Deep bacterial infection</td>
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<tr>
<td>Short Hair Coat</td>
<td>Atopic Dermatitis</td>
<td>Pain</td>
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<tr>
<td>Not walked at all</td>
<td>Orthopedic / Spinal</td>
<td>Entrapped free hair shafts</td>
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<td>Housed outdoor only</td>
<td>Trauma</td>
<td>Apocrine gland inflammation</td>
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<td>Concurrent Behavior Problems</td>
<td>Neoplasia</td>
<td>Fibrosis</td>
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<td>Fungal infection</td>
<td>Reinforced behavior</td>
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<td>Foreign Body</td>
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<td>Parasthesia / Neuropathy</td>
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<td></td>
<td>Behavior Disorders</td>
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Predisposing factors are things that do not directly cause ALD but make initiation and progression of ALD more likely. This includes breed predisposition and short hair coat over affected limbs. One recent study, suggested an increase risk for ALD in dogs that were rarely or never taken for walks, dogs that were housed outdoors only.

Primary causes are conditions that initiate licking at the target site, setting up progression of changes that result in clinical lesions. Foremost among these are diseases that cause pruritus: food allergy and atopy. Less common causes include trauma, neoplasia, dermatophytosis, foreign body, osteoarthritis, parasthesia, neuropathy, and behavior disorder. A recent case series reported clinical lesions, resulting from a Kirshner pin, lymphoma, mast cell tumor, sporotrichosis and Leishmania. Behavior is often described as the most common cause for canine ALD. In our clinic, food allergy is the most common, followed by atopy; all other causes are rare, including behavior. In cases with a final diagnosis of primary behavior disorder, patients exhibited multiple behavioral problems; including, separation anxiety, phobia, or other stereotypic behavior, such as tail-chasing, circling, wool sucking, fly biting, or rhythmic barking. If a dog with ALD presents with additional behavior problems, then suspect a primary behavior cause; however, in the absence of concurrent behavioral
disorders, pursue food allergy, atopy, and other diseases first, while addressing behavior as a perpetuating factor.

Collaborative prospective studies with both dermatology and behavioral specialties need to be performed to better determine etiology and characteristics of primary behavioral ALD. A good model is a recent study of another “behavioral” dermatosis, psychogenic alopecia. This study evaluated 21 adult cats referred with a presumptive diagnosis of psychogenic alopecia; in 19 cats a primary pruritic disease was identified, with only 2 cats found to have a psychogenic cause. Food allergy was the most common diagnosis, confirmed in 12 of 21 cats. Like “psychogenic” alopecia, a behavioral cause for ALD should only be diagnosed when all causes of pruritus have been eliminated.

**Perpetuating factors** are conditions that result from licking and progress to an amplifying cycle of self-traumatic licking. The three most common perpetuating factors are (1) deep bacterial infection, (2) free keratin debris and subsequent pain and inflammation, and (3) behavior. In a recent prospective study, deep tissue bacterial infection was identified in 29 of 31 dogs (94%). One dog was culture positive for *Microsporum gypseum*. The most common deep tissue isolates were *Staphylococcus* (58%), *Pseudomonas* (8%), and *Enterobacter* (8%). Antibiotic resistance was unpredictable; 52% of isolates were resistant to three or more antibiotic drug classes commonly used for *Staphylococcal* pyoderma (cephalosporin, clindamycin, potentiated sulfonamides, amoxicillin/clavulanate, and fluoroquinolones). Methicillin-resistant *Staphylococcus* was isolated in 25% of cases. Surface culture was a poor predictor of deep isolates; therefore antibiotic selection should be based on culture obtained by biopsy or purulent exudates squeezed from deep in the lesion.

Another major cause for progression and perpetuation of the self-traumatizing lick is ruptured hair follicles, free hair shafts, and inflammatory response to keratin. Dogs start licking as a manifestation of pruritus, which may result in focal bacterial folliculitis, which is pruritic and stimulates more licking. In short-coated breeds, licking results in rupture of hair follicles and forcing of short, stiff hairs into the deep dermis. Keratin is phenomenally irritating to tissues and elicits a profound acute and chronic inflammation. Hair shaft foreign bodies are very painful and elicit continued licking. Over time, these changes progress to commonly described histopathologic features of ALD: ulceration, dermal fibrosis with a vertical streaking pattern, thickened and elongated hair follicles, free hair shafts, and diffuse pyogranulomatous to lymphocytic-plasmocytic inflammation. In the prospective study of 31 dogs, epichrine sweat glands were also found to be heavily involved, exhibiting periglandular inflammation (90%), hypertrophy (81%), inspissation (81%), dilation (71%), severe focal inflammation in the glands (hidradenitis; 29%) and glandular rupture with secretions free in the tissue (10%). The role of epithelial gland inflammation in the progression of ALD is unknown, but histopathologic changes are similar to proliferative end-stage (cauliflower) otitis in Cocker Spaniel dogs.

Behavior is more likely involved in progression and perpetuation of canine ALD rather than as a primary cause. Repetitive, “compulsive” licking in ALD has been compared to obsessive-compulsive disorder (OCD) in humans. While very little is known about neurophysiology and neurochemistry of dogs with ALD, humans have been studied extensively. Some human patients have abnormal neural pathway between the frontal lobes (consciousness and perception) and the caudate lobe of the basal ganglia (planning and execution of movements). As a result OCD patients demonstrate recurrent impulsive repetitive behaviors, such as hair pulling (trichotillomania), hand-washing, checking of lights, stoves, door locks, unplugged irons; the patient is consciously aware they just washed their hands, but the information that the action is completed and no longer needs to be done does not get processed properly and the patient repeats the behavior. This may be true in dogs with some stereotypic behaviors, but seems unlikely in ALD. Do dogs think “I just licked my paw, my paw needs licking?” In addition to neural pathway disorders, humans with OCD have low serotonin activity. Serotonin is a vital neuromodulator involved in nearly every aspect of behavior, response, and action. Repetitive motor activities in OCD patients increase serotonin activity, creating a self-medicating feedback loop that reinforces the behavior. Dogs with ALD may also experience reinforced feedback, where licking provides both a temporary alteration of local sensation (relief of pain/pruritus) and pleasurable increase in serotonin activity in the CNS. Partial clinical improvement with Selective Serotonin Reuptake Inhibitors (SSRI) supports this observation.

**DIAGNOSIS**

Diagnosis should focus on both primary cause and perpetuating factors. Use both dermatology and behavior history questionnaires to assist in early identification allergic or behavior disorders. Any pruritus or otitis? Think allergy; however, do not rule out allergy if ALD is the only manifestation of pruritus. If behavioral history shows
concurrent anxiety, phobia, or stereotypic behaviors, then more aggressive pursuit of behavior is warranted. In most cases, think food or atopy first, not behavior.

The initial minimum database should include, cytology, skin scrape for demodicosis, and dermatophyte culture. Documentation of the size and appearance of the lesion with digital photography, calipers, or tracing of the lesion through clear acetate is important for later comparison.

Biopsy for histopathologic confirmation and bacterial culture and sensitivity is also recommended. Histopathology is the most direct method for ruling out organic causes such as neoplasia or deep mycosis. Of greater value is deep tissue culture and sensitivity. 95% of dogs with ALD have deep pyoderma, and most have bacteria with unpredictable susceptibility to antibiotics. Since ALD may require prolonged treatment (2-6 months), antibiotic selection based on culture increases the opportunity for success. Surface swabs show oral contaminants or more routine surface bacteria. My method is sedation with IV medetomidine at 5-8 ug/kg and butorphenol 0.2mg/kg followed by local anesthetic block. Lidocaine is administered subcutaneously in a semi-circle proximal and under the lesion. Injections into the lesion may disrupt the dermal architecture and inhibit bacterial growth. If necessary, intravenous propofol can be administered to effect; however, propofol provides no analgesic activity. Use surgical scrub and aseptic surgical technique. With a sharp (new) 6mm punch biopsy collect a deep biopsy from the center of the lesion; with a scalpel blade, trim the epidermis from the dermis and submit only deep tissue for culture. If unable to biopsy, sample deep exudate by squeezing the lesion until a small quantity of exudate emerges from a follicular pore.

Elimination diet trial is an essential test for canine ALD. Following 8-12 week trial, ask – is the dog licking less and is the lesion smaller. The answer may be yes because of resolution of infection; therefore the true diagnostic test is provocative challenge with the original diet. Intradermal allergy testing or allergy serology to identify allergens for inclusion in allergen specific immunotherapy is indicated in any patient that fails to respond to elimination diet trial. Radiography of the affected limb may be helpful to evaluate for underlying osteoarthritis, implants, neoplasia, or deep mycotic infection. In chronic ALD, the presence of periosteal reaction on radiograph is a negative prognostic factor.

THREE PRONGED APPROACH TO THERAPY
Focus on THREE key components: (1) Pain Management, (2) Effective Antibiotic Therapy, and (3) Management of Primary Disease, failure in any one of these areas will likely result in poor response, recurrence, or progression.

Pain is perhaps the most underappreciated and therefore undermanaged perpetuating condition in ALD. Pain can occur from entrapped hair shafts and deep pyoderma can be a major factor that stimulates continued “compulsive” licking. Additionally orthopedic or neuropathic pain may be the primary or initiating reason. Use of analgesics such as non-steroidal anti-inflammatory drugs is the first line of therapy. Adjunctive therapy with gabapentin and/or amantadine may be useful, but has not been thoroughly researched. Gabapentin is an antiepileptic drug with utility in managing neuropathic pain. Amantadine is an NMDA receptor antagonist. Check with your local anesthesiologist for dosing guidance as ideal dosages have not been determined for Gabapentin or Amantadine in dogs.

Managing the deep bacterial infection requires a safe, effective, and convenient antibiotic that the owners and the animal can tolerate for a protracted periods. Because resistant bacteria are common, and because the owner will be administering oral antibiotics for prolonged courses, try to choose an effective antibiotic based on susceptibility profile that is administered easily, on a simple schedule. cefpodoxime or ornithoprim sulfadimethoxine one time daily is ideal for susceptible bacteria. Once daily fluoroquinolones marbofaxacin and enrofloxacin can be used for gram-negative infections where no other oral choice is rationale. Use the highest achievable dose or combining with a second antibiotic to minimize risk of developing resistant strains. Other choices based on culture can include cephalosporins, clindamycin, chloramphenicol, doxycycline, and amoxicillin/clavulanate. Always aim high with dose and duration, as relapse and failure are common.

Topical mupirocin ointment is excellent for Staphylococcus, including methicillin-resistant strains. Topical benzoyl peroxide gels and washes can be beneficial as a superficial antiseptic and to open hair follicles and facilitate removal of keratin debris. Epsom salt soaks may help. Other topical therapies with variable utility and efficacy include, fluocinolone and DMSO, flunixin meglamine, and capsain. A mixture of 1/3 liquid HEET and 2/3 Bitter Apple has also been described. Use caution with any topical therapy if therapy directs the dog’s attention to the area, causing increased licking rather than less. Ideally apply topicals then distract the dog.
Other treatments including therapeutic laser, surgery, cryotherapy, surgical laser ablation, radiation therapy, and acupuncture have been reported with variable success. I prefer to use laser ablation only after the primary disease is diagnosed and managed and antibiotics have been administered to maximal benefit. Patience is necessary; the remaining lesion is smaller, and contains only fibrosis, trapped hair shafts, and foci of bacteria. Manage as any open wound by second intention; prevent continued licking.

Treatment of primary allergic disease may include diet, allergen immunotherapy, cyclosporine (Atopica, Novartis), and short courses of steroids to break the itch-lick cycle. Use corticosteroid doses and protocols employed for routine atopic dermatitis; avoid higher, longer, or aggressive steroid usage simply because ALD is a more severe. Previous poor response to corticosteroids is probably due to deep pyoderma not insufficient steroids. High steroid doses are not more likely to resolve bacterial infection than low doses. Intralional steroids will prolong infection and ALD.

Behavioral therapy is focused on two areas – behavior modification and drugs. Seek expert advice for effective protocols for concurrent behavioral diagnosis (separation anxiety, phobia, or stereotypic behaviors). Behavior modification therapy may include avoidance of recognized triggers, counter-conditioning, and distraction techniques, such as social and environmental stimulation, exercise, and increased play. Aversion therapy with shock collars was reported to be beneficial in 4 of 5 cases. However, guidance from an experienced behaviorist is strongly recommended before using this therapy. Aversion is one of the hardest behavior modification techniques to apply effectively; 100% application of the stimulus is required; partial or intermittent application can actually reinforce the behavior rather than extinguishing it. Also aversive stimuli does very little to resolve pruritus or pain associated with impacted hair shafts and deep pyoderma. Drug therapy may help resolve perpetuating, self-medicating serotonin feedback loop; consider tricyclic antidepressant: clomipramine and Selective Serotonin Reuptake Inhibitor: fluoxetine hydrochloride.

Bandaging, using E-collars, muzzles, and other techniques to physically restrain the dog and preventing licking meets with mixed results. Early on in the management restraint may actually be counterproductive, as pain and pruritus are usually very high and the motivation to lick is powerful. Some dogs will resort to self-destructive licking around the restraints or at other limbs, resulting in worse disease not better. I prefer to wait until the lesion is improving and stimulus is reduced before attempting restraint. I will definitely use restraint following laser ablation or other surgical intervention.

**SUMMARY**

- ALD is a multifactorial disease with predisposing, primary, and perpetuating factors
- Pain-management is an important component of therapy
- 95% of acral lick lesions have deep bacterial infections
- Bacterial infection is less predictable than routine pyoderma
- Culture by biopsy or by squeezing up deep exudates
- Most dogs with primary behavior ALD exhibit other behavior problems

**SUGGESTED READING**

CANINE PYODERMA: A DERMATOLOGISTS SECRETS REVEALED

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Introduction: Pyoderma can be defined as a pyogenic, or pus-producing, bacterial infection of the skin. Pyoderma is a common dermatitis seen in dogs, second only to flea-allergy dermatitis. Dogs seem to be much more susceptible to bacterial skin infections than humans or other domestic animal species. This may be due to differences in epidermal barrier (higher pH, less passive immunity in the form of lipids and antibacterial peptides, a thin, compact stratum corneum, lack of lipid-squamous plug in hair follicles, etc). Alternatively, dogs may have a higher incidence of underlying diseases that predispose to bacterial overgrowth. Regardless, dogs get pyoderma at high rates, pyoderma causes misery for our patients, our clients get frustrated by lack of response or frequent recurrence, and everybody’s quality of life suffers.

The usual suspects
• Staphylococcus intermedius: Coag-positive Staph. By far the most common isolate in dogs
• S. schleiferi and S. aureus: on the rise. Higher likelihood of multidrug resistance
• Gram negative organisms: Pseudomonas aeruginosa, Proteus mirabilis, E. coli, Enterobacter
• Atypical bacteria: Actinomyces, Nocardia, Mycobacterium (topics for another seminar)

Classification of pyoderma by...

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<thead>
<tr>
<th>Depth</th>
<th>Pattern</th>
<th>Location</th>
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<tbody>
<tr>
<td>(Irhke method)</td>
<td>(Encyclopedia method)</td>
<td>(Anatomist method)</td>
</tr>
<tr>
<td>Superficial</td>
<td>Puppy pyoderma (impetigo)</td>
<td>Folds: Lip, face, tail, perivulvar</td>
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<tr>
<td></td>
<td>Superficial spreading</td>
<td>(intertrigo)</td>
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<td></td>
<td>Folliculitis/Furunculosis</td>
<td>Friction areas: axilla</td>
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<td>Bullous impetigo</td>
<td>Trunk - generalized</td>
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<tr>
<td></td>
<td>Breed specific: German</td>
<td>Pododermatitis/Interdigital</td>
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<tr>
<td></td>
<td>shepherd, Dachshund, etc.</td>
<td></td>
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<tr>
<td>Deep</td>
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<tr>
<td>Bacterial</td>
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<tr>
<td>folliculitis/furunculosis</td>
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<td>Cellulitis</td>
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Clinical Outcome (my preference)
• Simple: resolves and does not recur
• Chronic recurrent: resolves with significant periods between episodes, but returns frequently
• Treatment failure: no response, no resolution or recurs in less than 7 days of ending therapy
Simple
- Overgrowth or infection of resident or opportunistic bacteria
- Usually no significant underlying disease
- Responds rapidly to topical antiseptics alone or systemic antibiotics
  - Chlorhexidene shampoo
  - Cephalosporin x 3 weeks
- Does not recur
- Not too frustrating for owner or challenging for veterinarian
- Examples
  - Impetigo (puppy pyoderma) – transient pustular pyoderma. Usually self-limiting
  - Secondary to poor grooming – folliculitis, matted fur, etc
  - Secondary to recognized and resolvable dermatitis – ectoparasitism

Recurrent pyoderma
- Recolonization and overgrowth by resident Staphylococcus rather than a failure to “eliminate” infection.
- Typically greater than 2 weeks between episodes. If less than one week probably treatment failure.
- Chronic Recurrent Pyoderma is almost always due to ongoing underlying disease
  - Non-parasitic allergic dermatitis: Atopy, Food, Contact
  - Parasite hypersensitivity: Flea, Cheyletiella, Sarcoptes, other regional parasites
  - Primary parasitism: Demodex, fly-strike,
  - Endocrine: hypothyroidism, hyperadrenocorticism
  - Hair follicle disorders:
    - Comedones (Schnauzers, Hairless breeds)
    - Follicular dysplasias (Doberman, other color-dilutes, Black-haired breeds)
    - Sebaceous adenitis (Poodles, Vizslas, Akitas, Samoyeds, etc).
  - Immune-deficiency:
    - True immune-deficiencies are very very rare
    - IgA, complement, Pelger-Huet, Chediak-Higashi, Neutrophil migration
    - Breeds: German shepherds, Irish Setters
  - Staphylococcal hypersensitivity
    - Response to Staphylococcal superantigens, exotoxins, other proteins.
    - Minor overgrowth results in profound inflammation and pruritus.
    - Clinically, recurrent pyoderma characterized by intense pruritus that resolves with antibiotic therapy alone.
    - Less common than actually diagnosed

Diagnostic approach to underlying diseases

<table>
<thead>
<tr>
<th>“Is it a rash that itches or an itch that rashes?”</th>
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<tbody>
<tr>
<td>If pruritus resolves with antibiotic therapy</td>
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<tr>
<td>Hypothyroidism</td>
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<tr>
<td>Follicular dysplasia</td>
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<tr>
<td>Comedone syndromes</td>
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<tr>
<td>Immune-deficiency</td>
</tr>
<tr>
<td>Sun-damaged skin</td>
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<tr>
<td>Primary Staphylococcal hypersensitivity</td>
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*That is, successful antibiotic therapy. Confirm with cytology demonstrating elimination of bacteria

- History: helps order differential diagnoses
  - Age of onset:
    - Atopy: 6months – 6 years
    - Food: any age, but if greater than 6 years suspect food over atopy
  - Breed
    - Food allergy: Bulldogs, Labradors, SharPei, German Shepherd, Cocker Spaniel.
    - Atopy: All Terriers, Golden Retriever, Dalmatian, WHWT, Bulldogs.
  - Seasonality
    - Seasonality is strongly suggestive of atopy or flea allergy dermatitis.
Non-seasonality does not help, as atopy can be year round.

- Response to steroids
  - In general atopics are responsive to steroids.
  - Poor response to steroids suggests food and infection, but does not rule out atopy.

- Life style and other animals in household
  - Started 3 weeks after visiting friends house whose dog also severely itch? Hmm.
  - Shelter animals, puppies, kittens, multicat households – think parasite.

- Physical examination
  - Characteristic lesions:
    - Atopy: anterior flexural surface of elbow. Posterior carpus between pad and accessory carpal pad.
    - Flea allergy: caudal dorsal region to base of tail
    - Sarcoptes: Pinna, elbows, flank (not always)
    - Cheyletiella: Dorsum with lots of dry scale.
  - Pinnal-pedal reflex: Rapidly scratch the leading edge of the pinna with a finger nail. If the ipsilateral leg starts stratching, then positive. Positive in majority of sarcoptes dogs, while negative with most other pruritic diseases. A rough tool, but if positive, then a parasite treatment trial is strongly encouraged.
  - Front half or back half?
    - If itches primarily on the back half of patient – rule out fleas
    - If itch focuses primarily on front half – atopy, food, other
  - Otitis
    - If no infection, but erythema is present, atopy generally affects the pinna and opening most, while food generally affects the horizontal and vertical canal more. If infection present, no help.
    - Pinna without canal – Sarcoptes.

- Diagnostic testing for every patient!
  - Cytology: Bacteria and Yeast. Occasionally Dermatophyte endospores
  - Skin scrape
    - Superficial – Sarcoptes and Cheyletiella. Negative skin scraping does not rule out either parasite; however, if you get lucky and find sarcoptes then no need to keep going until these mites are eliminated.
    - Deep – Demodex

- Further diagnostic testing for majority of cases
  - Parasite treatment trial
    - Revolution (selamectin) every 2 weeks for 3 treatments
    - Interceptor (milbemycin) 2mg/kg once weekly for 4 weeks
    - Ivermectin 300mcg/kg once weekly for 4 weeks. Do not use in ivermectin sensitive breeds. Step up to full dose over 4 days.
    - Frontline (fipronil) is not effective at eliminating Sarcoptes
  - 8-week elimination diet trial followed by challenge feeding
    - Duck/Potato, Rabbit/Potato, Kangaroo/Oat are my favorite novel protein diets. Recent study showed poor results with Venison or Fish based test diets; may be fine maintenance diets.
    - Hydrolyzed protein diets are getting better. Some reactions can still occur (GI and Pruritus). Suspect corn starch may be culprit or tiny amounts of less hydrolyzed proteins that are always still in there.
    - Amino acid formulation currently being evaluated – may be the answer.
    - Provocative challenge is the diagnostic part of the test!
    - Food serology has very low positive predictive value (11%); however, if positive to > 5 foods, then food allergy is more likely, just not necessarily to the foods listed.

- Specific allergen testing
  - Does not diagnose atopy
  - Purpose is to identify allergens for immunotherapy
Serology
• Measures allergen-specific IgE in circulation
• No correlation between amount of IgE and severity of disease
• No correlation between serum IgE and Intradermal allergy testing
• Highly variable between laboratories and within individual
• Less influenced by drug therapy
• Easy to do in office

Intradermal allergy testing: Direct measure of reaction to allergen exposure
• Requires drug withdrawal
  o Anti-histamines and Topical steroids - 2 weeks
  o Oral steroids - 4 weeks and Depo-medrol - 8 weeks

Basics of treatment – Details under treatment failure

Initial visit
• Focus on primary disease
• Systemic antibiotic for 3-6 weeks.
• Appropriate shampoo/conditioner if generalized or Bactoderm if localized.
• Aggressive flea control

Recheck 2-4 weeks – ask client to rank 1-10: pruritus, odor, appearance of skin. Repeat cytology.
• If good response, treat for 1-2 weeks beyond “cure” and proceed to maintenance therapy.
• If not improved – evaluate all causes for treatment failure listed above
  o Client compliance – verify and reinforce
  o Antibiotic selection, dosage, and interval
  o Consider culture if you truly suspect resistance
  o Repeat skin scraping and DTM to be sure you didn’t miss the common differentials
  o Any time dermatitis fails to respond to appropriate therapy for current diagnosis → biopsy.

Maintenance therapy
• Treat primary underlying disease
• Shampoo/conditioner every 1 to 2 weeks life long

Treatment failure
• Client compliance: Much more likely than true antibiotic resistance.
  o In humans, one study found that as many as 60% of prescriptions are never filled!
  o Of the prescriptions filled, only 40% are taken at the correct dosage, frequency, or duration.
  o Once daily dosing increases compliance
    ▪ Cefpodoxime (Simplicef), Enrofloxacin (Baytril), Marbofloxacin (Zeniquin)
    ▪ Ormethroprim sulfadimethoxine (Primor)
  o If can’t use one of these, BID protocols are still better than TID.
  o Single injection with Cefovecin (Convenia) improves compliance by taking the opportunity to fail away from the owner. Also useful for difficult to pill patients or during food trials
  o If it makes them vomit or have diarrhea, then they are probably not going to use it.
  o If they can’t get pill into the patient, then they are probably not going to use it.
  o Point of purchase vs. pharmacy dispensing: more likely to use if easy to obtain
  o Be specific – dose, frequency, duration. Repeat, demonstrate, put it in writing.
  o Phone call follow ups in 5 days. Tremendous return of value for effort

Wrong antibiotic
  o “The most expensive antibiotic is the one that doesn’t work”
  o Choose drug based on efficacy first, convenience second, cost third.
  o Great: Cephalosporin, Clavamox, Oxacillin, Fluoroquinolone (<5% resistance)
  o Okay if susceptible: Clindamycin (22% are resistant), Lincoxin (22%), Erythromcyn (28%), Chloramphenicol (30%), Trimethoprim-sulfonimides (up to 70%)
  o No no no! Bad choice: Penicillin, Ampicillin, Amoxicillin, Tetracycline (40-83% resistance)
  o Fluoroquinolones, Clindamycin concentrate in wbc, great choice for purulent deep pyoderma.
  o Caution with Sulfonamides
    ▪ Must measure STT before and 5 days into therapy (offsets cost benefit)
    ▪ Commonly implicated cause of adverse drug reactions (EM, IMHA, ITP)
    ▪ Blocks organification of iodine in thyroid → classic clinical & lab hypothyroidism

Inadequate dose or interval
  o More common in larger dogs than smaller dogs – common sense
Often underdose in attempt to save on cost. False economy → prolonged or ineffective tx
Always round up to next most convenient dose.
Fluoroquinolones – always aim high!
  - Bactericidal effect is Dose-dependent not time-dependent.
  - Highest achievable concentration spike above MIC that kills bacteria
  - For Baytril: 5mg/kg SID is better than 2.5mg/kg BID (7.5 – 15.0mg/kg is even better if you are treating resistant bugs).
Cephalosporins and Augmented penicillins
  - Length of time above MIC is most important. Pay close attention to dosing interval.
  - Cephalexin has a shorter half life than Cefpodoxime, less forgiving for missed doses.
  - If using Cephalexin, owners MUST understand NO missed doses

**Inadequate duration**
- Client discontinued: Didn't respond fast enough, got better so they stopped, or adverse side-effects: appetite, vomiting, diarrhea.
- Initial prescription was too short
- Treat superficial infections for minimum of 3 weeks, deep for 6 weeks, scar tissue or furunculosis may take 12 weeks.
- General guide line is to treat for 1 week beyond apparent clinical resolution. May want to extend to 3 weeks beyond for deep pyodermas or patients with prior history of rapid recurrence.

**Antibiotic resistance:** uncommon to first-line antibiotics (Cephalosporin, Clavamox, Quinolones)
- S. intermedia
  - High levels of resistance to non-potentiated B-lactam antibiotics
  - Remarkable for not developing resistance to commonly used antibiotics.
  - Cephalosporins have been used globally in dogs, cats, and humans for 30+ years and we still rarely find any resistance. Great first line drug.
  - Starting to see increasing resistance to enrofloxacin in otic isolates.
  - Methicillin-resistant strains are out there.
- S. schleferi and S. aureus
  - More likely to be resistant to methicillin, oxacillin, and fluoroquinolones
  - Need a good bacteriology service to diagnose. Most simply type the isolate to coagulase positive Staphylococcus, look to see that it came from a dog, and call it intermedia. Additional steps required to speciate further.
  - Methicillin-resistant S. aureus (MRSA) is a serious zoonotic hazard
- Gram negative organisms: Proteus, Pseudomonas, E. coli
  - Rarely seen in simple, uncomplicated pyoderma
  - German shepherds
  - Immune suppressed patients: Chronic glucocorticoids, Cushing’s
  - Pemphigus foliaceus
  - Special sites: interdigital, pervulvar, lip fold
  - Culture these if rods seen on cytology

**When that pyoderma is not really pyoderma**
- Demodicosis
- Dermatophytosis
- Pemphigus foliaceus
- Malassezia dermatitis
- T-cell lymphoma
- Cutaneous drug eruption, erythema multiforme
- Sun-damaged skin

**Other factors**
- Poor antibiotic concentration in target tissue. Skin receives only 4% of cardiac output (vs 33% to muscle tissue or 25% to kidney).
- Sequestered foci in scar tissue (deep furunculosis, acral lick granuloma)
- Immune deficiency -
- Failure to diagnose and manage underlying diseases

**Beyond antibiotic therapy**

**Topical ointments and creams**
- Mupirocin (Bactoban™) - note the veterinary product Bactoderm™ has been discontinued
  - Derived from a naturally occurring Pseudomonas product that inhibits the local competition.
Very effective against Gram-positive organisms, including Methicillin-resistant Staph
Not so great against Pseudomonas (for obvious reasons)
Good penetration into deep tissue
Useful for fold pyoderma, chin acne, acral lick granuloma

- Silver sulfadiazine (Silvidene™)
  - Great choice for gram negative infections
  - Open wounds and burns
- Avoid long term use of “triple threat” antibiotic-antifungal-steroid combinations.
- Resistance to aminoglycosides is increasing in skin isolates from dogs (up to 28%).
- Acidifying sprays/wipes. Useful for prevention of recurrence not active disease.

Shampoo therapy
- Adjunctive treatment of active infection as well as long term management of recurrent pyoderma.
- Advantages
  - Broad exposure to larger surface area than achievable with lotions, ointments
  - Direct treatment of target organ using products that are not useful systemically, but are still excellent antiseptics.
  - Very little resistance to ingredients in topical antiseptic shampoos
- Goals
  - Mechanical remove of dirt, oil, debris, and follicular plugs
  - Decrease numbers of bacteria causing pyoderma and folliculitis
  - Decrease recolonization and overgrowth by native flora after pyoderma resolved
  - Restore normal barrier function with moisturizers, emollients, and other.
- Clip long-haired dogs first to maximize treatment of skin rather than hair.
- Contact time is crucial for effective management: 10-15 minutes
- Apply twice weekly until resolved then once every 1 to 2 weeks for maintenance.
- Selection
  - Chlorhexidine best for bacteria on the surface of the skin.
    - Bactericidal in concentrations between 2-4%
    - Causes damage to cellular membrane resulting in leakage of cytoplasm.
    - No known transmissible resistance factors → can’t induce resistant strains
    - Not effective against Pseudomonas
    - Combine sulfur, salicylic acid for treatment of seborrheic patients
    - Combine with Miconazole or Ketoconazole for dogs with cytologic or historical Malassezia dermatitis
  - Benzoyl-Peroxide
    - Disrupts microbial cell membrane, oxidizes and lowers pH
    - Excellent antiseptic. Comparable to Chlorhexidine in concentrations of 2 – 3%.
    - Higher concentrations may be irritating or cause rebound scaling.
    - Excellent degreasing action, very useful in seborrheic patients, especially if combined with sulfur.
    - Follicular flushing action makes Benzoyl Peroxide shampoos the top choice for management of bacterial folliculitis and demodicosis.
  - Ethyl-lactate
    - Changes to ethanol and lactic acid.
    - Also has excellent follicular flushing activity
    - Very few side-effects – useful in sensitive animals or cats that may react with erythema, pruritus, irritation, and scaling to Benzoyl-Peroxide
  - Acidifying shampoos most useful for preventing recolonization rather than treatment of active infections
  - If at first you don’t succeed try a different product

Client communication essentials
You are treating the skin not the hair
Contact time is critical for success (bring a clock or timer)
Focus on problem areas first (longer time on critical area)
Keep massaging for full 10 minutes - don’t just lather and wait. WORK IT!
Praise owners for their efforts
• Leave on conditioners augment shampoo therapy
  o Residual Chlorhexidine provides ongoing antiseptic action to enhance elimination of active infections and suppress recolonization.
  o Microencapsulation prolongs action of active ingredients
  o Can also be used as a lotion in between baths.

Whirlpool
  • Hydrotherapy with chlorhexidine or other antiseptic added to water
  • Provides physical removal of crust, debris, trapped bacteria
  • Increases cutaneous blood flow
  • Useful for deep pyoderma, cellulitis, folliculitis/furunculosis, demodicosis, open wounds, and burns

Anti-inflammatory therapy:
  • May be useful for nodular pedal furunculosis and other foreign body reactions
  • May mask signs of pyoderma, resulting in premature discontinuation of antibiotic.
  • Antibiotics with anti-inflammatory benefit: Tetracyclines, Clindamycin, Metronidazole
  • Steroids? Very useful for acute pyotraumatic dermatitis (hotspots). Definitely avoid in deep pyoderma, demodicosis, or for prolonged usage.
  • Cyclosporin? Beneficial for atopic dermatitis, but research has not specifically evaluated pyoderma. Several cases of nodular pedal furunculosis did not respond until I started Cyclosporin…atopy or inflammation? Hmm.

Immune modulation
  • Staphage lysate - SPL™ (Delmont Laboratories, Swarthmore, PA 800-562-5541)
    o From S. aureus strains, contains large quantities of Protein A (exotoxin)
    o Stimulates B and T cell response against S. intermedius in dogs.
    o Double-blind, placebo control study supports benefit claims.
    o Give 0.5ml SQ twice weekly for minimum of a 12 week trial to judge benefits. If useful – give 1.0ml once every 1 to 2 weeks for life.
    o Manufacture recommends discontinuing corticosteroids before using SPL
  • Immunoregulin™ (Immunovet, Tampa, FL 813-621-9447 subcorp of Neogen 800-477-8201)
    o Bacterin from Propionibacterium acnes
    o Stimulates macrophage activation, lymphokine production, enhance cell mediated immunity, and increase natural killer cell activity.
    o Most useful for difficult deep pyoderma rather than prolonged maintenance therapy.
    o Give with systemic antibiotics
    o Dose by weight of dog
      ▪ Up to 15lb: 0.25 – 0.5ml
      ▪ 15-45lbs: 0.50 – 1.0ml
      ▪ 45-75lbs: 1.00 – 1.5ml
      ▪ Over 75lbs: 1.50 – 2.0ml
    o IV twice weekly for 2 weeks, then once weekly until resolution of active infection
    o If used for long term maintenance give once monthly.
    o IV route of administration limits client acceptance.
    o Do not administer SQ or IM (necrotizing dermatitis, yuck)
    o Do not give concurrently with glucocorticoids
    o Has been associated with anaphylaxis, fever, chills, anorexia, depression
  • Oral “immune stimulants”
    o Limited evidence supporting for usage. Plenty of anecdotal stories.
    o Levamisole: predominantly a T-cell stimulant
      ▪ Effect in animals with T-cell deficiency or dysfunction
      ▪ Limited or no effect in healthy animals
      ▪ Adverse reactions: GI, hepatic, neurotoxicity, agranulocytosis, erythema multiforme, and toxic epidermal necrolysis have all been reported.
      ▪ 2.2mg/kg q48hrs reported to benefit 10% of dogs
    o Cimetidine: Blocks H2 receptor on T-suppressor cells
      ▪ 3-4 mg/kg BID up to 6-8mg/kg TID has been recommended
Few side-effects. Few demonstrated benefits in chronic pyoderma
  - Interferon-alpha (Roferon-A, Roche, Nutley, N.J):
    - Recombinant human cytokine that promotes cell-mediated immunity.
    - Give 1000 – 2000 IU orally SID
    - Comes as 3 million IU in 0.5ml syringe.
    - Dilute in 100ml sterile saline, divide in 0.5ml aliquots (60,000 IU/ml). Freeze.
    - Dilute aliquots with 29.5 ml saline to get 30ml (1000 IU/ml) as needed.
    - Very few side-effects at this dosage

Extended antibiotic regimen
- Consider if recurrent pyoderma in spite of effective treatment of underlying disease AND shampoo or immunomodulation is ineffective.
- Also useful in cases of primary staphylococcal hypersensitivity
- Do not use in place of thorough diagnostic investigation for primary disease.
- Prefer to use Cephalosporins due to low incidence of acquired-resistance.
- Recommend against using fluoroquinolones, Clindamycin, or Clavamox due to possible selection for resistant bacteria. Okay if no other choices
- Strongly advise against using any potentiated sulfonamides long term due to high risk of irreversible damage to lacrimal glands, adverse drug reactions (erythema multiforme, hemolytic anemia, thrombocytopenia), hypothyroidism, fever, joint pain, etc etc etc.
- Protocols
  - 2 days on, 5 days off. (Give full dose on Sat and Sun, Off Mon through Fri)
  - One week on, one week off
  - Do not use sub-therapeutic doses daily

Some specific conditions worth some final comments

Mucocutaneous pyoderma: Cause for depigmentation and painful inflammation on nasal planum and lips. German Shepherds seem especially prone. Easily confused with Discoid Lupus Erythematosus both clinically and on biopsy. Some cases may warrant “antibiotic trial” prior to biopsy.

Vulvar fold pyoderma: Painful, ulcerative dermatitis associated with staphylococcus, E. coli, Pseudomonas overgrowth and infection. This is a surgical disease, not a medical one. Antibiotic therapy prior to surgery is great, but prognosis for long term success is miserable without surgical intervention. If you don’t feel comfortable performing episoplasty refer to surgical specialist…your patient and client will thank you.

Acral lick granuloma: Historically misclassified as a primary behavioral dermatosis. Lick granulomas are more often than not expression of allergic disease, coupled with deep pyoderma and foreign-body reaction to free hair shafts in ruptured follicles. Lick lesions are complicated by behavioral reinforcement, but are rarely primary behavioral problems. Treat lick granulomas as deep pyoderma with allergic trigger and you will be much more impressed by your results. Treatment ideas: Cephalosporin at adequate dose for a minimum of 12 weeks. Topical mupiricin ointment (Bactoderm™) BID. CO2 laser surgery to ablate scar tissue and foreign body reaction to ruptured hair shafts. Manage allergy.

Scalded Skin Syndrome: Actually this is a human disease characterized by colonization by Staphylococcus aureus strains that produce exfoliative toxins A or B. This causes separation of Stratum corneum from underlying living layers of epidermis, resulting in a shiny appearance to the lesion and profound erythema, pruritus, and inflammation. Similar skin disease has been reported in dogs, with profound inflammatory pyoderma characterized by “shiny” lesions. Similarly Staphylococcus induced “Pemphigus foliaceus” has been associated with exfoliative exotoxin producing strains of Staphylococcus. Aggressive long term antibiotic and topical antiseptic therapy is recommended for both cases. Relapse is common.

Suggested reading:
1. DeBoer DJ. Management of chronic and recurrent pyoderma in the dog. In Bonagura JD, Kirk’s Current Veterinary Therapy Xll. 611-617. 1995
Guide to Management of Canine Pyoderma

History: Gear towards diagnosing underlying disease: Age of onset? Seasonality? Diet? Higher risk for parasite exposure? Regular flea/tick control? Previous response to antibiotics/steroids/thyroid supplementation? Is it an itch that rashes or a rash that itches?

Physical exam: Distribution? Concurrent signs? Superficial or Deep? Greasy or Dry?

Initial diagnostics:
- 4 essential tests: Cytology, Scraping, DTM culture, and Parasite treatment trial
- If appropriate: Thyroid panel, Food trial, Allergen-specific testing, screen for Cushing’s

Initial therapy:
- Systemic antibiotic for 3-6 weeks.
  - Convenia (injection, re-evaluate for second injection in 14 days)
  - Simplicef (SID)
  - Cephalexin or Clavamox (BID)
  - Baytril, Zeniquin (SID) if gram negative. Do not use first line for gram positive infections.
- Appropriate shampoo/conditioner if generalized or Bactoderm if localized.
- Aggressive flea control – “Golly, this probably isn’t fleas Mrs. Johnson, but I’d sure hate for Fluffy to get fleas while we are doing all these tests to figure out what is causing her problems” Or “Ya know, I believe in controlling the things we can. I can’t control ragweed pollen, but I can control fleas”

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Dose (mg/kg)</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefovecin Convenia</td>
<td>8</td>
<td>1 or 2 injections</td>
</tr>
<tr>
<td>Cefpodoxime Simplicef</td>
<td>5 – 10</td>
<td>SID</td>
</tr>
<tr>
<td>Enrofloxacin Baytril</td>
<td>5 – 20</td>
<td></td>
</tr>
<tr>
<td>Marbofloxacin Zeniquin</td>
<td>2.75 – 5.5</td>
<td></td>
</tr>
<tr>
<td>Orbifloxacin Orbax</td>
<td>2.5 – 7.5</td>
<td></td>
</tr>
<tr>
<td>Difloxacin Dicural</td>
<td>5 – 10</td>
<td></td>
</tr>
<tr>
<td>Ormethoprim-Sulfadimethoxide Primor</td>
<td>27.5</td>
<td></td>
</tr>
<tr>
<td>Cephalexin</td>
<td>22 – 30</td>
<td>BID</td>
</tr>
<tr>
<td>Amoxicillin-Clavulanic acid Clavamox</td>
<td>15 – 22</td>
<td></td>
</tr>
<tr>
<td>Clindamycin Antirobe</td>
<td>5 – 10</td>
<td></td>
</tr>
<tr>
<td>Trimethoprim-sulfadiazine Tribrisen</td>
<td>15 – 30</td>
<td></td>
</tr>
<tr>
<td>Lincomycin</td>
<td>20 -30</td>
<td></td>
</tr>
<tr>
<td>Oxacillin</td>
<td>22</td>
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</tr>
<tr>
<td>Cloxacillin</td>
<td>20 – 40</td>
<td></td>
</tr>
<tr>
<td>Erythromycin</td>
<td>10 – 15</td>
<td></td>
</tr>
</tbody>
</table>

Recheck: 2-4 weeks – ask client to rank 1-10: pruritus, odor, appearance of skin. Repeat cytology.
- If good response, treat for 1-2 weeks beyond “cure” and proceed to maintenance therapy.
- If not improved – evaluate all causes for treatment failure listed above
  - Client compliance – verify and reinforce
  - Antibiotic selection, dosage, and interval
  - Consider culture if you truly suspect resistance
  - Repeat skin scraping and DTM to be sure you didn’t miss the common differentials
  - Any time dermatitis fails to respond to appropriate therapy for current diagnosis → biopsy biopsy.

Maintenance therapy:
- Treat primary underlying disease
- Shampoo/conditioner every 1 to 2 weeks life long
- Immune modulation therapy (personally I like Staphage Lysate)
- Consider extended antibiotic regimen
Suds not drugs: Topical therapy for Methicillin-resistant Staphylococcal pyoderma

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INTRODUCTION
Veterinarians see a lot of bacterial skin infections. Indeed bacterial dermatitis is the 3rd most common insurance claim reported for dogs by Veterinary Pet Insurance. In most cases the infection is associated with colonization by Staphylococcus pseudintermedius. S. pseudintermedius is a resident organism on the skin that acts as an opportunistic pathogen. Staphylococcal pyoderma is not spontaneous, but is rather due to changes in the microenvironment that favor opportunistic colonization, over population and subsequent infection. This is often referred to as bacterial overgrowth syndrome. Common primary diseases that create the conditions necessary for bacterial overgrowth include atopic dermatitis, food allergy, ectoparasites, hypothyroidism, and hyperadrenocorticism. Since many of the underlying disease that makes it easy for S. pseudintermedius to create a clinically relevant pyoderma are chronic, frequent relapses occur even after successful treatment of the initial infection. We recognize this as chronic reoccuring superficial pyoderma, epidermal collerettes, pustular pyoderma, malodorous seborrhea, friction fold dermatitis, and bacterial folliculitis. For many years management of bacterial skin disease focused on systemic antibiotics with antiseptic shampoo utilized as adjunctive to assist or accelerate resolution. While useful topical antiseptics were not critical to successful outcome of simple superficial pyoderma or folliculitis. In general, wild type strains of Staphylococcus pseudintermedius are susceptible cephalosporins, augmented amoxicillin, semi-synthetic penicillins, or any number of other antibiotic classes. However in the last 10-15 years there has been a steady rise in incidence of methicillin-resistant Staphylococcus isolated from canine patients. While methicillin-resistant Staphylococcus aureus (MRSA) usually occurred in patients with close contact to a human carrier or contaminated environment, methicillin-resistant Staphylococcus pseudintermedius (MRSP) seems able to colonize and infect susceptible dogs without an identified human carrier; we suspect it is capable of become a normal resident organism on dogs and transmission can occur dog to dog, human to dog, environment to dog is on the rise. Now MRSP is a common isolate from dogs with Staphylococcal pyoderma (cite a couple studies here). Worse still, MRSP antimicrobial susceptibility pattern is not limited to beta-lactam antibiotic resistance, but can include resistance to 3 or more classes of antibiotics routinely used in veterinary medicine including fluoroquinolones, sulfonamides, macrolides, tetracyclines, etc. As a result veterinarians are frequently left with less desirable systemic antibiotics such as chloramphenicol, rifampin, and aminoglycosides. Several analyses of data demonstrated that the single most significant risk factor for having a MRSP infection in a dog is previous use of antibiotics. So in dealing with a methicillin-susceptible Staphylococcal or MRSP dermatitis there is strong motivation to find effective alternatives to systemic antibiotics.

SHAMPOO THERAPY
Water itself is therapeutic for dermatologic disease. Water provides physical removal of irritants, allergens, and loosening of crust, scale. Water hydrates the stratum corneum, softens keratin, and reduces transepidermal water loss. One study demonstrated, whirlpool bathing alone without any additional agents other than water has demonstrable reduction in pruritus. The hydrating benefits of water therapy are improved when followed with an emollient or oil layer that assists in retention of water in the epidermis after thorough soaking. Since the skin is located on the outside of the dog, shampoo is an ideal vehicle for delivery of antiseptic agents to reduce bacteria overgrowth and infection. Imagine how the veterinarian managing pneumonia would rejoice if they had a method to exteriorize the lungs and bathe them in a safe and effective antiseptic before tucking them gently back into the patient! With skin infections it is possible to fully resolve superficial pyoderma and bacterial folliculitis without relying on systemic antibiotics.

The most common active antiseptic ingredients in commercially available veterinary shampoo products are benzoyl peroxide, chlorhexidine, ethyl lactate, and acetic, boric, malic acid mixtures. Many of these will also be combined with an imidazole product for management of concurrent Malassezia dermatitis. Additional ingredients can be added to enhance antimicrobial therapy. A carbohydrate, such as mannose, d-galactose, or l-rhamnose is added to inhibit bacterial adherence to keratinocytes. TrisEDTA may have a synergistic antimicrobial action by damaging bacterial cell walls. Phytosphingosine (a pro-cerumide) is directly antiseptic in high concentrations and may increase epidermal barrier function resulting in resistance to future colonization. Sulfur salicylic acid is frequently combined with benzoyl peroxide to enhance keratolysis and debris removal.
Regardless of the product selected contact of the active ingredient with the target organism is necessary for efficacy. That means – frequent and correct use by owner, removal of obstacles to correct use. First, are the owners able to bathe the patient frequently? In the case of managing active MRSP that may mean daily or every other day bathing. As an adjunctive to systemic antibiotics or in the interest of preventing bacterial overgrowth syndrome and relapsing bacterial infection that may mean 1-2 times per week. Is the patient amenable to bathing? Do the owners have the facilities? Do they have back problems or other physical obstacles? Troubleshoot with the owners – can they bathe outdoors? Use a walk in shower/bath with a detachable handheld nozzle? Negotiate a price package with a local groomer? Pay a neighborhood kid? Or, if critical to outcome of therapy, I strongly recommend offering therapeutic bathing in your clinic.

Does the patient have a long, thick coat? The goal is contact with the skin and hair follicles not the hair itself. If so, a short groomed coat is better than a long, thick coat. Rarely is a surgical clip warranted as this may further traumatize the skin. If there is excessive debris, dirt, crust, adherent scale, or seborrhea obstructing the skin, then use of a pre-bath with a shampoo designed for seborrhea is useful prior to application of the medicated shampoo. For deep pyoderma, prolonged hydrotherapy with pulsatile action, whirlpool, or simple warm water soak is highly beneficial to dilate the vascular plexus, soften crusts, open hair follicles, and open draining tracts. Then application of the antiseptic shampoo or rinses has a larger impact. Ideally the product should be aesthetically pleasing to the owner. This may include odor, luxurious texture, moisturizing, or even the shape and color of the bottle.

Verbal communication and frequent encouragement is required to increase owner compliance and adherence to the medical plan. Explain the key benefits of bathing: (1) physical removal scale, crust, debris, irritants, and allergens (2) moisturizing the skin (3) reduced pruritus, (4) reduced infection, (5) reduced odor, (6) repairing or restoring epidermal barrier function. It is in the owner’s and their dog’s best interest to bathe their dog frequently; by doing so they can reduce the need for systemic therapy. Tell owners to “Treat the problem area first, then the rest of the body, rinse in reverse order.” When most owners bath their dogs, they get the dog wet, put a line of product down the spine and swish around with their hands for 5-10 minutes then rinse. 80% of the product and 80% of the time is spent on the patient’s back. That is not particularly effective if most of the infection is on the ventral neck, axilla or groin. By telling owners to start on the problem areas first, you direct the majority of time, product, and attention to the most affected skin. Then work other areas before rinsing in reverse order. Even if the owner is trying to rush through the process they are certain to get at least 5 minutes contact time on lesional skin. If the patient is a long coated dog, then clipping the hair may enhance skin contact time as well.

**RINSES**

After shampoo therapy, the patient is rinsed but still sits before the owner wet, free of dirt, debris, crusts, and scale. The skin is hydrated. The hair follicles are open. This is the ideal time to lock in hydration, clobber any remaining bacteria, or apply a product with residual antimicrobial action. In the case of MRSP, I have two favorite rinses: Dakin’s Solution or accelerated hydrogen peroxide (Pure Oxygen, Ogena Solutions). Dakins solution is a 0.5% sodium hypochlorite solution that was produced for wound therapy during World War I, prior to the advent of penicillin. Now that we are once again dealing with Staphylococcus with limited susceptibility to routine, safe, efficacious antibiotics, Dakin’s solution has reemerged as an effective topical therapy for MRSA and MRSP pyoderma. Dakins solution in full or ½ strength can be purchased premade or can be made easily at home by combining 3 common house hold ingredients: water (32 ounces), 5.25% bleach (3 ounces), and baking soda (1/2 teaspoon). Since organic debris greatly inhibits the action of Dakin’s solution it is used after bathing or on otherwise clean skin. Generally I prefer half-strength solution, using the above formula with only 1.5 ounces of 5.25% bleach. Owners apply with sponge after a bath, soak to the skin until thoroughly wet, do not rinse. Because bleach can discolor fabrics, I advise owners to wear clothes they would paint in, apply outside, and take dogs for walks until dry. The solution can also be placed in a spray bottle to apply to focal areas in between baths. White dogs can get an orange discoloration to the fur.

An alternative to Dakin’s solution is Stabilized or Accelerated Hydrogen Peroxide (Pure Oxygen, Ogena Solutions). Accelerated hydrogen peroxide is an enhanced or stabilized hydrogen peroxide with proven action against MRSA, virus, and fungal pathogens when used as an environmental cleaner (Accel or Virox, Ogena Solutions). Pure Oxygen is a modification of the cleaner that is appropriate for use directly on patient’s skin. My clinical observation of the product is that accelerated hydrogen peroxide can be as or more effective as Dakin’s solution, less noxious for owners, and less likely to stain or discolor fur or fabric. Either Dakin’s or Pure Oxygen solution can be sponged or sprayed onto the skin to the point that it appears wet then allowed to dry. For deep pyoderma definitely want to sponge on or otherwise completely soak affected area.
Vetericyn (Innovacyn Inc) is a stabilized oxychlorine product with a neutral pH. This product also has demonstrated in-vitro activity against both antibiotic susceptible and methicillin-resistant strains of Staphylococcus and is an excellent commercial alternative if owners are reluctant to use Dakin’s solution.

OTHER TOPICAL THERAPY
In specific cases there are additional therapies that can augment antiseptic shampoo/rinses. For owners that are unable or unwilling to bathe their dogs frequently many of the same antiseptic ingredients such as chlorexidine can be found in sprays, lotions, or mousse products designed to be applied and left on the skin. For fold pyoderma or localized dermatitis is prefer to use wipes, pads, and ointments/gels. In addition to the common antiseptic ingredient containing products also consider using Nisin wipes (Preva wipes, DVM pharmaceutical a Bayer company). Nisin is an antimicrobial peptide that was developed and marketed for treatment and prevention of bovine mastitis. It is particularly effective against Staphylococcus, including methicillin-resistant strains. Nisin is not effective against Pseudomonas. Mupirocin ointment is an excellent choice for Staphylococcus and is recommended frequently for lip fold pyoderma or focal deep pyoderma, but has little action against gram-negative bacteria. Silver sulfadiazine is a favorite for Pseudomonas. Hyperosmolar honey or sugar therapy is highly effective in management of deep wounds, burns, or otherwise severely compromised skin with secondary bacterial contamination.

Protocol for MRSP with topical alone
(1) Deep soak, whirlpool, or pulsating hydrotherapy prior to medicated bath. Clip hair if necessary
(2) Benzoyl Peroxide Shampoo – focus on problem area first the rest of the body. Deep massage for 5-10 minutes then rinse thoroughly
(3) 3-4% Chlorhexidine Shampoo – same process as Benzoyl Peroxide. Rinse.
(4) Accelerated Hydrogen Peroxide or Dakin’s Solution rinse. Soak to skin. Do not rinse.
(5) Repeat DAILY for 10-14 days then reassess. If resolved, then repeat 2 times per week for 4 weeks. If not resolved, continue DAILY therapy switching up topical products as needed.

Protocol for maintenance therapy of dogs with high probability of relapse
(1) 3-4% Chlorhexidine Shampoo – focus on past problem areas first, then the rest of the body. Rinse in reverse order.
(2) Apply rinse of choice – antiseptic, antipruritic, or intensive moisturizing
(3) Repeat 1 to 2 times per week
(4) If unable to bath weekly, then bathe a minimum of every 2-3 weeks and use topical spray or mousse with chlorhexidine 2-3 days per week

SUMMARY
Safe, effective topical antiseptic therapy can be used alone to resolve superficial pyoderma, bacterial folliculitis, and in some cases deep pyoderma when faced with multidrug resistant bacteria. Continued use of topical antiseptics after resolution can decrease the frequency and severity of relapsing or recurrent pyoderma associated with chronic skin diseases such as atopic dermatitis, food allergy, demodicosis, hypothyroidism and hyperadrenocorticism. In all cases, antiseptic shampoo/rinse is a useful adjunctive therapy with systemic antibiotics to maximize probability of successful outcome

SUGGESTED READING:
• May ER. Bacterial Skin Diseases: Current thoughts on pathogenesis and management. **Vet Clin Nor Amer: Sm Anim Pract.** 36:185-202, 2006
Dr. Angus graduated from University of California Davis in 1994. After obtaining his degree in Veterinary Medicine, he worked in a private small animal and emergency practice for five years. Dr. Angus completed his residency in dermatology at the University of Illinois and became a Diplomate in the American College of Veterinary Dermatology in 2003. He remained at the University as a visiting clinical professor until 2004, where he received recognition as a teacher of excellence. Dr. Angus joined Animal Dermatology Clinic in 2007 and sees patients in Pasadena, CA.

Dr. Angus has written extensively for journals, veterinary textbooks, and is frequently invited to speak at national and international conferences. Currently Dr. Angus serves as a member of the ACVD Education Committee and is on the editorial boards for the Journal of the American Animal Hospital Association and Veterinary Dermatology, the official journal of the European Society of Veterinary Dermatology.