Diagnosing and Managing Cutaneous Adverse Food Reactions
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The ACVD task force on canine atopic dermatitis (cAD) defined cAD as a genetically-predisposed inflammatory and pruritic skin disease, most commonly associated with IgE antibodies to environmental allergens. This author believes that the definition should be expanded to include food allergens with or without IgE involvement. Regardless of the trigger symptoms of cAD may wax and wane leading to confusion as to whether the pruritus improved because of a therapy or in spite of a therapy. It is important to remember that there are many other causes for pruritus in the dog. In veterinary medicine the criteria for diagnosing cAD has evolved over time. Historically 1 of 2 sets of criteria have been used for making the diagnosis of cAD. The problem with these previous criteria is the former was never validated while the later had a limited sample size. The most current guideline was proposed by Favrot. Please note that before applying these criteria to a pruritic dog, other causes of pruritus, such as ectoparasites or infectious causes, need to be ruled out. This is the reason you shouldn’t use the criteria alone to make a diagnosis of cAD. History, physical examination, diagnostic testing and response to treatment should also be evaluated.

The criteria used to establish a diagnosis of cAD include
1. Onset of signs under 3 years of age
2. Dog living mostly indoors
3. Glucocorticoid-responsive pruritus
4. Pruritus sine materia at onset (i.e. alesional pruritus)
5. Affected front feet
6. Affected ear pinnae
7. Nonaffected ear margins
8. Nonaffected dorso-lumbar

Using these criteria, if 5 criteria are matched, and ectoparasites and infectious causes have been ruled out, the sensitivity and specificity are about 85% and 79% respectively. This means that using only this criteria, a wrong diagnosis will be made about 20% of the time.

Once you have established a diagnosis of cAD it is important to identify triggers that may cause the cAD to flare up. Triggers include
1. Environmental allergens
2. Food allergens
3. Ectoparasites
4. Infectious (bacterial, Malassezia)

This lecture is going to focus on food allergens as the trigger.

Food allergy (FA) is recognized as a potential cause of various dermatological and gastrointestinal (GI) signs in the dog and cat. The exact incidence of FA is unknown. However, the term “allergy” is often used indiscriminately. Acquaintance with exact terminology is important when dealing with FA.

The current terminology of adverse food reactions is advised by the “American Academy of Allergy and Immunology” and the “National Institute of Allergy and Infectious Disease.” Adverse food reactions (food sensitivity) are divided into two categories: immunological and non-immunological reactions. Food allergy (food hypersensitivity) implies an immunological reaction following food intake. Non-immune mediated reactions are indicated as food intolerance (FI). Food idiosyncrasy, food toxicity, food poisoning, anaphylactic food reaction, pharmacological and metabolic food reactions are all forms of FI.

Clinical signs of cutaneous manifestation of an adverse food reaction (CAFR) are identical to that of environmental triggered cAD. The only clue that the dog may have a CAFR is that there MAY be GI signs present. In regards to an environmental trigger, the only definitive clue is if the dog has a history of seasonal symptoms.

An elimination diet trial (EDT) is the ONLY diagnostic tool that is useful in dogs with suspected adverse reactions to food. In vitro testing, biopsies, intradermal skin testing and gastroscopic food sensitivity testing are not reliable for diagnosing FA. Be aware that an EDT doesn’t give any information about the underlying immunologic mechanism. Although FI can also be identified with an elimination diet it is generally accepted that most of the animals with adverse reactions to food do suffer from FA if cutaneous signs are present.

The first step in performing an EDT is to identify 1 protein and 1 carbohydrate that the dog has not previously eaten and feed that to the dog for 60 days. No other food, treats, flavored medications, etc should be fed during the EDT. The dog is then re-examined 30 and 60 days after beginning the EDT. If symptoms resolve, the dog is then “challenged” with his original diet, expecting exacerbation of the pruritus within 14 days. Within 14 days of going back on the EDT, symptoms should once again resolve.
What diet should be used to diagnosis CAFR? The choices are a commercial novel protein, a limited antigen or a home cooked diet. A diet can only be “hypoallergenic” if the animal was never exposed to the food components before. The identification of what is truly a novel protein for any given individual is determined by a very detailed dietary history. Because of the enhanced complexity of pet foods, it has become more difficult to compose a suitable elimination diet.

Regardless of what type of diet is used to diagnose CAFR there are a number of potential pitfalls to avoid. A common mistake made during food trials regardless of the diet used is using flavored heartworm preventative. This was reported in an abstract in which there were 12 dogs with natural occurring CAFR to either soy or corn. The author fed a flavored heartworm preventative fed to each dog. This preventative contained pork liver and soy (Interceptor). A clinical score (CS) was assigned based on the severity of skin and otic disease. After 1 pill 10/12 dogs had an increase in CS. In 5/12 dogs the values peaked on day 2 post challenge while in 5/12 dogs it occurred on day 5.

Another potential problem is the use of supplements or medications during the food trial. In a study by Parr et al, the authors tested 7 supplements for the presence of soy, pork, or beef antigens. Three were flavored OTC products and 4 were veterinary therapeutics. All OTC test products produced ELISA results in agreement with their ingredient lists. ELISA testing of veterinary therapeutic products did not agree with either their ingredient lists or product inserts because of other ingredients not listed. In 1 product the “artificial beef flavor” was made using pork liver and 1 arthritis product listed “natural flavors” which was determined to be a spray-dried digest derived from pork liver. Another potential problem identified was administering supplements/medications that were in a gelatin capsules. This is because the gelatin is derived from beef or pork. This lead the authors to recommend that veterinarians contact manufacturers of oral therapeutics prior to prescribing them during a dietary elimination trial to determine the other ingredients in those products that may not be listed on the ingredient list or product insert.

Mislabeling is not limited to supplements. A study was done using 12 dog foods (eleven novel protein diets and one hydrolyzed diet) from five different manufacturers, both international and Italian, for potential contamination by animal origin ingredients that were not mentioned on the label. The food was analyzed using both the official method (microscopy to identify bone fragments of different zoological classes (mammalian, avian and fish) and by polymerase chain reaction (PCR) for the identification of DNA of animal origin. In 2/12 samples the results of both analyses match the ingredients listed on the label. In the remaining 10 samples, microscopy detected bone fragments from 1 or 2 unlabeled zoological classes. In 6/10 samples there were undeclared avian fragments, 5/10 had fish and 4/10 had mammalian fragments. In two samples, microscopy analysis identified a contamination that would have otherwise passed unobserved if only PCR had been used. However, PCR identified the DNA of undeclared zoological class in 2 samples. The conclusion by the authors was that dogs might fail to respond to commercial limited antigen diets because such diets are contaminated with potential allergens. Both PCR and microscopy analysis are required to guarantee the absence of undeclared animal sources in pet foods. Lastly a study by Okuma et al collected 52 commercial dog and cat food products from southern California and on line. They tested the foods for the presence of eight meat species (bovine, caprine, ovine, chicken, goose, turkey, porcine, and equine) using real-time polymerase chain reaction (PCR). Of the 52 products, 31 were labeled correctly, 20 were potentially mislabeled because they either (1) contained meat species that were not included on the product label (16) and/or (2) did not contain meat species that were included on the product label (7) - note some food had both problems. One food contained a non-specific meat ingredient that could not be verified. Pork was the most common undeclared meat species detected. There was also a trend to substitute lower cost ingredients, such as poultry meats, for higher cost ingredients, such as beef and lamb. These studies support the position that before ruling out AFR, a novel protein home-made diet trial should be performed.

An appropriate elimination diet should contain 1 new, highly digestible protein or a diet that contains hydrolyzed proteins. Ideally a homemade diet (HMD) should be fed. This is the type of diet the author uses. A HMD consists of one protein and one carbohydrate. The protein usually is rabbit, venison, goat, ostrich, emu or alligator. White or sweet potatoes, oats, quinoa or rutabaga are appropriate carbohydrate sources. It is mixed 1 part meat and 3 parts carbohydrate and the dog is given 1-2 cups of the mixture/10#.

HMDs should not include ANY other ingredients. The dog must not ingest any other food, treats, tidbits, etc including items used to hide medication in. Avoiding gelatin capsules should be attempted. This may be difficult because some medications only come in a capsular form (e.g. modified cyclosporine). The problem with HMDs is that they are nutritionally inadequate for growth and maintenance therefore they are not using in growing dogs or for long term maintenance. Because they are not very calorically dense most animals will lose weight on these diets. If a dog has a body score of 4/9 or less, this author does not use a HMD. Although a HMD is not nutritionally balanced nor complete, supplements are not necessary, nor used, during the short test period. When a HMD is given during a prolonged time, it is recommended to consult a veterinary nutritionist to formulate a balance diet.

Although the gold standard for diagnosing CAFR is a HMD there are circumstances where the author will use a commercial diet instead. Examples include owners who will not cook for the dog, if the dog doesn’t tolerate HMDs (typically because of weight loss but some dogs will become lethargic on them or have GI disturbances). They are not fed to growing dogs.

Commercial novel protein diets (NPDs) can be used to diagnosis CAFR and also can be used long term to maintain a dog with CAFR. A variety of NPDs are available for dogs. These diets are readily available but do not have a 100% negative predictive value (false negatives occur 25-50% of the time). A number of studies have demonstrated the problems associated with NPD. In the first study...
they fed dogs with proven CAFR either venison/rice, chicken/rice or catfish/rice commercial dog food. When fed the venison dog food 85% of the dogs with CAFR reacted while 52% and 47.5% reacted to chicken and catfish dog food respectively. More recently 3 of 4 over the counter (OTC) dog foods that didn’t list soy on their ingredients list had soy identified via ELISA testing. More disturbing was the study that reported 3 out of 4 OTC dog foods that specifically stated “NO SOY” had soy found when ELISA testing was performed. Note that in the same study 2 of 3 hydrolyzed soy diets had intact soy identified.

Commercial hydrolyzed protein diets (HPDs) contain proteins that been enzymatically hydrolyzed to smaller molecules. This reduces the MW of the original protein which leads to a decrease in the antigenicity and allergenicity of the protein. This means that the molecules are too small to evoke a cross binding between IgE on the surface of the mast cell. This prevents degranulation of the mast cell and IgE-mediated (Type I) hypersensitivity. This is a key point, if the CAFR in that dog is not caused by IgE but by some other mechanism (e.g. type IV which is a T cell driven disease) the size of the molecule doesn't not matter and the diet will be ineffective. The optimal MW of a protein hydrolysate in dogs has not been agreed upon. Note that these diets are only partially hydrolyzed. This means that only a percentage of the protein is hydrolyzed- there is still some intact protein remaining. In the humans, peptides with a MW as low as 3000 Da are still capable of an allergic reaction. Free AA are not allergenic, but are not suitable in foods because of their bitter taste, high osmolarity (leading to diarrhea) and very high costs. As with the NPD, HPD are not able to diagnose CAFR in all dogs- they probably miss about the same percentage as the NPD.

Regardless of which diet is used there are a few points to discuss. Many owners believe that food additives (dyes and preservatives) are common food allergens in dogs, yet there has not been even 1 published case report documenting this. The length of time for the diet depends on the dog’s response or failure to respond. It should be continued until clinical signs resolve OR 60 days, whichever is shorter.

Which ingredients cause the most reactions? In 265 dogs reported collectively by 12 different studies, beef, dairy products, and wheat accounted for two thirds of reactions. Reactions to corn, pork, rice, and fish were rarely reported in dogs. In the April 2013 issue Veterinary Dermatology a letter to the editor reported the most common ingredients causing CAFR in 330 dogs- beef, dairy, chicken and wheat accounted for 78% of the reactions. Of 56 cats reported collectively by 10 studies, beef, dairy products, and fish accounted for 80% of reactions.

Maillard reactant products are formed when proteins are cooked with carbohydrate. They can increase or decrease the allergenicity of proteins, depending on the food component. This phenomenon may explain the apparent increase in allergenicity of proteins in commercial pet foods compared to fresh proteins. Because of this, the author suggests that when preparing the HMD the protein and carbohydrate should be cooked in separate pots.
Pemphigus

Pemphigus foliaceus (PF) is the most common form of pemphigus and is probably the most frequently diagnosed autoimmune skin disease (AISD) affecting cats and dogs. In general, PF is a disease of young to middle aged animals. Any dog may develop PF but Chow Chows and Akitas have a higher incidence in the author’s practice.

Historically, the owner may report that the lesions wax and wane or are progressive. The progression of the disease may be slow, especially cases with only facial involvement, or the dog may develop acute eruptions (most commonly associated with generalized disease). With the generalized form the dogs frequently will be febrile, may have limb edema and have constitutional signs. Pruritus with any form varies from non-existent to moderately intense.

There are 3 primary distribution patterns of PF -facial (most common) form which involves the bridge of the nose, nasal planum, periorbitally, pinnae (especially in cats); a footpad form (cats may present only with paronychia) and a generalized form where lesions usually begin on the face and then spread.

Because there is involvement of the hair follicles, multi-focal to diffuse alopecia is frequently present. The primary lesions of PF are large nonfollicular pustules (there are also follicular pustules present). The pustules that are present in a bacterial pyoderma usually involve the ventral abdomen and/or trunk and are much smaller than those seen with PF. Other lesions include epidermal collarettes, yellow brown crusts and erosions.

Differential diagnosis would include any pustular, crusting and scaling disease such as: pemphigus erythematosus; zinc responsive dermatosis (especially with foot pad involvement); metabolic epidermal necrosis (especially with foot pad involvement); bacterial and fungal (dermatophytosis) infections; demodicosis, DLE (facial/nasal form); erythema multiformae; mycosis fungoides; Leishmaniasis; and sebaceous adenitis.

Diagnosis

A cytologic prep of a pustule or crust should be performed. Microscopic findings would include acantholytic keratinocytes, either individually or in clusters, surrounded by NON-degenerative neutrophils and/or eosinophils- bacteria should not be seen. Histopathology is the only definitive means to diagnose pemphigus. An intact pustule (or if none are present, a crusted lesion) should be biopsied. Infectious diseases that produce proteases, such as a bacterial pyoderma or a dermatophyte infection (Trichophyton mentagrophytes), can breakdown the intracellular glycoproteins (desmoglein) leading to acantholysis. Because these infectious diseases mimic PF histologically, you should request special stains for both bacteria (gram stain) and fungi (GMS, PAS) anytime a there is a histopathologic diagnosis of PF.

Prognosis

PF may be drug related, either drug-induced or drug-triggered. The drug-induced form PF is caused by a drug and upon removal of the drug, sometimes with a short course of immunosuppressive treatment, the disease resolves. Drug-triggered PF occurs when a drug stimulates a genetically predisposed individual to develop PF. Typically, this form of PF must be managed long term, similar to idiopathic PF. Currently there is no way to identify which cases of drug related PF are drug induced and which ones are drug triggered. In fact there is no test that can be used to predict how well a case of PF will respond to treatment.

A study at NCSU revealed that 6 of 51 dogs (11.7%) with PF were weaned off all medication and stayed in remission for >1 year. Recognizing that PF is a sunlight aggravated disease, it was interestingly the dogs in this study were from areas (NC or Sweden) with high UV light exposure. In this report the dogs took 1.5–5 months of therapy before the disease was in remission. The drug(s) were then slowly tapered and then all therapy was stopped. The total duration of immunosuppressive therapy varied between 3 and 22 months. These dogs stayed in remission for the entire follow up period (1.5–6 years after treatment). Supporting this finding is a study from the University of Pennsylvania that reported that 10% of their cases went into long-term remission after weaning off medication.

This study performed at the University of Pennsylvania suggests that dogs with PF survived longer when given antibiotics (usually cephalaxin) in addition to their immunosuppressive regimen. This is in contrast to the author’s clinical observation that if dogs with PF do develop a concurrent pyoderma it only occurs AFTER being placed on immunosuppressive therapy. Supporting the author’s observations is a study from CSU that reported that there was no difference in survival when antibiotics were part of the initial treatment. In the study from University of Pennsylvania the survival rate was approximately 40% with 92% of the deaths occurring by 1 year. Other researchers have reported having a long-term survival rate of approximately 70%.

Cats may have a better prognosis than dogs with this disease. In the same report from the University of Pennsylvania, only 4/44 cats treated died (from their disease or therapy) during the study period. In the author’s practice, survival at 1 year also exceeds 90%. In addition, a significant number of the cats are eventually able to have all medications discontinued without suffering a subsequent relapse.
**Treatment**

Managing any AISD takes frequent rechecks and alertness to complications associated with immunosuppressive therapy such as demodicosis, dermatophytosis and bacterial pyoderma. Interestingly the author has rarely seen a dog with PF that had a secondary pyoderma at initial presentation. It is more common to develop after beginning immunosuppressive therapy. If a patient was controlled and then has a relapse or if the patient has been improving and suddenly worsens, there are 2 possibilities. The PF (which does wax/wane) is flaring up OR that the dog developed a secondary infection due to immunosuppression. If the new lesions are folliculocentric you must also rule the big 3 folliculocentric infections – bacteria, demodex and dermatophyte.

Skin scrapings, Wood’s light examination (screening test) and impression smears are the minimum data based that should be performed when a dog is presented with these lesions. Whether or not you need to do a fungal culture at this time depends on the how frequently you see dermatophytosis in your practice and what is seen on cytology (acantholytic keratinocytes, cocci, demodex mites). If dermatophytosis is commonly seen in your practice then a fungal culture should be performed. Otherwise a fungal culture and a repeat skin biopsy can be considered second tier tests to be performed if the case doesn’t respond to appropriate therapy (eg antibiotics)

In addition to the treatment options listed below, shampoo therapy should be included for symptomatic treatment of the crusting dermatitis. Pending biopsy results, if intracellular cocci are seen on cytology the author will dispense cephalaxin (10-15 mg/# bid-tid), unless there is a suspicion that it is a case of cephalaxin induced PF. If only extra cellular cocci are seen, then topical shampoo therapy with an antiseptic (eg chlorhexidene, benzoyl peroxide, etc)

Treatment must be individualized for each patient since there is no “best” treatment that works in all PF patients. This is why monitoring the progress of the disease closely by PHYSICALLY examining the dog or cat is critical for successful management of PF. It is especially important to recheck the patient prior to any adjustment in medication. When devising a treatment plan, be sure to consider the severity of the disease so that the treatment side effects are not worse than the disease itself.

There may be regional differences in how aggressively PF needs to be treated. Some of this may be due to the differences in the gene pools of the patients. But since PF is a sunlight aggravated disease, it also may be related to the differences in sun exposure. Regardless of the locale, sun avoidance should be part of the treatment for PF.

Because diet has been implicated as a cause of PF (endemic) in humans, the author will review the dietary history and consider dietary modification if the initial response to therapy is poor

Vitamin E (400-800 IU bid) and essential fatty acids may be used as part of the treatment since these nutrients have anti-inflammatory properties and anti-oxidant activities.

Glucocorticoids (GC) are the main stay of therapy for AISD. They may be applied topically or administered systemically depending on the severity of the disease and the amount of the body involved. Since some cats can’t metabolize inactive prednisone to the active form, prednisolone, ONLY PREDNISOLONE should be used in cats. In dogs either prednisone or prednisolone may be used. The author has seen cases of feline PF, which were well controlled on prednisolone, but when prednisone was dispensed relapsed, only to go back into remission once the cat was placed back on prednisolone- all at the exact SAME dosage and frequency.

For localized disease the author will apply a potent topical steroid product bid until clinical remission (not to exceed 21 days) and then tapered slowly over the next few months. Be sure to have the owners wear gloves when applying this product. If this treatment is unsuccessful the one of the following systemic therapies will be instituted.

In dogs with more extensive disease or those that fail topical therapy, prednisone or prednisolone is administered at 1 mg/# bid for 4 days then ½ mg/# bid for another 10 days. The dog is rechecked every 14 days. If the disease is in remission, the dose is decreased 25% at each recheck examination. The author defines “remission” as the absence of any active lesions (no pustules and any crusts that are present are easily removed with the underlying epidermis appearing pink rather than erosive). DON’T TAPER THE DOSE TOO QUICKLY. The goal is to maintain the dog on 0.25 mg/# or less every other day of prednisone/prednisolone. If this is not achievable, then azathioprine is added to the therapy (see below). Some dermatologist will use the combination therapy from the onset, but because at least 75% of the dogs in the author’s practice can be maintained on just GC and there are additional risks and costs associated with this drug the author considers this a second tier therapy. Only if the dog fails to respond to GC, or can’t be managed with every other day administration, will the author add azathioprine to the therapy.

For cats, ONLY prednisolone is used and in fact only prednisolone is stocked in the author’s pharmacy- this is to avoid the inadvertent administration of prednisone to a cat. The dose for cats is 1 mg/# bid for 14 days. From that point forward the management of the cat with prednisolone is the same as the dog. If the disease is not controlled with prednisolone then CHLORAMBUCIL (see below) is added to the therapy NOT AZATHIOPRINE!!!

If an animal fails to respond to prednisolone other immunosuppressive agents (see below) will be added to the therapy

Animals on chronic GC, regardless of dose should have a CBC, serum chemistry profile, urinalysis and urine CULTURE (monitoring for asymptomatic bacteriuria) every 6 months. The recommendation for performing a urine culture, even with a normal urinalysis, is best exemplified in 2 reports. In these reports, dogs had been receiving steroids for a minimum of 6 months. The incidence of UTI ranged from 21%-39%. In addition, pyuria was not identified in 48% of the samples that yielded growth. There was
not a correlation between the incidence of UTI and the frequency of drug administration (eg alternate-day versus daily), the type of GC or dosage administered or the duration of therapy (minimum 6 months). Lastly, clinical signs of UTI ranged from 0-32% of the cases. These 2 studies support the recommendations of performing urine cultures on dogs who receive steroids for at least 6 months whether or not they are symptomatic of a UTI. Also it stresses the need for a urine culture whether the urinalysis is normal or not since urine sediment analysis alone was not an adequate means of detecting urinary tract infections in these dogs.

Azathioprine (AZA) is an antimetabolite that is a competitive inhibitor of purine. Purine is necessary for DNA formation, so in the presence of AZA, defective DNA is formed preventing cell replication. It has a lag phase of four to six weeks before it reaches its full effectiveness. The drug is administered concurrently with GC. The initial dose of azathioprine is 1.0 mg/# sid. Once remission is achieved, and the dog is either off of GC, or the lowest dose of GC has been obtained, AZA is then tapered every 60-90 days. Usually the author will decrease the frequency, not the dose of azathioprine, first decreasing it to every other day and then if the disease is still in remission, to every 72 hours. A CBC, platelet count, serum chemistry profile are performed every 14 days for 2 months, then q 30 days for 2 months then q 3 months for as long as the dog is on azathioprine. Potential adverse effects include anemia, leukopenia, thrombocytopenia, hypersensitivity reactions (especially of the liver) and/or pancreatitis. AZA should not be used in cats- it may cause irreversible bone marrow suppression.

Chlorambucil (CAL) is used in cats and in dogs who failure to respond to azathioprine or can’t tolerate it. The protocol/precautions/monitoring for CAL is the same as w/AZA. The induction dose is 0.1-0.2 mg/KG/day. Because tetracycline and niacinamide (T/N) have a variety of anti-inflammatory & immunomodulating properties the combination has been used in treating a variety of immune mediated skin diseases, such as discoid lupus erythematosus, vesicular cutaneous lupus erythematosus (idiopathic ulcerative dermatosis of collies and Shelties), lupoid onychodystrophy, pemphigus erythematosus, German Shepard Dog metatarsal fistulae, sterile panniculitis, sterile periadnexal granulomatous dermatitis (idiopathic sterile granuloma-pyogranuloma syndrome), vasculitis, dermamoytomysis and cutaneous histiocytosis. The author used to use this combination for any of the previous mentioned diseases if the disease is relatively mild. If any of these diseases fail to respond well to immunosuppressive therapy, T/N may also have been added to the therapy in dogs. Since the unavailability of tetracycline, the author has replaced it with either doxycycline or minocycline. Currently the author uses subantimicrobial doses of doxycycline. This has 2 advantages- 1 has minimum impact on oral and intestinal bacterial resistance and secondly makes the product cost effective. The dose is 2 mg/kg sid. At this dose the author has not seen the side effects that have occurred with tetracycline (anorexia, vomiting and diarrhea). The dosage for niacinamide in dogs <10 kg is 250 mg, q 8 hours and for dogs >10kg - 500 mg q 8 hours. If there is clinical response, which may take a few months, the niacinamide is slowly decreased from tid, to bid to sid while maintaining sid doxycycline. Side effects are rare but when they occur as usually due to niacinamide. These side effects include vomiting, anorexia, lethargy, diarrhea and elevated liver enzymes. The author has not tried the low dose doxycycline in cats yet but will try 10 mg sid (1/2 of a 20 mg tablet crushed in the food). When administering doxycycline be sure to use a liquid form or administer a pill in a meat bolus followed immediately with food. ESOPHAGEAL STRICTURES have occurred as a sequele to doxycycline use in cats!!!

Cyclosporine A (CSA), a calcineurin inhibitor, has been used orally at a dose of 5 mg/kg sid in cases of PF with poor results in dogs. Recently the author has used CSA at 5 mg/kg sid- bid with success either as monotherapy or as steroid sparing agent. Others report that using at 5–10 mg kg every 24 hours along with ketoconazole 5 mg kg every 24 hours has increased the treatment success rate. In a retrospective study of cases in which either CSA or chlorambucil was used concurrently with steroids (steroids alone were ineffective) the author concluded that CSA appeared to be as effective as chlorambucil for controlling feline PF when used in combination with steroids.

Recently topical tacrolimus has been reported to be effective in the treatment of facial PF and PE. The author has limited experience with this product.

Sulfasalazine (SSZ) is a sulfa that has both anti-inflammatory and/or immunomodulatory properties due to its prostaglandin synthetase and leukotriene inhibition. In the past it has been used for the treatment of colitis but more recently it has been used for neutrophilic vasculitis. SSZ is metabolized by colonic bacteria to 5-aminosalicylic acid (5ASA) and sulfapyridine (SP). SP is well absorbed, metabolized in the liver, and excreted by the kidney while 5-ASA is much less well absorbed. Because SSZ is metabolized to aminosalicylic (“aspirin”) this drug should be used cautiously in cats. The biggest concern with this medication is the possibility of developing irreversible keratoconjunctivitis sicca. This appears to be an idiosyncratic reaction that occurs more in smaller dogs but may occur in any dog. It is essential that you warn the owner that if the eyes become red or they notice an ocular discharge or squinting to contact you immediately so that you can do tear testing. Other side-effects associated with this drug include anemia, KCS and hepatotoxicity so a CBC, serum chemistry profile and Schrimer tear test are performed every 14 days for 2 months, then q 30 days for 2 months then q 3 months for as long as the dog is on SSZ. In cases of neutrophilic vasculitis that fail SZA treatment w/dapsone may be effective, however, dapsone appears to be more toxic than SZA. The dose is 20-50 mg/kg tid (maximum 1 gm/dose), usually beginning with 20-30 mg/kg tid. Once the disease is in remission, the dose is slowly tapered.

Specific treatment approach- for mild cases of facial PF (or cases of pemphigus erythematosus), a topical glucocorticoid is used. For generalized forms, or in cases with severe facial and/or footpad involvement, prednis(ol)one should be used as described above.
As long as the disease is in remission at each recheck, the steroids are tapered as previously described. If the disease is not in remission at the first 14 day recheck or it can’t be kept in remission with steroids at a dose of <0.25 mg/# q 48 hrs, then either azathioprine (dogs) or chlorambucil (cats) is added to the treatment.

If the disease is not responding to the above treatment, CONFIRM that the diagnosis is correct (be sure to have ruled out dermatophytosis, demodicosis and bacterial pyoderma) then, changing to either dexamethasone or triamcinolone may be helpful. Use 0.05-0.1 mg/# bid of either drug, as the starting dose, and then taper as previously discussed.

As a “rescue” treatment for refractory cases of PF, high dose GC pulse therapy has been reported to be successful. Pulse therapy is followed by ½ mg/# bid of prednisolone and then taper as described previously. There are 2 protocols for pulse therapy:

1. 11 mg/kg of methylprednisolone sodium succinate (mixed w/250 ml of D5W) IV sid x 3-5 days
2. 10 mg/kg once daily for 3 days of prednisone ORALLY

**Lymphoplasmacytic lichenoid dermatitis**

Historically discoid lupus erythematosus (DLE) was considered an auto-immune disease whose symptoms were localized to the skin. Diagnosis was made using the same approach as in cases of PF- signalment, detailed history, physical findings, histopathology changes and response to therapy. In the dog, DLE is the 2nd most common autoimmune skin disease. The author has never recognized it in a cat. It has been suggested that there is no age predilection, but in the author’s experience it seems to be more common in young to middle-aged dog. Collies, Shelties, German shepherd dogs, Siberian huskies and Brittany spaniels are at risk breeds.

Clinical findings include depigmentation, erythema, erosions, crusts and alopecia. When the nasal planum is first affected there is loss of its normal cobblestone appearance and it develops a slate gray appearance. Depigmentation, erythema, erosions and crusts may occur over time. DLE usually begins on the nasal planum and may process to involve the bridge of the nose. It may also involve the lips, periorcular region, pinnae, and genitalia. Dogs affected with DLE are not clinically ill.

Differential diagnoses may include mucocutaneous pyoderma, pemphigus complex, cutaneous drug reaction, erythema multiformae, cutaneous lymphoma, uveodermatologic syndrome, SSC, solar dermatitis/collie nose and systemic fungal infections.

Mucocutaneous pyoderma (MCP) (the author feels a better name is “antibiotic responsive dermatitis” since bacteria are not seen histologically) is a crusting disease that may affect the lips, nasal planum (exclusively), the bridge of the nose, periorcular region, genititals or anus. Clinically it is indistinguishable from DLE. There is no identifiable cause for this disease and the diagnosis is based on the signalment (adult dog, most commonly in German Shepherd dogs (or mixes)), clinical appearance and distribution of the lesions and most importantly response to antibiotic therapy.

In the past MCP was differentiated from DLE based on histopathologic findings. DLE was diagnosed when a lichenoid lymphocytic to lymphoplasmacytic interface dermatitis with hydropic degeneration and/or individual necrotic keratinocyte involving the basal cell layer, pigmentary incontinence and a thickened basement membrane was present. Mucocutaneous pyoderma would be diagnosed histologically when a lichenoid plasmacytic to lympho-plasmacytic infiltration was present without an interface change and without basal cell damage. HOWEVER, this criterion has been called into question with a study that reported that histologically mucocutaneous pyoderma and DLE are indistinguishable! In that study, dogs were separated, based on histologic findings, into 3 groups, ones with lymphocytic lichenoid interface dermatitis with hydropic degeneration; ones with plasmacytic lichenoid dermatitis, and lastly ones with a mixture of the first 2 patterns- lymphoplasmacytic lichenoid, interface dermatitis with hydropic degeneration. The authors then evaluated whether the group responded to antibiotics or immunomodulating therapy. There was no statistical difference when histopathologic features were compared between the 2nd and 3rd groups! The author now believes that all cases of canine nasal dermatitis should have a 30 day course of cephalaxin prior to immunomodulating therapy - in fact prior to biopsy a 3-4 week course of a cephalosporin is appropriate and may establish a diagnosis without needing to biopsy the lesion!

A better way to approach cases of nasal dermatitis that presents clinically as the “typical” DLE is to recognize that this is a reaction pattern rather than a disease. This reaction pattern (lymphoplasmacytic lichenoid dermatitis) may be antibiotic responsive or may require immunomodulating therapy. Since the biopsy findings will be identical in both cases, a 30 day trial of a cephalosporin prior to biopsy should be administered. This is the same approach I would apply to those cases of “DLE” that involve other areas, such as the perivulvar region or in cases of chelitis.

**Diagnosis**

Dogs with DLE are clinically healthy and are normal hematologically and serologically (including a negative ANA). Historically the histopathologic changes consistent w/DLE included a lymphocytic to lymphoplasmacytic lichenoid interface dermatitis w/hydropic degeneration of basal keratinocytes. Scattered apoptotic keratinocytes may also be present. Failure to respond to a 30 day course of a cephalosporin is also required for the diagnosis.

**Treatment**

When treating dogs with DLE it is important to avoid aggressive therapy since it is primarily a cosmetic disease. Occasionally the lesions seem to bother the dog because of pruritus. It is therefore important to treat cases in proportion to the severity of the
symptoms. Be sure that the therapy is not worse than the disease. The author treats this disease in a stepwise progression with each step added to the previous therapy except where noted. The steps are as follows: Cephalexin 10-15 mg/# bid-tid for 30 days (since DLE and MCP are indistinguishable); if the dog does not respond to the cephalexin, then the cephalexin is discontinued and the following treatment is begun, sun avoidance, sun screens and vitamin E and omega 3 fatty acids. Niacinamide and doxycycline are as begun as previously described. If after 60 days the dog doesn’t respond to this treatment the next step is topical GC (beginning with a moderately potent GC). If after 60 days there is no response then stop the doxycycline and niacinamide and begin systemic prednisone (anti-inflammatory doses) that is slowly weaned over a period of months to achieve the lowest possible dose.
Demodex canis is the dog follicular mite, while Demodex injai is found within sebaceous glands and ducts. D. cornei lives in the stratum corneum.  

Neonates are thought to acquire mites from their dam during nursing. Direct transmission, other than from dam to the pup rarely occurs.

Dogs may have either localized or generalized disease. There is no universally accepted definition of localized vs generalized disease but recently it has been suggested that with localized disease there are no more than four lesions with a maximum diameter of to 2.5 cm. Demodicosis is also categorized based on age of onset- those less than 12 months of age (18 months in large or giant breeds ) are considered juvenile onset while older dogs are considered adult onset. The prognosis is excellent for the localized form either in puppies or adult dogs while the generalized form carries a more guarded prognosis.

Demodex causes disease when there is an overgrowth of the commensal mites either associated with a genetic defect (juvenile onset) or immune suppression (adult onset). In the adult dog, hyperadrenocorticism (iatrogenic or spontaneous), hypothyroidism, leishmaniasis, or chemotherapy are the most identifiable causes of adult onset generalized demodicosis.

The lesions include non pruritic alopecia, scaling, follicular casts, follicular papules/pustules (if a secondary bacterial infection is present), comedones, crusts, erythema, hyperpigmentation, and lichenification. Pruritus is variable but is mild except in cases with a secondary bacterial folliculitis.

Lesions frequently involve the face and/or forelegs and may progress to affect other body sites. Since the lining of the external ear canal is epidermis, demodicosis may cause a bilateral ceruminous otitis externa. As the disease progress dogs may develop a deep bacterial folliculitis and furunculosis and draining tracts. In those cases peripheral lymphadenopathy, lethargy and fever are commonly present. In some patients their presentation is exclusively pododemodicosis. In these cases a deep bacterial folliculitis and furunculosis is frequently present and the feet are swollen and painful leading to lameness.

In contrast to D.canis and cornea, D. injai tends to be associated with a greasy hair coat on the dorsum of the trunk. Many times alopecia is not present and only a low number of mites may be found on skin scrapings. It has been reported that terriers, especially wire haired fox terrier and West Highland white terrier, are at risk of developing this form of demodicosis.

Since demodicosis is a folliculocentric disease it will look identical to follicular lesions caused by a bacterial pyoderma and dermatophytosis. Superficial (for D.cornea) and deep skin scrapings (for the other species of demodex) are the most reliable method to diagnose demodicosis.

To perform a deep skin scraping it is best to squeeze the skin prior to and during the scraping to push the mites out of the hair follicles. Scrape the skin in the direction of hair growth until capillary bleeding occurs. When lesions are present on the face or paws the animal should either be sedated before scraping or a hair pluck/trichogram may be performed in an awake animal. Hair plucks are performed with mosquito hemostat forceps that grasp and pull out hairs. It is best to collect hairs from the leading edge of the lesion. To increase your yield, squeeze the skin as you are plucking the hairs and be sure to collect a large number of hairs (50–100). Take the collected hairs and lay them on a slide containing a drop of mineral oil and add a cover slip. Sample multiple sites in each patient. Trichograms, or in cases of pustular demodicosis examination of the exudate, will detect Demodex mites in about 85% and 100% of the collected hairs and lay them on a slide containing a drop of mineral oil and add a cover slip. Sample multiple sites in each patient.

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Recently it has been reported that applying tape to a skin lesion and then squeezing the skin is as an effective way to identify demodex mites in dogs. A study was performed to confirm this observation. Specifically the study was to evaluate and compare the sensitivities of acetate tape impression deep skin scraping for the diagnosis of canine demodicosis. They concluded that squeezing the skin followed by acetate tape prep was found to be as sensitive as deep skin scraping for the diagnosis of canine demodicosis. Unfortunately the author has not had the same experience.

Be sure to collect samples from multiple sites and note the site that the sample is collected from since localized disease is treated differently than generalized disease. When examining the slides you need to evaluate for the approximate number of each stage that is present (eggs, larva, nymph and adults). Also note how many of the mites alive vs are dead. These results will be important to compare to future skin scrapings as you are monitoring the dog’s response to therapy. With effective treatment a decreasing number of immature mites and the disappearance of eggs should occur. The number of live mites should also decrease. In all cases of demodicosis be sure to perform an examination of an otic swab. Otodemodicosis is identified by collecting roll swabs from each ear.  

Unfortunately the author has not had the same experience.
using a cotton swab that has been dipped in mineral oil. The sample collected is place onto a glass slide that also has a drop of mineral oil on its surface. A cover slip is applied and then the sample is examined. If samples are collected as described it would be extremely uncommon to miss the presence of demodex mites. Occasionally this may occur, even with properly performed skin scrapings and hair plucks, if the dog has scarring due to chronic disease or because of the thickness of their dermis (therefore the deeper depth of their hair follicle making expulsion of the mite more difficult) (i.e. Shar-Pei).

If demodicosis is strongly suspected, but no mites are found on skin scrapings and hair plucks, skin biopsy is recommended to rule in or rule out their presence.

How to treat a dog with demodicosis depends on whether it is localized or generalized. In cases of localized demodicosis, less is best. In many cases, especially juvenile onset, the disease will spontaneously resolve within a couple months. Miticidal therapy is not required unless the disease becomes generalized. Since the progression of localized disease to more generalized form is not influenced by whether the localized form is treated or not, treatment of localized disease is not necessary. However, in the author’s practice “benign” topical treatment is prescribed. This is done so that if the disease does progress, the owner feels that something had been done to try to prevent for occurring. Topical therapy with benzoyl peroxide shampoo and/or gel can theoretically be helpful due to its antibacterial properties and follicular flushing activity. Due to its suppressive effect on the immune system you should avoid using any steroid containing product (topically or systemically) in patients with demodicosis (localized or generalized). Ensuring a proper diet and intestinal deworming program should also be part of the treatment of dogs with demodicosis. To evaluate the effectiveness of treatment, a follow up examination, including repeating skin scrapings, should be performed in 30 days.

Treating a dog with generalized demodicosis requires much more aggressive therapy than localized. Multimodal therapy, a common approach that is used to treat other diseases (eg arthritis, atopic dermatitis or congestive heart failure) will be necessary when treating generalized demodicosis. Acaricidal therapy and treating secondary bacterial infections if present is required for both adult and juvenile onset disease. In adult onset cases attempts should be made to identify and treat the underlying systemic disease.

Dogs with juvenile onset generalized demodicosis, in addition to the above mentioned treatment should be neutered. This is important not only to prevent the propagation of this genetic defect but also estrus may trigger recurrence of clinical disease.

As mentioned previously, in cases of adult onset generalized demodicosis attempts should be made to identify and treat the underlying disease. Evidence shows that successful treatment of an underlying cause increases the likelihood that adult onset demodicosis can be cured. In the author’s practice, diagnostics performed in cases of adult onset generalized demodicosis include a CBC, serum chemistry profile and a urinalysis. Depending on the age of onset, abdominal ultrasound and thoracic radiographs may be included in the minimum data base. Because of the influence that bacterial pyoderma or generalized demodicosis has on evaluating thyroid or adrenal gland disease, evaluation of these organs is delayed until any secondary bacterial infection has been resolved and the demodicosis has improved or is in remission.

Specific treatment of generalized demodicosis is outline in table 1. This table is the result of the most recent consensus guidelines written by an international group of dermatologists. The author has indicated in bold the approach used in his practice.

Since dogs may look normal clinically but still have active disease (as determined by the presence of mites on skin scrapings) treatment must be continued beyond clinical resolution. Parasitic cure is defined as multiple negative skin scrapings, including lack of dead or fragmented mites, on 3 consecutive monthly visits. Skin scrapings should be used to determine the therapeutic end-point. This end point is reached when the dog looks normal clinically and skin scrapings have been performed monthly on the 4-6 most severely affected areas and have been negative for 3 consecutive visits. If during a visit the skin scraping is positive, it is important to compare the number of live and dead mites and the number of each stage of the mite life cycle to the previous visit. An indication of effective treatment is that during therapy the number of live mites found on skin scrapings and the number of immature mites should be reduced from the previous visit. If this doesn’t occur, therapy should be re-examined and possibly changed.

How to treat a dog with severe generalized disease

1. Perform cytology and if there is evidence of a deep bacterial skin infection or the dog has been treated previously with antibiotics a bacterial culture and sensitivity. With inflammatory cells and bacteria present, appropriate oral antibiotic therapy is required.
2. Use topical therapy with chlorhexidene or benzoyl peroxide shampoo weekly to possibly twice weekly. (Unless amitraz is being applied)
3. There are several treatment options for the treatment of canine demodicosis. The best option will depend on the legalities pertaining to the use of veterinary pharmaceutical products in the country of residence, the finances of the owner and the clinical situation. However, independent of the treatment specifics the dog should be neutered because dogs in need of mite treatment should not be allowed to breed, and the disease may relapse in cycling bitches.
   a. Amitraz weekly or every 2 weeks in a concentration of (0.025–0.06%) can be used. Dogs with a medium to long hair coat need to be clipped, and skin should stay dry between rinses to avoid washing off the drug.

Table 1- Summarized treatment of canine demodicosis *

Treatment of a dog with severe generalized disease

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   a. Amitraz weekly or every 2 weeks in a concentration of (0.025–0.06%) can be used. Dogs with a medium to long hair coat need to be clipped, and skin should stay dry between rinses to avoid washing off the drug.
Rinsing should be performed in well-ventilated areas. The author only uses this therapy if the dog has failed to respond to ivermectin or is a herding breed. Please note that amitraz is EPA registered and doesn’t EVER allow any off label use (label states 1 bottle/2 gallons every 14 days)

b. Milbemycin oxime may be administered orally at a dose of 1–2 mg/kg/day. Moxidectin orally (see below) is in the milbemycin family, is much less expensive than milbemycin, and is used if the dog fails to respond to ivermectin (again a non herding breed)

c. Moxidectin as a spot-on in combination with imidacloprid may be used weekly. This spot-on formulation has a markedly higher success rate in dogs with milder disease.

d. Ivermectin at an oral dose of 0.3–0.6 mg/kg (0.4 mg/kg) or moxidectin at 0.2–0.5 mg/kg p.o. daily are further options. With both drugs, a gradual increase from an initial dose of 0.05 mg/kg to the final dose (of 0.4 mg/kg) within a few days is recommended to identify dogs that cannot tolerate those drugs. Monitoring for neurological adverse effects should occur throughout the course of therapy. Ivermectin is the treatment of choice in the author’s practice.

e. Doramectin weekly at 0.6 mg/kg p.o. or SQ is a possible treatment. A gradual increase from an initial dose of 0.1 mg/kg to the final dose seems prudent to identify dogs that cannot tolerate the drug and will show neurological adverse effects.

So to summarize- this report states that “There is good evidence for the efficacy of weekly amitraz rinses and daily oral macrocyclic lactones such as milbemycin oxime, ivermectin and moxidectin for the treatment of canine demodicosis.”

Other recommendations are

- Dogs should be evaluated monthly, and treatment should be continued until 3 consecutive visits with multiple negative skin scrapings have been achieved.
- Treat secondary bacterial infections
- Factors predisposing to demodicosis, such as malnutrition, endoparasites, endocrine disease, neoplasia and chemotherapy, should be identified and corrected to maximize response to therapy.


**Diagnosis and management of malassezia dermatitis**

**Overview**

*Malassezia* is a genus of lipophilic yeast found as a commensal of the skin and mucosal surfaces that may cause skin disease in a variety of mammalian species. In normal dogs these organisms are present in very small numbers on the skin (fold areas-lip, vulvar, axillae, interdigital), oral and anal mucosal surfaces, in the ear canals and in the anal sacs. In contrast to *Candida*, MD is not associated w/recent antibiotic administration, in fact, there appears to be a symbiotic relationship between the surface staphylococcal organisms and the yeast. It is theorized that the organisms produce growth factors and micro-environmental changes (eg inflammation) that are beneficial to each so it is not uncommon to see concurrent infections w/Malassezia and staphylococcus. Why do animals develop *Malassezia* dermatitis (MD)? There have been numerous studies comparing the strain of *Malassezia* organisms found on skin of affected dogs vs. the skin of unaffected dogs. To date there has not been an identifiable difference in virulence and/or adhesion in *Malassezia* organisms found on skin of affected dogs vs. the skin of unaffected dogs. Since the organism virulence doesn’t explain MD, the explanation seems to be the host response to *Malassezia* organism. Both type I and type IV hypersensitivity reactions to *Malassezia* have been identified in dogs w/MD. Disorders that affect the barrier function of the skin (eg pruritic skin disease) or the cutaneous lipid content (eg hypothyroidism) are risk factors for developing MD

**Signalment**

There is no age or sex predilection

**History**

MD is always secondary to another skin disease. A clue that MD may be present is that the clinical features and/or the previously effective therapy of the underlying disease become ineffective. For example, pruritus that was seasonal becomes nonseasonal; the distribution of the pruritus changes, responsiveness to previously effective antibiotic and/or glucocorticoid therapy is decreased. Any allergic animal whose pruritus (intensity or distribution) or the therapeutic responsiveness of the pruritus changes suddenly should be evaluated for MD, pyoderma and ectoparasites.

**Clinical findings**

On physical examination lichenification, erythema, greasy exudate, dry scale, papules, plaques, alopecia or hyperpigmentation may be present. A moist dermatitis with a musty odor is not an uncommon clinical finding. Pruritus may vary from mild to intense and erythema may be present with minimal pruritus especially interdigitally.

The lesions may be focal or generalized and the distribution of the lesions overlaps with other pruritic diseases. Affected areas include interdigitally, intertriginous areas, face, nail folds, perioral (lateral muzzle), pinna and flexor surface of the elbow.
**Diagnosis**

MD may cause a folliculitis that is clinically identical to staph pyoderma. Therefore if there are follicular papules, epidermal collarettes or lichenification you can’t assume that there is a bacterial component to the skin disease without performing skin cytologies. Remember to include skin scrapings for ectoparasites as part of your minimum data base.

Identifying *Malassezia* organisms budding yeast from the affected area is necessary to establish a diagnosis of MD. Tape impression or direct impression smear are the most common method used for sampling affected areas.

The question is “how many is too many organisms?” A previous report found that normal dogs had 1 yeast per 2700 oil field. MD is confirmed when, on cytology, you find ANY field that has more 1 organism OR if there is 1 organism every 1-3 fields (1000X).

The ACVD task force on atopic dermatitis discussed MD as a complication of atopic dermatitis. The task force states that “Surface cytology of the skin and ear is useful to determine whether or not *Malassezia* or *Staphylococci* are present at lesional sites. Making antimicrobial treatment decisions based solely on microbe numbers is incorrect and inappropriate.” The article goes on to discuss that the host response to these normal organisms determines the severity of clinical signs. Their recommendation was “the result of cytology might better be limited to the sole report of ‘presence’ or ‘absence’ of detectable bacteria or yeast”.

**Treatment**

In order to prevent recurrence of MD the underlying cause must be identified and treated. As previously mentioned any disease that disrupts the barrier function, the lipid content of the skin surface, the cutaneous microclimate or host defense mechanisms may predispose the animal to MD. These include hypersensitivities (atopy, cutaneous adverse food reactions), ectoparasites (demodex, sarcoptes, and fleas), endocrinopathies (hypothyroidism, hyperadrenocorticism), metabolic diseases (metabolic epidermal necrosis), neoplasia (cutaneous T-cell lymphoma) and excessive skin folds. Genetic factors, as seen in Bassett hounds, predispose a dog to maintaining higher number of *Malassezia* organisms on their skin, putting them at greater risk for developing MD.

Unless the MD is very focal, the author prefers both topical and systemic therapy. This combination will be the most successful treatment of MD. Eliminating MD as the cause of pruritus is important so that when the dog is rechecked any remaining pruritus is a result of the underlying hypersensitivity reaction, not the MD.

There are a variety of effective topical agents including selenium sulfide, miconazole, ketoconazole, clotrimazole and chlorhexidine. In the authors experience any shampoo that contains at least 3% chlorhexidiene or contains 2% chlorhexidine combined w/an azole is effective. Shampooing should be followed by a leave on conditioner containing an antifungal ingredient such as 2% miconazole. Depending on the severity and extensiveness of the lesions the frequency of application varies from daily to 3x/week.

Ketoconazole (KCZ) 5-10 mg/kg sid was the systemic drug of choice. Since the drug is now unavailable fluconazole (5-10 mg/kg/day). Another choice, especially for hard to medicate dogs is itraconazole 5 mg/kg given 2 consecutive days/week. A less costly therapy is terbinafine (30-40 mg/kg sid w/food). Regardless of which treatment is chosen the treatment should be continued for 14 days beyond clinical resolution BASED ON YOUR examination (not a phone call) with a minimum treatment time of 21 days. Please note that griseofulvin is ineffective against *Malassezia*.

Be sure to evaluate the dog for concurrent superficial bacterial pyoderma since MD and pyoderma occur simultaneously in dogs. In cases of concurrent superficial bacterial pyoderma, antibiotic therapy should be used simultaneously.
Antibiotics
A consensus statement has been released with the purpose of guiding practitioners in the diagnosis, treatment and prevention of superficial bacterial folliculitis (SPF). These guidelines, like the previous guidelines published concerning antibiotic use for treating urinary tract infections, are the result of a committee consisting of veterinary internists, pharmacologists, microbiologists and dermatologists. In this article it is stated that “there is concern among some members of this panel about the potential selective effects of third generation cephalosporins (cefodoxime and cefovecin) on the Gram-negative microflora, due to their broader spectrum of activity compared with first generation cephalosporins”. The following is the author’s position on the use of these broad spectrum antibiotics in the treatment of SPF.

Cefpodoxime is a 3rd generation cephalosporin (broad spectrum) effective for most Staphylococcus infections that occur in dogs. The company believes that this drug should be a first line antibiotic instead of using the narrower spectrum antibiotic, cephalixin, in the treatment of SPF. The concern about using a broad-spectrum antimicrobial is that they affect a wider variety of microorganisms and their use may select relatively resistant strains of non targeted microorganisms. Even if these microorganisms are non pathogenic, they can be a source of resistance genes for pathogens. A cited advantage of cefpodoxime over cephalixin is that it is a once a day antibiotic leading to better owner compliance. This belief of higher compliance rate with once daily medication vs. twice daily has been dispelled in a study that revealed there is no difference in compliance with once daily versus twice daily dosing. Also be aware that there are numerous studies showing that once daily cephalixin at 30-40 mg/kg is as effective as splitting this dose and administering q 12 hours. However these were not peer reviewed studies so this is NOT my recommendation. But these studies do suggest that missing 1 dose of cephalixin is not catastrophic. Recognizing that missing one dose of a once daily pill would be the same as missing TWO doses of a twice daily pill the author believes that there is no advantage of medications that are given once daily vs. twice daily. Note if once daily dosing is important there are other antibiotics that would be more appropriate to dispense when treating SPF such as clindamycin (5-10 mg/#) or one of the potentiated sulfas. Another advantage mentioned is that the cefpodoxime pill is easier to administer than cephalixin capsules. Cephalixin is now available as a chewable tablet (Rilexine® Virbac) that helps make administration of cephalixin much easier. Other concerns about cefpodoxime as a 3rd generation cephalosporin will be discussed below.

Cefovecin is a parenterally administered 3rd generation cephalosporin that has tremendous value when used properly (selectively). It too is a broad spectrum antibiotic when compared to cephalixin. In New Zealand it is approved for infections due to Staphylococcus intermedium, ß-haemolytic Streptococci, Escherichia coli and/or Pasteurella multocida and Proteus spp. In Canada it is approved for skin infections in dogs due to Staphylococcus (pseudo)intermedium, Streptococcus canis and Escherichia coli. It is also approved for canine urinary tract infections caused by Escherichia coli and Proteus mirabilis. In cats it is for skin infections caused by Pasteurella multocida, Prevotella bivia, Bacteroides fragilis, and Staphylococcus (pseudo)intermedius. This wide spectrum is in contrast to is compared to chewable cephalixin (Rilexine® Virbac) which is only approved for the treatment of superficial bacterial pyoderma caused by Staphylococcus (pseudo)intermedius. Because of the previously mentioned issues, the author believes that this drug should be reserved for cases where the owner is unable to orally medicate the dog or cat or the animal can’t tolerate oral antibiotics. The concern about using this medication is that therapeutic drug concentrations (above MIC) are only maintained for 7-14 days post injection, depending on the infectious agent, while sub-MIC tissue levels persist for up to 65 days. The question is whether this prolonged subtherapeutic blood (tissue?) level will enrich the environment for the proliferation of resistant bacteria. Will adverse reactions require prolonged treatment due to the prolonged systemic drug clearance? What are the long-term effects on injection sites, especially in cats? Most of these questions have not been answered, even by the company. The following is from the Convenia drug insert (New Zealand)

“Cefovecin is a long acting broad spectrum fourth group cephalosporin. Cefovecin may persist in the body for approximately 4 to 5 weeks; therefore, adverse event monitoring should be carried out for a similar amount of time”. (note USA insert states that reactions may require prolonged treatment due to the prolonged systemic drug clearance (65 days) “Prudent Use: It is prudent to reserve third generation cephalosporins for the treatment of clinical conditions which have responded poorly, or are expected to respond poorly, to other classes of antimicrobials including first generation cephalosporins. Use of the product should be based on susceptibility testing and take into account official, and local, antimicrobial policies. Indiscriminate use of Convenia could contribute to the development of antibiotic resistance.”

An additional concern about 3rd and 4th generation cephalosporins is that they are a risk factor for developing extended spectrum beta- lactamase (ESBL) producing bacterial infections. Extended-spectrum beta-lactamases (ESBLs) are mutant beta lactamases found in Enterobacteriaceae (E. coli, K. pneumoniae, etc) and are a concern in human medicine because they cause serious, potentially
life threatening infections. These bacteria are not only resistant to beta lactam antibiotics but are frequently multi- drug resistant being resistant to non beta lactam antibiotics such as aminoglycosides, fluoroquinolones, tetracyclines, chloramphenicol, and sulfamethoxazole-trimethoprim. This wide ranging resistance greatly limits effective treatment options. The genes encoding this resistance are mediated by plasmids and/or mobile elements which allows horizontal transfer between the same and different species of Enterobacteriaceae. Horizontal transmission allows wide spread dissemination between human bacteria or between human and animal bacteria. In contrast to FQ and 3rd generation cephalosporins, first generation cephalosporins have not been reported to be a risk factor for such resistance.

Bottom line – we should be very selective when dispensing any antibiotic but especially third- and fourth-generation cephalosporins in the treatment of SPF. The most convincing argument against using these newer drugs as a first line antibiotic is since there are disagreements about the long term impact of these drugs on bacteria, and since cephalexin works well in most cases, why would you change?

Antipruritic
Oclacitinib is a JAK inhibitor approved for the treatment of canine pruritus. Cytokines bind to unique cell membrane receptors and activates specific intracellular pathways. JAK is one such intracellular pathway. Once triggered, the JAK pathway activates, via phosphorylation, intracellular proteins call Signal Transducer and Activator of Transcription (STAT). These proteins bind to specific DNA regulatory sequences in the nucleus to activate or repress cytokine production. JAK 1 is involved in the production of cytokines (IL-2, IL-4, IL-6, IL-13 and IL-31) that trigger and perpetuate the clinical signs of pruritus and cutaneous inflammation. Oclacitinib inhibits the activation of JAK 1 thereby decreasing the amount of pro-inflammatory and pruritogenic cytokines produced. It is approved for use in dogs as an antipruritic agent. This oral medication is dosed at 0.4-0.6 mg/kg bid for 14 days then sid. It appears that this drug, when effective, works very quickly, sometimes within hours. However a noticeable number of dogs will become pruritic when switching from bid to sid. In those cases, make sure you are using the 0.6 mg/kg dose- if not, then increase to that dose. If that dose is not effective when given sid, then try splitting the daily dose into bid. Please be aware that this drug will mask pruritic diseases such as sarcopites, flea allergy dermatitis, pyoderma and Malassezia dermatitis. These are diseases that should be treated with ectoparasiticides for the former 2 or antimicrobials for the latter 2 rather than masking the pruritus with medication. As is true with any drug used in the treatment of atopic dermatitis, it should be used as a temporary therapy as you are trying to identify and manage the underlying cause (eg adverse food reaction (food trial), ASIT for environmental atopic dermatitis). The author monitors CBC, serum chemistry profile, urinalysis and urine culture q 6 months for dogs on prolonged treatment. To date only a few dogs have had adverse events (neutropenia/leucopenia) that resolved with discontinuation of the drug.

Sublingual immunotherapy
Recently sublingual immunotherapy (SLIT) has become available to veterinarians for the treatment of canine atopic dermatitis (cAD). The author has some reservations about the use of this therapy for cAD. Recognizing that SLIT has been used for many years in Europe for the treatment of human asthma we can review the information that is available in that species. The vast majority of studies and protocols in humans are for rhinitis/asthma and NOT atopic dermatitis. A review in human medicine (2006) found the following

1. Dosing summary
   a. The studies included doses that varied by 30,000-fold
   b. Frequency of dosing varying from daily to weekly
   c. Duration of treatment varying from 2 months to 5 years

   Their conclusion was that SLIT is an effective treatment (for rhinitis or asthma) but it was unclear what the proper dose, treatment schedule and overall duration of treatment was to be effective.

   Other review articles found that the cumulative monthly dose varied between 0.017 and >500 times the customary subcutaneous maintenance dose. In addition that each manufacturer uses its own standardization, formulation, and administration schedules. In a review of SLIT for human atopic dermatitis the authors could only find 1 DBPCR. That study evaluated the efficacy and safety of SLIT using housedust mite containing drops. They concluded that for mild–moderate disease there was significant improvement but there was no improvement in cases of severe disease. But it went on to say that standardized treatment was essential to ensure therapeutic efficacy. They used 80 umg protein concentration/day once daily with instructions to Patients were instructed to keep the drops under the tongue for 1–3 minutes and then swallow. Note in this study the treatment group had a total efficacy rate of 77.78% (cured + marked improvement) vs. 53.85% in the control group. These were statistically significant but look at the placebo effect! The other important finding was that during the first year of immunotherapy there was no difference between placebo and SLIT response and the difference was only noticeable at 2 years. In 2015 there was a systematic review to evaluate the evidence supporting the use of SLIT for hAD? They could only find 5 studies to fit their criteria. They found that in 4/5 studies there was an improvement in AD but in 2/4 there was a substantial placebo effect making the true effect of SLIT difficult to determine. They found serious
shortcomings such as lack of control group, lack of randomization, data analysis was not by intention to treat. The group graded 1 of the studies to have moderate quality, 2 to have low quality and 2 to have very low quality.

As you review the studies in veterinary medicine concerning SLIT and eAD you will note that all studies except for 1 have the same very serious limitations- they are open studies, there are no placebo groups and only the study only applies to mite sensitive dogs. Also the studies state that there are statistically significant changes in CADESI and PVAS but don’t state if this translated into CLINICAL improvement- for example pruritus may go from +10/10 to a +7/10- statistically different but not clinically different. In the 1 DBPCR study that has been done to date in veterinary medicine, they found that overall the percentage of dogs that improved >40% were in the control and 66% in the active group. Once again look at that placebo response! Two problems with this study-1 they don’t state if the response rate is statistically different and also the criteria that has been establish states there must be at least a 50% improvement to be considered clinically significant- so why did that study use a 40% cutoff?

Lastly, things that give the author great pause about this whole subject is that there are some companies that refuse to tell the veterinarian what is in the SLIT formula that they expect us to give to our patients. In addition the different antigen companies are using different strengths in their SLIT (one company offers a dilution of 20,000 pnu or 40,000 pnu whichever you want – but doesn’t give guidelines how to chose), different volumes and different frequency (Sid vs bid). So how can they all be effective? The author uses SLIT in very limited, specific situations such as when owners are absolutely adamant that they won’t give SCIT and won’t’ bring the pet in for you to give the injection, an animal that has had a severe reaction to SCIT or if the animal fails to respond to SCIT after 1- 1 ½ years. I tell the owner that we really don’t know how successful this method is but that it is very safe to try.

**Antifungal**

Itraconazole (Sporonax ®-Janssen Pharmaceuticals- 100 capsules and 10 mg/ml oral solution)) is a member of the azole family of antifungal agents. Imidazoles (Imidazole family (thiabendazole, clotrimazole, ketoconazole, miconazole and enilconazole) and triazoles (itraconazole and fluconazole) make up this family of drugs. All azoles are potent inhibitors of ergosterol synthesis (a main membrane lipid of fungi) via inhibition of a microsomal cytochrome P450 enzyme (14 △ sterol demethylase) (see table 1). Since mammalian cytochrome P450 is involved in glucocorticoid and sex hormone synthesis (androgens), depending on which azole, the dog’s cortisol and androgen levels may decrease during therapy. This is more of a potential problem w/ketoconazole then w/itraconazole (ITZ) because ITZ is more selective for the fungal enzyme than the mammalian form. Itraconazole has been used in veterinary dermatology for many years to treat subcutaneous (eg Sporotrichosis) or systemic (eg cryptococcus, histoplasmosis) mycotic infections. More recently it has been used for treating cats (and occasionally dogs) for dermatophyte infections. It has also been found to be very effective for the management of Malassezia dermatitis. For cats w/dermatophytosis the author uses "pulse" therapies (i.e., daily therapy for 1 week, then one week off, then one week on, etc) at a dosage of 5-10 mg/kg/day. It is better absorbed if given with food. Side effects of itraconazole in dogs or cats include anorexia, GI disturbances, hepatopathies and in dogs (when using higher doses (10 mg/kg)) vasculitis. It is teratogenic so it is not to be used in pregnant animals. For dog’s w/Malassezia dermatitis, 5 mg/kg, 2 consecutive days/week is as effective as daily administration.

Fluconazole (Diflucan®, Pfizer Pharmaceuticals) is another alternative for the systemic treatment of Malassezia but until recently has been more expensive than either ketoconazole or itraconazole. The dosage is similar to ketoconazole 5-10/kg once daily- GI absorption is unaffected by food intake. The residual effect of fluconazole is similar to itraconazole. Fluconazole is eliminated primarily via the kidneys so administering this drug to a dog w/hepatic disease could be advantageous over the other azoles. Dosage adjustments for dog’s w/renal compromise are necessary.

Terbinafine is an allylamine antifungal agent used in human medicine for the treatment of dermatophyte infections. An advantage of terbinafine over the azoles is that terbinafine has minimal effect on the cytochrome P450 enzyme system as opposed to the azoles. Clinically this translates into fewer drug interactions especially compared to ketoconazole. This drug is effective for dermatophytes (when used w/lime sulfur) and Malassezia and can be used in both cats and dogs. The dose is cats and dogs is 30-40 mg/kg sid however there is a study that used the following dose for dermatophytosis (used w/lime sulfur dips)= cats < 2.8 kg – 62.5 mg, 2.8-5.5 kg- 125 mg and in cats > 5.5 kg 1 tablet.
Alopecia in the dog is a common clinical finding. It is most commonly associated with pruritus due to allergic skin disease. There are also many nonpruritic causes of alopecia. Since the skin and hair can only “react” in a limited manner regardless of the triggering event, signalment, history (hx), physical exam (PE) and laboratory testing (eg skin scrapings, skin biopsies, fungal cultures, endocrine testing, intradermal testing, etc) will be needed to help determine the underlying cause.

Once congenital, pruritic or infectious causes of focal to multifocal alopecia have been eliminated as a cause, the remaining alopecic diseases are associated with inflammation or interface dermatitis. Note that the inflammation may only be histologically apparent, not clinically observable. These can only be differentiated based on microscopic examination of skin biopsies. Vaccine induced alopecia is an example of an inflammatory alopecic disease. When performing a skin biopsy in an alopecic disease it is best to submit an elliptical shaped sample that has the tip of one end in the alopecic region and the other tip in the normally haired area. Be sure to request that the sample is sectioned from tip to tip (longitudinally) rather than transversely. This will allow the pathologist to see the progression of the lesion from early to late stages all on one sample.

Vaccine induced alopecia is most commonly associated with rabies vaccination and occurs due to ischemic changes in the skin. The alopecia occurs 2-12 months after administering a rabies vaccine. Small white breeds of dogs seem to be at risk for developing these lesions. SQ or IM injections have no impact on the occurrence of this reaction. Lesions consist of scaling, focal (occasionally multifocal) areas of alopecia, plaques, hyperpigmentation, nodules, erosions, crusts and cutaneous atrophy (scarring). The lesions may also develop at sites distant from the vaccination site. Histologically in addition to typical vasculitis changes, septal panniculitis and focal lymphoid nodules will be seen. Rule-outs are fairly limited but should include demodiosis, dermatophytosis, allergic skin disease and bacterial skin disease.

Dermatomyositis is an ischemic genodermatosis in collies and shelties involving both the skin and muscles. When it occurs spontaneously in adult dogs of other breeds there is only skin involvement. The onset of clinical disease in the inherited form is between 6 weeks and 1 year of age- usually occurring before 6 months of age. The lesions may be fairly limited and heal as the puppy matures or they may progress. Usually the lesions stop progressing by the time the dog is a year old. The cutaneous lesions, which are usually the predominant clinical sign, include focal to multifocal areas of alopecia, scaling, crusts, erosions, ulcers, depigmentation, hyperpigmentation and scarring. These lesions occur on the face, mucocutaneous junctions, carpal and tarsal regions and the tip of the tail and ears. Onychodystrophy may also be present. Secondary bacterial pyoderma may occur. Muscle involvement, which only occurs in the inherited form, tends to be proportional to the severity of the skin lesions and is usually identified subsequent to the cutaneous lesions developing. These dogs may develop megaesophagus or muscle atrophy involving the muscles of mastication and ambulation. Differential diagnoses for the skin disease include demodiosis, dermatophytosis, superficial bacterial folliculitis, DLE, cutaneous drug reaction, erythema multiformae, vasculitis and epidermolysis bullosa simplex. In the author’s experience, puppies are mostly commonly presented with limited facial lesions that the breeder claims are wounds/scar from the other puppies or from a cat in the household. Diagnosis is based on signalment, physical examination and histopathologic changes consistent with a vasculopathy.

Treatment for ischemic skin diseases would include avoiding the trigger and various immunomodulating drugs. For vaccine-induced alopecia the treatment options include pentoxifylline or surgical excision of the affected area. Pentoxifylline is a methylxanthine derivative that increases RBC deformability and lowers blood viscosity thereby allowing for better blood flow through narrowed/edematous vessels. It also suppresses synthesis of proinflammatory cytokines such as IL-1, IL-4, IL-12 and TNF-α. Pentoxifylline is administered at 15 mg/kg tid. There may be a 30-90 day lag before full clinical response is seen.

Other treatment options for ischemic dermatopathy include tetracycline (or doxycycline) and niacinamide. These drugs are used with, not replacing pentoxifylline. Doxycycline and niacinamide (D/N) have various anti-inflammatory & immunomodulating properties. The dosage for niacinamide in dogs or cats <10 kg is 250 mg q 8 hours. For dogs >10kg - 500 mg of niacinamide q 8 hours are administered. Doxycycline is dosed at 2 mg/kg q 24 hrs. If there is a clinical response (may take 2-3 months) the treatment is decreased from tid, to bid to sid. Side effects are rare but include vomiting, anorexia, lethargy, diarrhea and elevated liver enzymes from niacinamide and hepatotoxicity from doxycycline.

If there are focal lesions that fail to respond to the previous treatment, topical glucocorticoids (GC) may be added. The topical products are applied bid until clinical remission (not to exceed 21 days) and then tapered slowly over the next few months. Be sure to have the owners wear gloves when applying these products. Please note that topical steroids may cause pu/pd/polyphagia. This sensitivity to steroids is quite variable and may occur in unexpected situations. Topical tacrolimus (0.1%) may be used in cases that fail to respond to topical steroids, the pet has side effects to the topical steroid or for the dog that needs long term topical treatment to control the disease.
If the disease is more widespread or fails to respond to the previous treatments, prednisone may be used. It is administered at 1 mg/kg bid for 14 days. The dog is rechecked every 14 days. If the disease is in remission, the dose is decreased 25% every 14 days. The author defines “remission” as the absence of any active lesions. DON’T TAPER THE DOSE TOO QUICKLY. The goal is to maintain the dog on 0.25 mg/# or less every other day. Another option for SEVERE cases would include azathioprine along with the oral GC. The initial dose of azathioprine is 2.2 mg/kg sid. Once remission is achieved, and the dog is either off of GC or the lowest dose of GC has been obtained, AZA is then tapered usually every 30-60 days. When tapering AZA, the author will decrease the frequency, not the dose of azathioprine, first decreasing it to every other day and then if the disease is still in remission, to every 72 hours. When using AZA, a CBC, platelet count and serum chemistry profile are performed every 14 days for 2 months, then q 30 days for 2 months then q 3 months for as long as the dog is on AZA. Potential adverse effects include anemia, leukopenia, thrombocytopenia, hypersensitivity reactions (especially of the liver) and/or pancreatitis.

Cyclosporine (Atopica®) may be effective in some cases of ischemic dermatopathy. Be sure to use modified cyclosporine (Atopica®) since unmodified CSA is not absorbed as well. The dosage is 5 mg/kg sid.

Sulfasalazine (SSZ) is a sulfa that has both anti-inflammatory and/or immunomodulatory properties due to its prostaglandin synthetase and leukotriene inhibition. In the past it has been used for the treatment of colitis but more recently it has been used for vasculitis. Side effects associated with this drug include anemia, KCS and hepatotoxicity so a CBC, serum chemistry profile and Schirmer tear test are performed every 14 days for 2 months, then q 30 days for 2 months then q 3 months for as long as the dog is on SSZ. The dose for SSZ is 20-50 mg/kg tid (maximum 1 gm/dose), usually beginning with 20-30 mg/kg tid. Once the disease is in remission, the dose is slowly tapered.

Sebaceous adenitis (SA) is an inflammatory disease of the sebaceous glands. Some people will separate this disease into the granulomatous form (Standard Poodle form= SPf) that is seen in Standard Poodles, Akitas, Samoyeds, Old English and Belgian sheepdogs and the short coated breed form seen in the Viszla, Weimeraners and Dachshunds. The author believes this later form is not sebaceous adenitis but rather part of the syndrome known as sterile granuloma/pyogranuloma syndrome (sterile periadnexal granulomatous dermatitis) and will not be discussed in this lecture.

A genetic basis has been identified in Standard Poodles and is believed to be an autosomal recessive trait. Both the spontaneous and genetic forms of the disease occur in young adult to middle aged dogs.

Clinically the dog with the SPf will have adherent white scaling, follicular waxy “casts”, and matted hair from the waxy scale, varying degrees of hypotrichosis (including alopecia) and a dull appearance to the hair coat. In Standard Poodles many of the remaining hairs lose their curls. Secondary bacterial folliculitis may be present and result in pruritus. SPf tends to begin on the dorsum, especially the head and then progress caudally and distally onto the extremities.

Early histopathologic changes that are found with the granulomatous form include a nodular granulomatous to pyogranulomatous reaction in the ischemic region of the hair follicle that is unilateral (sebaceous glands are unilateral), follicular and surface hyperkeratosis (clinically will appear as scaling). In the end stage of the disease, the inflammation has resolved and you will be left with perifollicular fibrosis, follicular atrophy and absence of sebaceous glands. Treatment for the SPf includes treating secondary bacterial or Malassezia infections. Pre-bath spraying with baby oil, bathing with a keratolytic shampoo (eg sulfur/salicylic acid containing product) and follow with a humectant. Keratolytic agents will cause desquamation of the cornified epithelium, basically loosening the outer layer of the skin (SC). Oral omega 3/6 combination products at double the bottle dose and evening primrose oil (500 mg bid). The author has discontinued using oral Vitamin A for this disease. This is based on a study that revealed there was no correlation between vitamin A dosage and response to treatment nor any difference between dogs responding and those not responding to adding vitamin A to topical therapy. In addition, there is evidence that retinoids are the most potent pharmacological inhibitor of sebum secretion. Histological changes in sebaceous gland size can be seen after 8 weeks of treatment. The sebaceous glands have a reduced size and the sebocytes appear undifferentiated with decreased lipid accumulation. These are undesirable effects in treating sebaceous adenitis.

In a study oral cyclosporine was used to treat 12 dogs with SA (not just SPf). Ten of twelve dogs improved within 4 months however most needed topical therapy once the mCSA was discontinued. In summary, treatment with mCSA resulted in clinical improvement in dogs with SA, with the greatest improvement evident within 4 months after the initiation of treatment. The authors concluded that long-term treatment appears to be necessary to control the disease. The authors reported that there was some evidence that mCSA was of limited benefit in dogs with chronic disease in which the perifollicular inflammatory reaction had already resolved. Therefore, treatment with mCSA should be initiated as early as possible during the course of the disease.

A subsequent study is only available in abstract form so details are lacking. This study involved 20 dogs with SA. Initial therapy included essential fatty acid supplementation with a total gamma linolenic acid dose of 10–20 mg/kg once daily and an antiseborrhoeic shampoo twice weekly. All animals were assessed at 3 weeks. An improvement in coat condition was noted at this time, but there was no evidence of hair regrowth. Treatment was started with topical cyclosporine. Twenty-five millilitres of cyclosporine (Neoral oral solution, 100 mg/mL) made up to a total volume of 250 mL of liquid with sterile water (making it a 1% solution) was applied to the coat once daily followed by an emollient spray. At a 6-week recheck, further improvement was noted. In
some cases, new hair regrowth was apparent. In six dogs, blood samples were taken at 9 weeks to measure blood levels of cyclosporine. In no case could cyclosporine be detected. Therapy was successful in every case, but was deemed too labor intensive by the owners of some dogs. Despite good initial improvement in their dog’s skin condition, they were lost to follow-up. In all other cases, once hair had regrown after 8–12 weeks, the frequency of application could be reduced to once or twice weekly.

In a study using 9 dogs Lucas et al used a 0.4% CSA solution. He made the solution by mixing four 100 mg capsules in 100 mL vegetable oil. The solution was applied twice per week. Clinical improvement was noticed in all dogs, and total hair regrowth occurred in 4 months. Topical (0.4%) cyclosporine A applied twice a week was well tolerated and efficacious in the symptomatic treatment of sebaceous adenitis in dogs.

Lastly there was a study that revealed that the combination of topical treatment and oral CSA gave the best results. Differences between the treatment protocols are marginal. Topical treatment, both alone and in combination with CsA, appeared to reduce scaling more effectively than CsA alone. Both therapies reduced alopecia. In the study there was some evidence suggesting a synergistic benefit on both scaling and alopecia if both treatment options were combined. Inflammation of the sebaceous glands was reduced the most by a combination of both CsA and topical therapy. There was evidence that regeneration of sebaceous glands is best achieved by CsA, either given alone or in combination with topical treatment.

The next group of alopecic diseases that will be discussed are the ones that are diffuse or symmetrical on examination. The first group we will discuss are the endocrinopathies. Hypothyroidism is one of the most over-diagnosed endocrine disease in the author’s referral practice. Hypothyroidism is most commonly caused by an immune mediated destruction of the thyroid gland. Middle-aged medium sized to large breed dogs are the most commonly affected dogs. Clinical findings that have been associated with hypothyroidism are quite extensive and will not be reviewed here. A few dermatologic clues would include seborrhea sicca or oleosa, poor hair regrowth (seems to be a more common complaint than spontaneous alopecia), recurrent bacterial pyoderm and a dry, dull hair coat. Alopecia (triangular in shape) just caudal to the nasal planum is another finding that suggests hypothyroidism. The “frizzies” may be seen in Golden retrievers and Irish setters. CBC, serum chemistry profile and urinalysis may reveal mild nonregenerative anemia, hypercholesterolemia and hypertriglyceridemia. Thyroid testing is needed for a definitive diagnosis of hypothyroidism. Thyroid tests that are of value include Total T4 (TT4), free T4 by equilibrium dialysis (fT4ed), thyroid stimulating hormone concentrations (cTSH), thyroglobulin autoantibody (TgAA), T4 autoantibodies (T4ab) and T3 autoantibodies (T3ab). Details of these tests sensitivity and specificity are beyond the scope of this lecture.

The thyroid profile requested by the author includes TT4, cTSH, TgAA, T4ab, T3ab. The author will have a fT4ed added to the profile if there are T4ab present, if non-thyroidal illness is present or the dog has received drugs known to affect the thyroid. In general DOGS MUST NOT HAVE RECEIVED TOPICAL OR ORAL STEROIDS FOR 30 DAYS OR REPOSITOL STEROIDS FOR 3 MONTHS BEFORE TESTING THE THYROID. Also, they must not have received sulfas drugs for at least 30 days. For dogs with hypothyroidism, after 1 month of therapy (L-thyroxine 0.02 mg/kg bid-use BRAND NAME ONLY), a blood sample is submitted 4-6 hours post pill for a TT4. The levels should be in the upper range of normal or even a little higher than normal.

A far more common endocrinopathy seen by the author is hyperadrenocorticism (HAC). It is not the purpose of this lecture to discuss all the symptoms of HAC but a few points must be made. In dermatology it is NOT uncommon to have a dog with HAC present without pu/pd or a potbelly appearance and may ONLY have a recurrent pyoderm, poor hair regrowth or non-inflammatory truncal alopecia. If there is a suspicion that the dog may have an endocrinopathy (based on PE, cbc, serum chemistry and urinalysis results) then it is important to first rule out HAC since a dog with HAC may have a low thyroid profile due to the influence that steroids have on the thyroid gland. The 2 screening tests that are used by the author are the ACTH stimulation and the LDDS. If the dog has a history of steroid exposure, then an ACTH stimulation test is performed. If the dog has no recent steroid exposure, then the author prefers to begin with a LDDS test. Note that 1 normal screening test doesn’t rule out HAC. The author believes that the sensitivity of the LDDS is much better than the ACTH stimulation. Treatment for HAC is based on the severity of the clinical signs. Either trilostane or mitotane may be used for treatment.

Dyscyclic follicular diseases of unknown etiology (post clipping alopecia, alopecia X, seasonal flank alopecia) are diseases in which the hair follicle is structurally normal but it is not cycling properly. Rule outs for these dyscyclic diseases include the endocrinopathies already discussed and also hyperestrogenism (sertoli cell tumor associated).

Alopecia X is a syndrome of unknown etiology. Theories abound as to the cause including an adrenal sex hormone imbalance, an abnormal metabolism of hormones by the hair follicle or a hormone receptor problem at the follicular level. The later theory is supported by the observation that hair regrows at the site of skin biopsies. This ability to induce hair regrowth by localized trauma would suggest a local inhibition of hair cycling rather than systemic. Alopecia X occurs in plush coated breeds and in poodles. It occurs in young adults of either sex or reproductive status. Clinically these dogs lose their guard hairs, beginning on the neck and progressing to the shoulders, trunk and thighs. Eventually the dog may have a woolly, cream color coat. In some dogs this may progress to alopecia with hyperpigmentation. Diagnosis is based on signalment, hx, PE and ruling out (r/o) other alopecic diseases. Histopathology can support but not diagnosis Alopecia X. That is because the findings with Alopecia X resembles other dyscyclic alopecic diseases such as hypothyroidism, hyperadrenocorticism, gonadal sex hormone abnormalities, recurrent flank alopecia and
post clipping alopecia. Histologically, these diseases are characterized by many specific (follicular atrophy, telogenization of follicles with excessive trichilemmal keratinization (flame follicles), orthokeratotic hyperkeratosis, follicular keratosis, sebaceous gland atrophy), but nondiagnostic (nondiffereniating) findings. An adrenal sex hormone panel stimulation test can be performed but it is of questionable value in the author’s opinion. Treatments that have been used with variable success include neutering, sex hormone replacement (estrogen OR testosterone), low dose lysodren, melatonin, trilostane, growth hormone and thyroid supplementation. All of these treatments may cause a temporary improvement in the alopecia (nonspecific anagen induction?) but rarely is the hair coat returned to normal. Also these medications (other than melatonin) are associated with potentially significant side effects. In the author’s practice, if a diagnosis of Alopecia X is made then the client is counseled about the choice in treating a cosmetic disease with potent drugs. Neutering is recommended if it is an intact animal. If the alopecia fails to respond to the neutering, a therapeutic trial with melatonin 3-6 mg tid for 90 days is performed.

Seasonal flank alopecia (SFA) is a nonscarring alopecia that has been reported in a variety of breeds, but it has been reported to be more common in Boxers, Airedales and Bulldogs. The etiology is unknown. Some people think that it is caused by a “melatonin deficiency” since many of the dogs develop the lesions in the fall, when melatonin levels should be increasing and some dogs respond to melatonin administration. But there are some cases that the hair is lost in the spring and regrows in the fall so it makes this etiology impossible. The disease occurs in young adult dogs and will begin most commonly in the fall with spontaneous resolution in the spring. This disease may occur once and never recur, it may recur each year with each episode involving larger areas of the body, or it can occur once and never completely resolve. The lesions involve the flanks and sometimes the caudal lateral thorax. The alopecia is usually bilateral with annular lesions that may coalesce into polycyclic lesions with hyperpigmented and smooth glistening skin. Papules and pustules consistent with a bacterial pyoderma may develop in these areas. Diagnosis is based on r/o other nonscarring alopecias – hx alone may be diagnostic if it is a recurrent problem. Biopsy can support but not diagnose SFA. Treatment is again either a tincture of time or melatonin. Since the disease usually goes into spontaneous resolution it may be difficult to determine if the melatonin had any impact, especially the first time the disease occurs. In the author’s practice melatonin is more commonly used to prevent symptoms by beginning therapy just prior to the onset of the symptoms (if there is a seasonal pattern). Dose is as discussed previously.

Post clipping alopecia occurs primarily in the Arctic breeds. It has been theorized that these breeds have a very long telogen (resting) phase to their hair cycle in order to preserve a high protein substance (hair!). If the hair is clipped during the telogen stage, it will not regrow until it cycles back to the anagen stage. Others have suggested that when the hair is clipped there is decreased blood flow to the area (to minimize heat loss) leading to a decrease in growth factors. Diagnosis is based on hx and r/o endocrinopathies. Histopathology will reveal follicles of normal size but in most are in telogen. Treatment is tincture of time or sometimes a 7-10 days course of thyroid supplementation (will stimulate anagen resolution) or a 90 day trial of melatonin.

The structural follicular dysplasias -color linked, non-colored linked and pattern baldness all have an abnormality not just of the hair follicle but also the hair shaft. Be aware that finding dysplastic hair follicles on histopathologic is not adequate evidence to diagnosis a structural follicular disease; there should also be dysplastic hair shafts. A study in 1998 reported that 46% of the dogs with an endocrine alopecia had dysplastic hair follicles but less than 1% had concurrent dysplastic hair shafts.

Colored linked alopecias include color dilution (mutant) alopecia (CDA) and black hair follicular dysplasia (BHFD). CDA occurs in dogs with a blue or fawn hair coat. These hair coat colors occur as a result of the effect of the “dilute” gene on black or brown hairs respectively. Any dog with a blue or fawn coat may be affected by CDA but not always. Dobermans and Great Danes are the most common breeds seen in the author’s practice affected by CDA. A dog with this autosomal recessive genodermatosis is born with a normal coat but as the dog matures, usually beginning at between 4 months of age and 3 years, it will develop varying degrees of hypotrichosis (including frank alopecia) affecting the “dilute color” areas only. The hair coat will become dull and there will be scaling and comedone formation. Secondary bacterial pyoderma are frequently present. The exact cause of the hair shaft abnormality is not known but is believed to be related to a dysfunctional melanin transfer from the melanosomes to the hair matrix or a defect in the storage of the melanin once it is in the hair shaft. The result is melanin clumping. This clumping leads to weakening and eventual fracturing of the hair shaft. Diagnosis is based on hx, PE, appearance of hairs on a trichogram, r/o other alopecic diseases (especially demodex, dermatophytosis, bacterial pyoderma and endocrinopathies) and is supported by histopathology. Microscopic examination of plucked hairs will reveal melanin clumping in the hair shafts and disruption of the normal hair shaft architecture. Treatment (other than elimination from the breeding stock) is directed toward managing the secondary pyoderma and seborrhea. Bathing, humectants, fatty acids +/- antibiotics are the mainstay of therapy. Melatonin, which can stimulate hair cycling, has also been reported to improve hair coats in some dogs. The author uses melatonin, 6 mg tid, as a 90 day therapeutic trial.

BHFD is an alopecic disease of dogs with bicolored or tricolored hair coats such as Boston Terriers, Basset hounds and Cocker spaniels. It has been reported to be inherited as an autosomal recessive trait. This tardive disease is also believed to be due to a defective transfer of melanin leading to melanin clumping that weakens the hairs and eventual fracture. Usually abnormalities of the hair coat are noted by the time the dogs are weaned. Initially changes consist of a dull hair coat affecting only black hairs. Eventually these areas become alopecic. As with CDA secondary pyoderma may occur. It may be easiest to think of BHFD as a localized form
of CDA. Histopathology is similar to CDA and diagnosis is based on signalment, hx, PE, appearance of hairs on a trichogram and can
be supported by histopathology. Treatment is the same as CDA.

Non-colored link follicular dysplasias have been reported in a number of breeds including Portuguese Water dogs, Irish Water
Spaniels and Curly Coated Retrievers. Between 6 months and 6 yrs of age (depending on the breed) these dogs develop symmetrical
hypotrichosis to alopecia usually beginning on the neck and progressing to the shoulders, trunk, tail and thighs. Any remaining
truncal hairs may have a color change (lightening). In dogs, estrogen receptors are present in telogen hair follicles and are important
in keeping hairs in this phase. In Irish Water Spaniels dietary change (avoiding soy which may contain phytoestrogens) has been
reported to be effective. Melatonin and trilostane both block estrogen receptors and may account for the effectiveness of these drugs
in a variety of canine alopecic diseases.

Pattern baldness alopecia (PBA) is also a tardive genodermatosis. The dogs are born with a normal coat but develop PBA at 6
months-1 yr of age. There are 4 different forms of this non-inflammatory, non-pruritic alopecia. One form occurs in male
Dachshunds. These dogs develop a slowly progressive alopecia and hyperpigmentation of the pinnae. A second form occurs in
primarily in female Dachshunds, Chihuahuas, Whippets, Manchester Terriers, Greyhounds, and Italian Greyhounds. This form is
identical to the first form except for the distribution of the alopecia. In this form there is progressive alopecia caudal to and involving
the pinnae, ventral neck, ventrum and caudomedial thighs. The 3rd form affects American Water Spaniels and Portuguese Water
Dogs (see above). The last form is seen affecting the caudolateral thighs of Greyhounds. Regardless of the form of the PBA,
diagnosis is made on signalment, hx, PE, ruling out other alopecic diseases and supported by histopathology in which there is
miniaturization of hair follicles and shafts with normal adnexa. There have been reports of some dogs improving with melatonin.
What would you do? An interactive session where a real case is presented for the audience to diagnose and manage

This case presentation will focus on a typical allergic dog that is not responding to therapy as he has in the past. During this discussion we will focus on the step by step approach that should be taken to help address this dog’s problems in the most cost effective manner. Also we will discuss common pitfalls that occur in managing these cases and how to avoid them. We will discuss both the short term and long term therapy of an allergic dog. During the session we will learn which questions to ask, which tests to perform and which therapies should you use and which you should avoid. We will delve into how to interpret bacterial cultures using the MIC data and how it applies clinically to dosing and frequency of antibiotics. We will discuss which antibiotics are considered first tier and which are considered second tier when dealing with bacterial pyodermas in the dog.
The importance of the dermatological history can’t be overstated. Having a standardized dermatological history form for clients to fill out can be extremely useful and improve efficiency. Regardless of if it is obtained via paperwork or on direct questioning, there is basic information that should be known prior to the dermatological examination. It is remarkable how much of a differential diagnosis list or working diagnosis can be generated with history alone.

**What is the chief complaint?**
You immediately need to know why the pet is presenting to you, as it will help guide your historical questions and allow you to instantly identify to the client that you are addressing why they brought the animal in. If you don’t do this, they can become frustrated as you proceed to questions that in their mind could be irrelevant.

**What is the signalment of the pet, when was it acquired and from where?**
Many skin conditions have a strong predilection for certain breeds, ages and genders of the pet. For example, if a 4-month-old puppy presents with acute facial swelling, huge submandibular lymph nodes and a papular/pustular rash on the muzzle, juvenile cellulitis would be the top differential. If a young Persian cat obtained from a cattery presented with non-pruritic alopecia, dermatophytosis would be the top working diagnosis until proven otherwise.

**What is the age of onset of the dermatological condition?**
The age of onset when dealing with pruritic disease is extremely useful information. Pruritus beginning before 6 months of age is most often seen in parasitic diseases, allergies (most often flea allergy or food allergy) and dermatophytosis. Middle-aged pets would include the above but also tend to emphasis allergies (food and atopic dermatitis). When older pets present with new pruritic skin disease food allergies are a top differential, as are more unusual causes of pruritus in older animals, such as mycosis fungoides (cutaneous T cell lymphoma). Furthermore, certain hormonal and autoimmune diseases are more likely to occur at certain times in a pet’s life than others.

**What is the seasonality of the dermatological condition?**
The presence of seasonal pruritus makes atopic dermatitis and/or flea allergic dermatitis more likely. If seasonality is present during which time the patient’s symptoms fully resolve and then return after a substantial period of time, certain conditions, such as food allergies and endocrinopathies are unlikely and can usually be ruled out.

**Questions about the pet’s immediate environment: is the patient indoor/outdoor; if outdoor what percentage of the time; what kind of exposure to the non-home environment do they have: i.e. how frequently do they board, go to dog parks, doggy day care, etc. Are there other pets in the household? If so, what species and are they affected with dermatological disease as well. Are any humans in the house affected with dermatological disease?**
Determining the nature of the pet’s environment is very important. Animals that have a history of leaving the home environment can be more at risk to be exposed to parasites (fleas, sarcoptes) and infectious agents (dermatophytosis, viral infections). Symptoms triggered by environmental changes such as a recent move or addition of a new pet can all help give clues to if the condition could be allergic or parasitic. Knowing if any animals or people in the household have skin disease can be very important, as it would make contagious or zoonotic conditions a consideration.

**Is the patient pruritic? If so, what is owner’s numerical assessment using the pruritus score (0-10)?**
In a pruritic patient, it is helpful to have the client assess the pruritus scale for you at each appointment. This helps gauge progress and provides documentation that allows you to track seasonality/waxing and waning in your records. Different conditions have typical levels of pruritus that are expected. Canine sarcoptic mange and feline notoedric mange are some of the itchiest skin diseases that occur, with most owners observing 10/10 on the pruritic scale. Hormonal and autoimmune diseases are typically minimally pruritic, although the presence of a secondary infection can create a level of pruritus that can mimic allergies. Similarly, canine demodectic mange is classically considered a non-pruritic disease, which is why many demodectic dogs that are pruritic from secondary bacterial infection are commonly misdiagnosed as allergic and erroneously treated with glucocorticoids.

**What types of symptoms is the patient displaying?**
It is important to clarify the dermatological symptoms that the owner is observing including, but not limited to: pruritus, alopecia, rashes, pustules, blackheads, erythema, hives, crusting or the presence of growths or nodules.
What are the locations of the symptoms?
Many conditions have predilections to manifest at certain locations. A dog that has front paw licking and recurrent ear infections is typically food allergic and/or atopic. Pemphigus foliaceus would be the top concern in a cat with crusting on the nail beds, pinna, and around the mammae. Because lesions can come and go and because the dermatological examination may not indicate the location of a pet’s problems (especially in allergies), having the owner tell you where they perceive symptoms is extremely important. A pruritic dog that comes in looking 100% normal but whose owner reports non-stop chewing at the base of the tail needs to be treated for flea allergies before proceeding to other differentials, regardless of if fleas or flea dirt are present.

Does the patient have any other previous problems?
Knowing about other concurrent or previous diseases can be very important. Dogs with a history of inflammatory bowel disease (IBD) that develop pruritus may be more likely to have a dietary allergy. Herpes virus and calicivirus would be concerns in a cat with a history of upper airway viral disease that has developed facial lesions and pruritus.

Does the patient have any concurrent gastrointestinal symptoms? How many bowel movements does the patient have daily? Are they prone to vomiting/diarrhea/loose stool/gas/perianal pruritus?
All these questions are asked to obtain if the patient is possibly displaying other symptoms of food allergies. Whenever I have a pruritic puppy with five-six bowel movements daily I have a serious discussion about diligent evaluation for underlying food allergies. If a patient like this persists with symptoms after one food trial I’m more likely to try a second food trial with a different diet before moving on to other causes of differentials.

What current medications is the pet on? What is the pet’s vaccination history? Has the pet received any medications/treatment for this condition and if so what was the efficacy of these treatments?
Certain drugs and vaccines can create drug reactions, and having a detailed history of all previously used drugs is very important. If the current pruritic condition is drug responsive, to what drugs is helpful information. Is the condition antibiotic or glucocorticoid responsive? Many allergy cases are glucocorticoid responsive, however some cases are not or may require higher than typical dosages. Knowing that the condition gets worse with glucocorticoid therapy would make you think of infectious conditions, such as dermatophytosis, demodicosis or possibly autoimmune diseases such as pemphigus foliaceus (PF). PF can be very pruritic and non-glucocorticoid responsive especially if the dosage of the glucocorticoids was not initially high enough. Knowing current medications before prescribing new therapy is critical as there are many drug interactions to be aware of. Do not use oral monthly spinosad flea treatments in patients receiving high dose ivermectin for parasitic conditions, as this can potentiate neurological side effects. Never prescribe glucocorticoid therapy to a patient receiving non-steroidal therapy, as this can cause stomach ulceration.
This will be a case based lecture, which each case being representative of a cutaneous manifestation of a systemic disease. This is meant to be a more interactive hour to help practitioners think about how to appropriately work up these more unusual cases. Conditions that will be covered include superficial necrolytic dermatitis (also known as shepatocutaneous disease), feline paraneoplastic alopecia, cutaneous xanthomas and nodular dermatofibrosis.
Dermatophytosis implies cutaneous infection with one of several species of keratinophilic fungi. Three species are responsible for the vast majority of clinical cases: Microsporum canis, Microsporum gypseum and Trichophyton mentagrophytes. Microsporum gypseum is a soil inhabitant, Microsporum canis is a zoophilic organism that has adapted to animals and is a normal inhabitant of the hair coat of some cats. Trichophyton mentagrophytes infections are usually associated with exposure to rodents or their environment. Dermatophytosis is a disease, which is both over diagnosed, as well as often overlooked. If clinicians rely on clinical signs alone the disease is over diagnosed. Since the organism usually causes a folliculitis, a common clinical sign is circular areas of alopecia with scale. These signs cannot be clinically distinguished from a staphylococcal folliculitis or demodicosis. However, due to the variety of other clinical presentations, dermatophytosis is often overlooked. Many patients will show papular eruptions with variable scale and crust and cats often times can display military dermatitis. Pruritus is also extremely variable; some cases are non-pruritic while others can be very pruritic. This may lead to an erroneous diagnosis of an allergic condition or other pruritic disease, with the subsequent inappropriate use of glucocorticoids. Without appropriate diagnostics, dermatophytosis can go undiagnosed for long periods of time.

Definitive diagnosis of dermatophytosis is made by positive fungal culture or identifying the organism by histopathology, although diagnosis is best made with positive fungal cultures. Dermatophyte test media (DTM) is a convenient fungal culture media commonly used by practitioners. Dermatophytes utilize protein and produce an alkaline by product that produces a red color change. However, after all the carbohydrates are utilized, the saprophytes can utilize the protein and turn the media red. The DTM cultures should be inspected daily. Suspected fungal growth can be lifted with clear plastic tape and stained with lactophenol cotton blue for characteristic macroconidia and fungal identification. Identifying the dermatophyte causing the infection is extremely important, as it will tell you where the pet contracted the fungal organism and how to best control it. If the source of the fungus isn’t addressed, reinfection after treatment is possible.

Other less accurate diagnostics include Wood's light fluorescence and direct microscopic examination of the hair. The Wood's light fluorescence is positive in only a small percentage of M. canis cases. Positive fluorescing hairs should be plucked for DTM culture or for direct microscopic examination. The direct microscopic examination requires a trained individual, and hyphae or arthrospores can be seen in 40-70% of cases. Diagnosis of dermatophytosis by Wood’s lamp examination is wrought with hazards. The Wood’s light is an ultraviolet light with a light wave of 253.7 nanometers filtered through a cobalt or nickel filter. When exposed to this UV light, hairs infected by M. canis may give a yellow/green fluorescence. The fluorescence is caused by the tryptophan metabolite produced by the organism. This test however is subject to numerous errors. False negative results may be obtained by inadequate examination. The lamp should be allowed to warm up for 5 minutes since the light wavelength is more stable at certain temperatures. Some hairs also need prolonged exposure to show fluorescence. Certain medications like iodine will also destroy fluorescence. False positive results are also common. It is essential to remember that only the hairs should fluoresce. Color changes to scale, crust or other material is not significant. Certain bacteria, specifically Pseudomonas or Corynebacteria may also cause fluorescence. It is imperative to remember that of the commonly encountered veterinary dermatophytes, only Microsporum canis will fluoresce and, then, only approximately 40% of the time. So while a positive Wood’s lamp test is meaningful, a negative test means nothing and further diagnostics should be undertaken.

Treatment

There are three keys to the appropriate treatment of dermatophytosis: environmental decontamination, topical treatment, and systemic treatment.

The environment should be addressed in every case of dermatophytosis you diagnose. This is the most important in cases of M. canis, as the spores can live in the environment for up to 18 months. Vacuuming, disinfection, steam cleaning, and discarding infected bedding are all important.

Topical therapy is palliative at best and in a number of cases is ineffective on its own. This is not surprising if you remember that this disease is causing a folliculitis and topical medications are just unable to penetrate the skin as much as needed. Many miconazole, ketoconazole and chlorhexidine based shampoos and rinses are available and can be applied 2 to 3 times a week. An older, reportedly effective topical is 2% lime sulfur, it can be tried at 5-7 day intervals. Shaving affected longhaired cats with generalized lesions may facilitate topical therapy. Shaving dermatophyte patients needs to be done with care. Not adequately cleaning/containing the shaved hair can cause release of infected hairs into the environment. If the pet is shaved too closely, microtrauma to the skin can occur which can facilitate infection of the fungus into the hair follicle.
There are numerous drugs that can be used when treating dermatophytes. Regardless of the drug chosen, the author prefers to treat through two-three consecutive negative fungal cultures at 2-4 week intervals. The first culture is usually taken 4-6 weeks into treatment, depending on the drug used and the clinical presentation, and only after clinical signs have resolved and a previously positive Wood’s lamp is now negative.

**Systemic oral medications used for treating dermatophytosis:**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Griseofulvin (microsized)</td>
<td>50-100mg/kg divided BID</td>
<td>Monitor CBC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Give with a fatty meal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Teratogenic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Do not use in FIV cats</td>
</tr>
<tr>
<td>Griseofulvin (ultramicro)</td>
<td>10-15mg/kg divided or as a single daily dose</td>
<td>Same as above</td>
</tr>
<tr>
<td>Itraconazole daily</td>
<td>5mg/kg once daily</td>
<td>Monitor liver values</td>
</tr>
<tr>
<td>Itraconazole pulse</td>
<td>5mg/kg once daily for 1 week, off one week, repeat</td>
<td>Monitor liver values</td>
</tr>
<tr>
<td>Ketoconazole</td>
<td>10mg/kg/day (dog)</td>
<td>Monitor liver values</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Not as effective</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Higher incidence of GI side effects in cats-so not recommended</td>
</tr>
<tr>
<td>Terbinafine</td>
<td>30mg/kg/day</td>
<td>Monitor liver values</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anecdotal efficacy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>May be safer in animals with liver issues</td>
</tr>
<tr>
<td>Fluconazole</td>
<td>5-10mg/kg/day</td>
<td>Monitor liver and kidney values</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Not always as effective</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Typically safe and well tolerated</td>
</tr>
</tbody>
</table>

**Other**

Lufenuron (Program®, Novartis) has been used for dermatophytosis treatment due to its anti-chitin properties. It is used at 100mg/kg every 14 days. There is a tremendous amount of controversy associated with its success. Controlled prospective studies have cast doubt on its efficacy. Some dermatologists use Program in conjunction with other systemic treatment, but it is not recommended to use as the main systemic treatment. Dermatophyte vaccines have been used in Europe to treat cattle and foxes, and have been available in the United States. However, for small animals they show little benefit and are not recommended by the author.
This two hour lecture will be purely cased based, going through several complicated dermatology cases. A variety of patients will be presented, and the discussion will help establish the thought processes used to manage cases that present as a diagnostic or therapeutic challenge.
Diseases of the nasal planum and footpads in cats and dogs range from life threatening diseases to benign conditions that require long-term therapy to maintain control. It is of the utmost importance to properly diagnose the diseases that affect these locations, as the treatment and prognosis varies greatly depending on the disease entity. It cannot be underestimated how valuable histopathology is in elucidating the majority of these diseases.

History
Taking a thorough history is the first step in determining the underlying cause of diseases of the nasal planum or footpads. Age of onset, breed, gender, location of lesions, systemic illness, spread to other animals/humans, husbandry conditions and chronicity/progression of disease all give clues to narrow down the differential list. For example, if a cat with a history of chronic upper respiratory tract infections starts developing ulceration of the nasal planum, feline herpesvirus dermatitis would be a top differential.

Physical examination
A complete physical examination is key. It is especially important when evaluating diseases of the paws to differentiate between diseases of the footpads versus interdigital pathology, as both can cause lameness and pain. Furthermore, the presence of lesions on locations other than the nasal planum and footpads needs to be noted, as this will affect the differential list. In addition, the lesion type should be determined to help assist with the differential diagnoses list.

Differential diagnoses
Tables 1 and 2 present the most significant diseases affecting the nasal planum and footpads of cats and dogs, as well as other key points about the diseases.

Diagnostic tests
Cytology/skin scraping
Cytology can be very helpful in cases involving the nasal planum and footpad to evaluate for things such as bacteria, acantholytic keratinocytes associated with pemphigus, and inflammatory cells that can give clues to the underlying etiology. Skin scraping can also be useful in certain cases to evaluate for parasitic causes of disease.

Fungal culture
Fungal culture should be performed to rule out dermatophytosis. In cases where acantholytic cells are seen on cytology and pemphigus is suspected, a fungal culture should definitely be performed as inflammatory, pustular dermatophytosis can cause acantholysis.

Skin biopsy
Definitive diagnosis of the majority of the diseases of the nasal planum and footpads are confirmed by histopathology. It is imperative that the clinician be comfortable choosing lesional skin, as this is the most likely to provide a definitive diagnosis. In general, ulcerated skin should be avoided, as the epidermis is no longer intact. As bacteria and/or yeast often colonize compromised skin, treatment with antimicrobials is usually indicated prior to taking biopsies. Furthermore, as diseases of these anatomical locations are often unusual, it is also recommended that biopsy samples be sent to a dermatopathologist or a pathologist with a special interest in skin disease, as the changes in some of these conditions can be subtle and require an experienced eye to diagnose.
<table>
<thead>
<tr>
<th>Feline Diseases and incidence</th>
<th>Anatomical Sites</th>
<th>Other key points</th>
<th>Predispositions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pemphigus foliaceus (Uncommon)</td>
<td>Nasal Planum</td>
<td>Pustules, hyperkeratosis, crust and pitting</td>
<td>Lesions can occur anywhere, but are especially common on the pinna, nail beds and nipples</td>
</tr>
<tr>
<td>Drug eruption (Rare)</td>
<td>Footpads</td>
<td>Ulcerative dermatitis</td>
<td>Highly variable in presentation and body parts affected.</td>
</tr>
<tr>
<td>Erythema multiforme (Rare)</td>
<td>Nasal Planum</td>
<td>Ulcerative or vesiculobullous dermatitis</td>
<td>Most common on the trunk and mucocutaneous junctions.</td>
</tr>
<tr>
<td>Herpesvirus dermatitis (Uncommon)</td>
<td>Footpads</td>
<td>Uncommonly causes an ulcerative/crusting dermatitis</td>
<td>Skin lesions commonly follow the path of the trigeminal nerve</td>
</tr>
<tr>
<td>Plasma cell pododermatitis (Uncommon)</td>
<td>Nasal Planum</td>
<td>Swelling with a layer of white, scaly striae</td>
<td>FeLV/FIV cats at higher risk</td>
</tr>
<tr>
<td>Systemic lupus erythematosus (Very rare)</td>
<td>Footpads</td>
<td>Erythematous, scaling, crust and pitting</td>
<td>Symmetric face, ear and paw lesions</td>
</tr>
<tr>
<td>Squamous cell carcinoma (Uncommon)</td>
<td>Nasal Planum</td>
<td>Under cutaneous horns or, rarely, an ulcerative dermatitis</td>
<td>Pinna, eyelids and lips commonly affected</td>
</tr>
<tr>
<td>Epitheliotropic lymphoma (Rare)</td>
<td>Footpads</td>
<td>Erythema, depigmentation or ulceration</td>
<td>Variable</td>
</tr>
<tr>
<td>Vasculitides (Rare)</td>
<td>Nasal Planum</td>
<td>Ulcerative dermatitis</td>
<td>Pinna, lips and oral mucosa</td>
</tr>
<tr>
<td>Mosquito bite hypersensitivity (Common)</td>
<td>Footpads</td>
<td>Papulocrusting, ulcerative dermatitis</td>
<td>Crusting, papular, erosive dermatitis, on the pinna and bridge of the nose</td>
</tr>
<tr>
<td>Eosinophilic granuloma (Common)</td>
<td>Footpads</td>
<td>Firm, erythematous or ulcerated footpad swellings</td>
<td>Often present in the oral cavity, on the chin and limbs</td>
</tr>
<tr>
<td>Canine diseases</td>
<td>Anatomical Sites</td>
<td>Other key points</td>
<td>Breed Predispositions</td>
</tr>
<tr>
<td>----------------------------------------------</td>
<td>-----------------------------------------------</td>
<td>-------------------------------------------------------</td>
<td>----------------------------------------</td>
</tr>
<tr>
<td>Pemphigus foliaceus (Common)</td>
<td>Pustular dermatitis that leads to crusting, alopecia, depigmentation, erythema and erosions</td>
<td>Hyperkeratosis and crusting</td>
<td>Chow Chows and Akitas</td>
</tr>
<tr>
<td>Pemphigus vulgaris (Very rare)</td>
<td>Vesiculobullous progressing to an erosive/ ulcerative dermatitis</td>
<td>---</td>
<td>None</td>
</tr>
<tr>
<td>Discoid lupus erythematousus (Common)</td>
<td>Erythema/crusting/depigmentation/scaling that leading to loss of cobblestone/ ulceration/erosion/ fissuring</td>
<td>Hyperkeratosis of the footpads is uncommon</td>
<td>German shepherds, Labrador retrievers, Collies</td>
</tr>
<tr>
<td>Drug eruption (Rare)</td>
<td>Ulcerative dermatitis or pemphigus-like lesions</td>
<td>Ulcerative dermatitis or pemphigus-like lesions</td>
<td>None</td>
</tr>
<tr>
<td>Erythema multiforme (Rare)</td>
<td>Ulcerative or vesiculobullous dermatitis</td>
<td>Ulcerative or vesiculobullous dermatitis</td>
<td>None</td>
</tr>
<tr>
<td>Uveodermatological Syndrome (Rare)</td>
<td>Depigmentation, rarely crust and erosion</td>
<td>Depigmentation</td>
<td>Akitas, Siberian huskies, Chows</td>
</tr>
<tr>
<td>Vitiligo (Uncommon)</td>
<td>Depigmentation</td>
<td>Depigmentation</td>
<td>Rottweilers, German shepherds, Dobermans</td>
</tr>
<tr>
<td>Nasal hyperkeratosis (parakeratosis) of Labrador retrievers (Uncommon)</td>
<td>Hyperkeratosis, crusting, depigmentation that can lead to ulceration and erosion</td>
<td>Hyperkeratosis of the footpads can be seen</td>
<td>Labrador retrievers and their crosses</td>
</tr>
<tr>
<td>Epitheliotropic lymphoma (Rare)</td>
<td>Depigmentation, scale, crusting, or ulcerative dermatitis Early lesions often develop around nasal planum</td>
<td>Depigmentation, hyperkeratosis or crusting.</td>
<td>Golden retrievers</td>
</tr>
<tr>
<td>Squamous cell carcinoma (Common)</td>
<td>Ulcerative erosive, swollen, erythematous, painful, necrotic dermatitis</td>
<td>Ulcerative dermatitis</td>
<td>Beagle, Dalmatian, Bull terrier</td>
</tr>
<tr>
<td>Zinc responsive dermatoses (Uncommon)</td>
<td>Erythema, crusting dermatitis</td>
<td>Hyperkeratosis and crust</td>
<td>Siberian husky, Alaskan malamute, American Eskimo, Samoyed</td>
</tr>
<tr>
<td>Mucocutaneous pyoderma (Common in general, rare on the nasal planum)</td>
<td>Crusting and erythema that can lead to fissuring</td>
<td>---</td>
<td>German shepherds and their crosses</td>
</tr>
<tr>
<td>Condition</td>
<td>Clinical Findings</td>
<td>Associated Conditions</td>
<td></td>
</tr>
<tr>
<td>-------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------</td>
<td>------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Superficial necrolytic dermatitis (Rare)</td>
<td>Crusting and erythema, moderate-severe hyperkeratosis and crusting which can lead to ulceration and fissuring</td>
<td>Erythema, hyperkeratosis and crusting of the mucocutaneous junctions</td>
<td></td>
</tr>
<tr>
<td>Distemper (Not uncommon)</td>
<td>Crusting and hyperkeratosis, Crusting and hyperkeratosis</td>
<td>Generalized impetigo Unvaccinated dogs</td>
<td></td>
</tr>
<tr>
<td>Systemic lupus erythematosus (Rare)</td>
<td>Erythematous, scaling, crusting, ulcerative and erosive dermatitis. Depigmentation and scarring can occur</td>
<td>Ulcerative, erosive, erythematous, crusting, or alopecic dermatitis. Lesions most common on face, ears and paws, lesions very variable, typically bilaterally symmetric German shepherds-medium to large breed dogs</td>
<td></td>
</tr>
<tr>
<td>Familial footpad hyperkeratosis (Rare)</td>
<td>---</td>
<td>Severe hyperkeratosis of the footpads, as well fissuring and the formation of cutaneous horns Abnormal nail growth has been reported</td>
<td></td>
</tr>
<tr>
<td>Vasculitides (Uncommon)</td>
<td>Crusting, ulcerative dermatitis. Depigmentation can occur</td>
<td>Ulcerative, necrotic dermatitis common on the pinna, lips, tail tip, periocular skin, and in the oral cavity</td>
<td></td>
</tr>
<tr>
<td>Dermatomyositis (Uncommon)</td>
<td>Depigmentation and scale. Ulceration if a vasculitic component is present</td>
<td>Muzzle, periocular, ear and tail tips commonly affected. Symptoms associated with myositis can also be seen</td>
<td></td>
</tr>
<tr>
<td>Hookworm dermatitis (Uncommon)</td>
<td>---</td>
<td>Hyperkeratosis and erythema leading to painful, pruritic paws Affects areas that typically contact the infected ground, such as the interdigital spaces, sternum and groin. Dogs housed in unsanitary environments</td>
<td></td>
</tr>
</tbody>
</table>

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Cats are not small dogs when it comes to pruritus. Diagnosing the underlying cause of itching in the cat can be difficult due to variations in clinical presentation and numerous possible etiologies. Many cats are secretive about licking and overgrooming, making it difficult to assess their true itch level. It is critical to be able to interpret historical information, identify and understand the meaning of clinical lesions, and know the appropriate usage of diagnostic tests when diagnosing and managing the pruritic cat.

### Historical information

#### Signalment

Age of onset and breed can provide clues to underlying etiologies. Pruritus beginning prior to six months of age is more commonly associated with parasitic diseases (*Notoedres*, cheyletiellosis, *Otodectes*), allergies (especially food and flea) and dermatophytosis. When pruritus begins in middle age, the differentials include those mentioned for younger animals, but allergic disease becomes more probable (food allergy and atopy). When pruritus begins in older animals with no history of prior skin disease, conditions such as epitheliotropic lymphoma, pemphigus foliaceus, Bowen’s disease and paraneoplastic syndromes should also be considered, although food allergy can present at any age. Finally, breed predilections exist for certain diseases, such as Persians for dermatophytosis and Siamese for food allergies.

#### Environment

Outdoor cats have greater exposure to mosquitoes, parasites (ex. fleas and *Notoedres*) and infectious agents (ex. dermatophytes and viruses). Knowing if other people or pets are affected can indicate if a contagious or zoonotic disease is present, such as dermatophytosis, cheyletiellosis, *Notoedres* or *Otodectes*. Psychogenic pruritus can be triggered by environmental changes, such as construction/remodeling/moving, or introduction of a new pet or person into the household. Siamese and their crosses seem to be at risk for psychogenic disorders, although it should not be assumed based on breed, and is diagnosed only after all other causes of pruritus have been excluded. If an animal's symptoms are fully medically responsive to non-behavior medications, psychogenic disease can be ruled out.

#### Previous drug and disease history

In cats with concurrent histories of pruritus and gastrointestinal disease (ex. inflammatory bowel disease), food allergy should be seriously considered. Atopic dermatitis needs to be strongly considered in pruritic animals with concurrent airway disease/asthma. Viral dermatoses should be suspected in cats with a history of upper airway viral disease that develop erosive facial lesions. Vaccines and drugs, even those perceived as safe, can trigger erythema multiforme and pemphigus foliaceus.

### Physical examination

#### Lesion distribution and type

Distribution of lesions, especially at the initial stages of the disease, can be extremely useful in narrowing a differential diagnosis list. Flea allergy cases are typically more severe over the lumbosacral, groin and dorso-cervical areas, whereas food allergies often focus on the head. Atopy symptoms can be variable, and can easily mimic food and flea allergy presentations. Cheyletiellosis tends to have a dorsal distribution, presenting with scale, papules and crusts. Dermatophytosis can be localized to a specific site or can present more generalized. Asymptomatic carriers can be seen with both cheyletiellosis and dermatophytosis. Pemphigus foliaceus usually targets the pinnae, bridge of the nose, claw folds and peri-mammary areas, but can also be generalized. These lesions tend to be thick crust, often honey-colored. The pustule stage can be super difficult to observe in pemphigus cats. Remember to submit crust when biopsying, as the is is where the diagnostic acantholytic cells are present in the highest numbers.

Being able to recognize and identify lesion types can provide valuable information in the evaluation of a pruritic cat. The following are the most typical lesion types seen in our pruritic cat patients.

- **Excoriations**, which are a nonspecific symptom, typically of scratching, are characterized by their linear shape and are most prevalent on the head and neck.

- **Erosions** are superficial lesions that are similar to excoriations but often wider. When due to scratching, erosions tend to be linear, while those associated with licking tend to be circular. They can often be associated with eosinophilic plaques.

- **Ulcers** can occur as focal non-pruritic lesions on the upper lip area, known as rodent or indolent ulcers. These lesions are one of the components in the triad of the eosinophilic granuloma complex (EGC). EGC lesions are reaction patterns typically indicative of an underlying allergy or hypersensitivity reaction, they are not their own disease. I.E. EGC lesions, including indolent ulcers, are symptoms of an underlying condition, typically allergies. Other conditions that can create ulcers on the body with variable degrees of pruritus include vasculitis, autoimmune diseases, drug reactions, and neoplasia.
Papules are small raised 1-5mm lesions that are often associated with crusts and are the most common lesions seen in miliary dermatitis. Like the EGC lesions, miliary dermatitis is the symptom of an underlying disease, not a disease itself, and can be associated with flea allergy dermatitis (most commonly), atopic dermatitis, bacterial folliculitis, cheyletiellosis, dermatophytosis, pemphigus foliaceus and drug reactions.

Plaques appear as moderate to well-defined elevations of the skin with erythema. Eosinophilic plaques, one of the EGC variants, are most commonly associated with underlying allergic disease. These plaques can be highly prone to secondary bacterial infection.

Eosinophilic granulomas are the third component of the EGC complex, and are characterized as firm, sometimes ulcerated, raised areas that are often found in the mouth or in a linear pattern on the body. It’s important to check the hard palate of allergic cats for this, I’ve seen cats come in on emergency with granulomas having worn through the palate and causing oral bleeding.

Alopecia that is associated with pruritus usually presents as broken-off, barbered hairs from over grooming, scratching or rubbing. Other lesions of pruritus are often present with alopecia; however, in some cases, broken/barbered hair is the only clue that the cat is pruritic. Thin flakes of shed epidermis characterize Scale, a nonspecific symptom that is commonly seen in cheyletiellosis.

**Diagnostic tests**

Dermatological diagnostic tests are powerful tools, that can often provide quick information as to how to manage a case. Cutaneous cytology is a rapid test that is easy and inexpensive to perform that can assess the presence of bacteria, inflammatory cells, fungal spores/hyphae, acantholytic cells and neoplastic cells. I perform cytology in almost every pruritic cat with dermatological lesions, aside from non-inflammatory alopecia, that I see. True bacterial pyoderma cases should demonstrate intracellular bacteria, usually within neutrophils, and, sometimes, within eosinophils. Eosinophils are a very common inflammatory cell seen in a variety of disorders, but are most commonly associated with ectoparasites, allergies and some forms of EGC lesions. Fungal spores or hyphae can be visualized in many dermatophyte cases, although a fungal culture should ALWAYS be performed for speciation, to verify the causative species to guild environmental treatment recommendations. Cytology can also be of value in some forms of cutaneous neoplasia, and, on rare occasion, can identify ectoparasites such as Cheyletiella, especially when adhesive tape is used. Acantholytic cells are suggestive of pemphigus foliaceus, although they can also be seen in dermatophyte cases and biopsy should always be performed to confirm the diagnosis. Skin scrapings are one of the most important diagnostic tests, and should be utilized on all pruritic cats, aside from those with seasonal symptoms, which automatically indicated atopic disease or flea allergies. Some of the more common parasites that can be identified include Cheyletiella blakei, Otodectes cynotis, Lynxacarus radosky, Trombica autumnalis, Felicola subrostratus, Notoedres cati, Demodex cati and gatoi. One of the most reliable ways to find Cheyletiella mites in both symptomatic and asymptomatic animals is to use a fine tooth comb on the entire hair coat for several minutes to collect dander and scale, and then examine under a cover slip with mineral oil.

The Dermatophyte test media (DTM), or fungal culture, is considered the gold standard to identify dermatophytes. Dermatophyte infections can present as pruritic infections with any lesion type. Dermatophytes utilize protein, thereby producing an alkaline by-product that produces a red color change. However, after all carbohydrates are utilized, any saprophyte contaminant can utilize the protein and turn the media red, and for this reason, DTM should be inspected daily for color change, and growth needs to be examined microscopically for evidence of macroconidia. Suspected fungal growth can be lifted with clear adhesive tape, stained with lactophenol cotton blue, and then examined microscopically. Speciation of the dermatophytes should always be performed to determine the source of infection to help prevent future re-infection. For example, if the dermatophyte is Trichophyton mentagrophytes caused by exposure to a rodent and the rodent is still around, the cat will continue to get re-infected. Woods light examination can be utilized in suspect dermatophyte cases, but only fluoresce in a small percentage of Microsporum canis cases, and positive fluorescing hairs should be plucked for culture for definitive diagnosis, as other things can cause false positive glows. Direct hair exams can also be a method of identifying dermatophytosis, as hyphae and spores can often be seen when the condenser is turned down, although cultures should always be performed to confirm the diagnosis. In cases of alopecia where pruritus levels are unknown, trichograms, to examine the tapered tip of plucked hairs, can help determine if the hairs were removed by self-trauma, in which case they appear fractured and jagged. This can especially be seen in hair from the caudalventral abdomen. Skin biopsies can be a powerful tool, when used in the correct case. Many specific infectious, parasitic, autoimmune and neoplastic diseases will be diagnosed via biopsy. Biopsies are indicated in unusual lesions or clinical presentations, or if a case is not responding to standard treatment. The various allergies look the same on histopathology, so biopsy is usually not used to diagnose them, and NEVER to differentiate between them.

If all non-allergic differentials have been ruled out, a systematic approach to allergies must be pursued, as three three common allergic disease, atopy, flea and food allergy, can look identical. The majority of allergic cats are flea allergic, and flea control trials should be performed to eliminate this differential. Several approaches can be taken to flea control trials. Because none of the products that can be used are repellants, it is virtually impossible to rule out flea allergy in an outdoor cat, but keeping cats indoors is not always feasible. One of the ideal methods of performing a flea trial, especially in outdoor animals, is to use the oral medication Nitenpyram (Capstar, Novartis) every other day, for a 4-6 week period. This product lasts for 24 to 36 hours, and must be re-
administered to provide continued elimination of newly acquired fleas. Another option is to use one of the topical formulations, such as imidacloprid (Advantage®, Bayer), fipronil (Frontline Plus®, Merial), dinotefuran/pyriproxifen (Vectra®, CEVA) or selamectin (Revolution®, Pfizer), off label every 2-3 weeks for a 4-6 week period. Diligent spinosad (Comforis, Elanco) every 3-4 weeks can be an effective flea trial as well. Please note that Vectra 3D® for canines contains permethrin at a level that can be highly toxic to cats, and care must always be taken to not use the canine product on felines.

When proceeding with the evaluation of food allergic dermatitis, a food elimination trial must be performed to rule out the disease, as serological testing is unreliable and inaccurate. Food allergic cats can have the same symptoms as atopic or flea allergic animals, but commonly display severe head and neck pruritus. The only way to diagnose food allergy is with an elimination diet that is fed for an 8-12 week period. The author prefers a diet trial consisting of home-cooked or limited protein based commercial diets, such as Royal Canin® (Innovative Veterinary Diets, IVD) duck, rabbit, or venison and green pea, and typically only utilizes hydrolyzed diets if the other diets are not eaten. When the owner is willing to home cook, they can be directed to www.balanceit.com, where they can purchase recipes and supplements. Because of the unique nutritional needs of felines, it is imperative that only balanced home cooked diets be fed, as feeding an unsupplemented diet for more than four weeks can create nutritional deficiencies. At the end of the 8-12 week period, the cat is re-challenged with the original diet and observed for exacerbation of clinical signs. Many food allergic cats are so severely pruritic that they need short courses of oral steroids or cyclosporine to control their itch, with the goal of being able to taper them off these medications as they proceed on the diet trial. Apoquel® (oclacitinib, Zoetis) is off label for cats, and is not recommended for use to control pruritus in the feline at this time.

The diagnosis of atopic dermatitis is made primarily on history, physical findings and ruling out all other pruritic diseases. Allergy testing is used to determine what specific allergens the patient is allergic to after the diagnosis has been made, typically to start immunotherapy. Intradermal skin testing, although considered the gold standard of allergy testing, is more difficult to perform in the feline due to the difficulty of performing and interpreting intradermal injections in the cat. Feline skin is thinner and more difficult to inject allergens into, and the degree of reactivity at the allergen injection sites is often flatter, producing false negatives. In-vitro allergy tests are also available which provide a reasonable alternative to skin testing, with some specialists preferring this method in the feline.
Pruritus is the most common symptom of skin disease in the dog. Proper management includes a methodical work up to determine the underlying disease, and treatment to alleviate symptoms with the fewest number of side effects.

Pruritus affects a large percentage of the pet population, and is one of the top causes of presentation of dogs to general practitioners, especially depending on the time of year. Because there are a varied number of conditions that can cause itching, it is important to approach this symptom methodically, and having a general algorithm in your head can be very useful. As soon as your history starts you are gathering critical information that is allowing you to formulate your diagnostic list and therapeutic plan. Key features of the dermatological examination then help formulate the differential diagnosis list (DDX) further, as well as notify where to take optimal samples for diagnostics. If you approach every itchy dog with a solid basic diagnostic and therapeutic plan you'll be much more successful then if you just administer steroids and hope the problem goes away.

The most common causes of pruritus in the canine are the allergic diseases (atopic dermatitis, food allergic dermatitis, flea allergic dermatitis), parasitic diseases (sarcoptic mange, cheyletiella, flea exposure, demodectic mange with secondary infection), and infections (yeast, bacterial, dermatophytic). Uncommon causes of pruritus that the practitioner needs to be aware of include autoimmune diseases (such as pemphigus foliaceus), neoplastic diseases (such as mycosis fungoides), drug eruptions/erythema multiforme, contact allergic dermatitis and psychogenic.

History
The importance of historical information can not be understated. Although you can not always expect the history alone to give you a specific diagnosis, it actually can in many cases and is critical information in all cases. It can be helpful to create a dermatology history questionnaire-if there is down time the client can fill it out before the appointment, and if not then you can use it to help trigger the most important questions to remember to ask. We have our form available online for clients to fill out and bring to the initial pruritus appointment.

I find the most important question to be where is the dog pruritic. Ask specifically about the face, feet and perineum, as people will often not associate the rubbing, licking and scooting seen in these locations as a sign of itchiness. Verify where the dog was initially pruritic and where they feel the most pruritic areas are currently. There are many recognized patterns of pruritus for specific diseases: flea allergic dermatitis tends to affect the caudal 1/3 of the body, especially on the dorsal lumbar region, tail, groin and thighs. Atopic dermatitis and food allergic can look identical on the face, ears, ventrum and feet, although food allergic dogs will sometimes have a history of perineal pruritus. Sarcoptic mange dogs tend to be itchy along the ear pinnal margins, elbows and hocks, although it can easily progress to generalized. Cheyletiella tends to favor the dorsal trunk.

Seasonality of symptoms is probably the second most important question that I ask. When symptoms are strictly seasonal the DDX instantly becomes atopic dermatitis, flea allergic dermatitis or insect bite hypersensitivity. When dogs have nonseasonal symptoms with seasonal exacerbations I always think about atopic dermatitis plus or minus a concurrent food allergy. Verifying if the symptoms started seasonally and then became nonseasonal is also useful.

I follow this with grading the pruritus level. I ask all owners to score the pruritus on a scale of 0-10 where 0 is asymptomatic and 10 is so itchy they have to pull the dog off themselves in the middle of the night due to pruritus. This acts as a reference point to monitor response to treatments and therapeutic trials. Clients will often overscore the itch level to increase your thinking the pet's issue is significant, but that's why it's useful to remind them at follow ups what they previously said for comparison. The conditions which tend to cause the most severe pruritus are sarcoptic mange (almost always a 10, but sometimes they are more mild to start, which can make them occasionally get misdiagnosed as allergies), flea allergic dermatitis, food allergic dermatitis and atopic dermatitis, although atopic dogs are more likely to wax and wane a bit depending on time of year and presence of infection.

I find some clients will freeze when asked to grade the pruritus on the 0-10 scale, so another thing I like to ask is percentage of improvement from last appointment. This is a super important question when making decisions about ongoing therapeutic management.

Age at onset of pruritus is a vital question in formulating a differential list. When significant pruritus affects very young dogs, especially less than 6 months of age, sarcoptic mange, demodectic mange with secondary infection, food allergic dermatitis and flea allergic dermatitis are the top differentials. Young food allergic patients can be very challenging to diagnose, as they don't always respond to the first diet tried, we are limited with the diets we can use for dogs on food trials under one year of age (royal canin venison and potato and royal canine HP) and they can be EXTREMELY itchy and not very responsive to anti-pruritics. Remember that apoquel is not recommended and is off label for dogs under one year of age. When pruritus affects dogs over 1 year of age (although it can be as early as 6 months) the main differentials are sarcoptic mange, demodectic mange with secondary infection, flea

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allergic dermatitis, food allergic dermatitis and atopic dermatitis. Atopic dogs classically first show signs between 6 months and 3 years of age, but I've seen dogs younger and older that were confirmed to be atopic. It is quite unusual for dogs over 7 years of age to develop atopic dermatitis unless there has been a major change in the environment (such as a move, increased allergens, exposure to parasites that pushes any subclinical symptoms over the threshold to cause itch). If a dog has never had any history of pruritic skin disease and then develops it later in life out of the blue, I check for infections (sarcoptes, demodex, dermatophyte, yeast, bacterial) and am more concerned about an unusual condition such as mycosis fungoides or pemphigus foliaceus. I have seen many older dogs present with pruritus secondary to skin infections caused by an endocrinopathy such as hypothyroidism or hyperadrenocorticism that aren't classically considered, but with marked, untreated secondary infections they most certainly can present for severe itching. It can be useful to ask these clients of the itch came first or if the rash came first, as an allergic dog/parasitic dog will typically start with itch first, but a dog that has itch secondary to a yeast or bacterial infection [triggered by something else, possible a "non pruritic" disease] will often get a rash first and then become itchy.

Verify if the dog has received any prior therapies and if so how useful they were and for what period of time. I specifically want to know the usage and usefulness of glucocorticoids, cyclosporine, apquel, antibiotics, topical therapy and parasite control (ideally drug, dose, route of administration and duration). The literature tends to generalize that flea allergic and atopic dogs are steroid responsive and that sarcoptic mange and food allergies are steroid resistant. Many food allergic dogs are VERY steroid responsive (39-63% of cases in reported in studies) and many atopic dogs will not respond to steroids at all. Atopic dogs tend to respond to cyclosporine better than food allergic dogs. It is still early for me to make a definitive statement about apquel other than it doesn't work to control pruritus in all atopic dogs, and I've seen it control the pruritus in dogs that didn't have atopic dermatitis (flea allergic dermatitis, food allergic dermatitis).

Lastly, ask if any other pets or contact animals are affected, and if the humans have any skin lesions or pruritus themselves. Infectious diseases such as sarcoptic mange, cheyletiellosis, dermatophytosis will affect other animals and humans. If other animals are not affected you can typically eliminate sarcoptic mange and cheyletiellosis from the differential list, but since pets can be inapparent carriers of dermatophytes, especially cats, I don't rule this out base on this information.

Physical examination

It's important to be able to perform a thorough dermatological (and otoscopic) exam on every pruritic patient, paying attention to note primary lesions (such as papules, pustule and crust), secondary lesions (excoriations, alopecia, erythema, lichenification, hyperpigmentation and scale) and lesions consistent with self trauma. The distribution of lesions can correlate directly with the site of pruritus DDX list above. Dogs with sarcoptic mange will often have crusting on the margins of the pinna as well as on the elbows and hocks, and many will have a positive pinna-pedal reflex. If a dog has been chewing its paws excessively (salivary staining can be a big clue to this), atopic dermatitis and food allergic are considered. Pay attention to erythema, hyperpigmentation and lichenification around the perineum, as many food allergic dogs will show this and the owner will not have reported perianal symptoms. Dogs with symptoms confined to sparsely haired "contact regions" especially with a compatible history, should have contact allergy considered. Dogs with large areas of acute moist dermatitis over the dorsal lumbar region and tail are considered flea allergic until failing the strictest of flea control regimes.

Initial diagnostics

I perform skin scrapings, to evaluate for sarcoptic mange, demodectic mange and cheyletiellosa, on every pruritic dog I see. If they don't have obvious lesions I'll be sure to focus on the hocks/elbows/pinna where sarcoptic mange tends to be the easiest to find (remember it's only found a small percentage of the time). The presence of a single sarcoptic mange mite or egg is diagnostic. Negative skin scrapings do not rule out sarcoptic mange, as even in dogs with the disease it's only found roughly 30-40% of the time. Demodectic mange isn't classically considered to be pruritic, so if found verify if there is secondary infection present, the most common cause of pruritus in these cases, OR if there an additional pruritic disease present.

Also extremely important is to perform skin surface cytology to verify the presence of bacterial or Malassezia infections. Cytology can be taken in a variety of ways, including surface swabs, impression smear and scotch tape prep. It is so important to be comfortable being able to diagnose these infections as they are a huge reason for failure to respond to treatment. If a dog has a significant bacterial skin infection that hasn't responded to previous appropriate antimicrobial therapy a bacterial culture and sensitivity is performed.

Other initial diagnostic tests include flea combing/evaluation of flea dirt, dermatophyte culture or wood's lamp in suspect cases, tape prep for Cheyletiella in dogs with suspicious scale.

Initial therapeutic plan

My first step is to make sure I've ruled out sarcoptic mange in animals that have that on their differential list, and my treatment of choice for this is Revolution® (selamectin, Pfizer) every two weeks for three doses to cover the lifecycle of the sarcoptic mite. This will also act as strict flea control in MOST pets, and addressing flea control is my next concern. If the dog is in a super high exposure area I'll consider adding in an oral flea pill monthly, or Capstar® (nitenpyram, Novartis). It can't be understated how important it is
that the environment and contact pets also be treated, otherwise failure is certain. It can take up to 6-8 weeks to see the results of implementation of strict flea control, and if the owner is slacking about letting new fleas come into the environment it is impossible to gauge the dog's response to this trial. My next step in the initial therapeutic plan is to always address skin infections appropriately based on the results of my initial diagnostic plan. If a dog is clearly food allergic or atopic this will be the day that I'll start my elimination food trial, unless the owner has a conflict that delays this (ex. the dog is going on antibiotics and they don't think they can administer antibiotics and change the diet simultaneously). Topical therapy is implemented to help assist in infection control/itch control. Whether to use and what form of anti-pruritic medication is based on the health of the patient, the severity of the disease, and my suspicion of what is causing the problem. If I have a young healthy 1 year old dog with sarcoptic mange that is a 10/10 itchy I'll give it oral steroids (I always avoid injectable steroids because of side effects and the fact that they're just not necessary in the practice of canine dermatology) to cut its itch/scratch cycle on day 1, knowing if I don't there will be a significant delay in achieving comfort, even if the mites and secondary infections are addressed. Conversely, if I have a newly moderately allergic dog with a severe Malassezia dermatitis secondary to suspect allergies I'll start with infection control and topicals and see how much of the pruritus can be controlled with infection control/addressing the underlying issue. There is no magic answer for when to use and not use anti-pruritics, but remember to consider the patient's health, don't use them as a crutch to not evaluate the underlying disease, and monitor them properly if used for extended periods of time.

Next steps
If the pet continues to be itchy after ruling out parasites/dermatophytes/infection and flea allergy several things must be considered. Firstly, if the case is unusual or not responding to therapy as it should pursuing a skin biopsy and submitting it to a pathologist with special interest in dermatology may be indicated. Second, you need to always truly verify that all infections have been fully resolved and that the the flea regime is strict and adequate. If all of these issues are addressed then the vast majority of the time you're left with food allergic dermatitis or atopic dermatitis. It can take more than one strict diet trial to find the perfect diet that works for a dog, and care must be taken that dogs are switched from flavored to non flavored supplements, flea control products and heartworm preventatives. This includes medications used to treat other conditions, such as if a dog is on carprofen for arthritis or phenylpropanolamine for urinary incontinence. If left with a diagnosis of atopic dermatitis then treatment should be aimed at minimizing symptoms with the fewest number of side effects. These treatments include allergen specific immunotherapy, topical therapy, fatty acids/antihistamines, or chronic anti inflammatory with medications like oral glucocorticoids, apoquel and cyclosporine, all of which require stringent routine bloodwork monitoring every 6 months (ideal).
Otitis cases are often complex and involve more than one etiologic component. This means the diagnosis and management of otitis externa is often much more complex than just recognizing what “caused” the ear disease. A successful approach to ear disease requires the understanding of what really is contributing to the pathology of any given ear, which requires that each component of the problem ear be recognized. The PSPP classification considers the etiologies as causes, which are diseases, or agents that directly produce inflammation in the ear and are Primary and Secondary. Factors are agents or elements of the disease or pet that contribute to ear disease and are divided into Perpetuating and Predisposing. For each cause or factor there is a prognosis, methods for assessing or monitoring as well as treatment options. The classification has been combined with prognostic labels, some educational diagrams, a table (Table 1) into a handout the PSPP System© which may be used to help organize a diagnostic plan, complete diagnosis, prognosis, treatment plan and educate the client. See attached PDF and it is also available to download at www.animaldermatology.com.

Table 1 from PSPP system©

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It is important to establish if a dog with chronic otitis hears. First this often changes my approach to a case. If hearing loss seems permanent and non reversible then total ear canal ablations and bulla osteotomy become better treatment options. Hearing loss is the main side effect of the procedure and if this were not an issue I would spend less time and expense trying medical therapy. In addition hearing needs to be determined prior to ear flushing and medicating with topical medications when otitis media is likely. It always surprises me how often dogs have fairly apparent hearing loss or deafness and owners are not aware of it. This is especially common when there are multiple pets in the household. It is important to ask questions about response to doors, cars pulling up, being called when outside and localizing the sound, sound sleeping and anything else that will help determine if there is significant hearing loss. Sounds should be made in the exam room when the dog is not paying attention to the veterinarian. It is important to not just see the dog responded to the sound but did it localize where the sound was coming from almost immediately. A problem may occur if a near deaf or deaf dog is not recognized in the examination and then the owner is warned about deafness as a side effect to the deep ear flush and treatment being sent home. After the procedure the client pays attention and recognizes there dog does not hear well then blames the treatment when in fact the dog had been deaf prior to the treatment. Brainstem auditory evoked response (BAER) testing is a more accurate way of assessing the dogs hearing. This allows one to assess hearing threshold, the level of sound that each ear detects and stimulates a brain response. It is being used to assess hearing loss and ototoxicity. Unfortunately it is not readily available.

Primary causes
Primary causes are usually the actual inciting agent or etiology that directly causes damage or inflammation to the ear canal skin. These can occur alone and induce otitis externa without any other cause or factor. The primary cause may be very subtle and often go unrecognized by the owner or even veterinarian until a secondary cause occurs. Once a primary etiology alters the aural environment secondary infections often develop. In the authors opinion the vast majority of cases will have a primary cause though they may not always be readily apparent. Idiopathic or not diagnosed was reported in 32 of 100 cases. In general practice foreign bodies and ear mites make up a significant number of cases and once they occur they may result in perpetuating factors that result in chronic ear...
disease. If not seen early in the process they may then present without the primary cause being readily diagnosed. That and atopic otitis without obvious skin disease likely are responsible for many of these cases called idiopathic or not diagnosed. Some of these may also occur when predisposing factors combine with secondary causes, but it is likely most of these cases have a primary cause that was unrecognized. The most common causes seen in a dermatology referral practice are atopic disease, food allergy, epithelialization or metabolic disorders. In general practice foreign bodies and ear mites are relatively more prevalent. It is critical too successful long-term management that a primary cause be found and either eliminated or control be secured. The diagnosis of the primary cause often is determined from the otoscopic exam, cytology, complete dermatologic history and examination as well as diet or therapeutic trials, and possible organ testing or biopsy of the skin in other areas or the external ear.

Secondary causes

The secondary causes do not create disease in a normal ear; they contribute to or cause pathology only in the abnormal ear. As such they occur in combination with primary causes or predisposing factors. Generally secondary causes of otitis externa are easy to eliminate once identified and when they are chronic or recurrent it is usually because primary causes or perpetuating factors have not been adequately addressed. Secondary causes in the past were often considered as primary causes or the “main” diagnosis of an ear case. (ie. Pseudomonas or Malassezia otitis) Even today many clinicians direct all their efforts at diagnosing and treatment of secondary causes. Although their treatment may be important, other causes and factors must be looked for. In some cases such as Malassezia, eliminating the concurrent predisposing factor or primary disease may result in the resolution of the secondary problem. Secondary causes are most often diagnosed with cytologic examination and culture and sensitivity testing when indicated.

A more recently recognized concern in otitis cases is the presence of biofilms. Biofilms are a community of bacteria that live in an extracellular polymeric matrix that increases resistance to antibiotics and host defense mechanisms. Biofilms are different than the planktonic or individual cells of bacteria that are what is most commonly studied when evaluating infectious diseases that fulfill Koch’s postulates. The extracellular matrix is composed of polysaccharides, DNA and proteins and is often referred to as SLIME, a physical characteristic that is associated with some biofilms seen in nature. These communities, originally associated with adhesion to solid surfaces, are known to occur in aggregates in some tissues.[2] The tissue aggregate form may further enhance mechanisms of survival in the affected tissue.[3, 4] The slime may also contribute to damage of the tissue and pathologic responses that occur. The biofilm increases resistance to antimicrobial agents by more than producing SLIME. In addition metabolic adaptations occur at a higher frequency in biofilms and the communities stimulate the development of persister cells. Persister cells are slow growing and do not grow in the presence of an antibiotic. They persist and are able to grow again once the antibiotic is gone. These biofilm infections are most often associated with chronic diseases and in humans middle ear and possible the external ear are sites of predilection.[5, 6] Forty percent of canine otitis strains of Staph. intermedia and Pseudomonas are capable of producing the extracellular polymeric substance of biofilms.[7, 8] Malassezia may also form biofilms.[9] So far biofilms have not been documented in canine otitis cases by two of the best methods for detecting biofilm infections, peptide nucleic acid-fluorescent in situ hybridization (PNA-FISH) and confocal laser scanning microscopy (CLSM). However I have seen cases that have aggregates present on cytologic examination of ear exudate. Seeing these three dimensional aggregates is suggestive and in humans the otitis media aggregates vary from 4-80 uM.[4]

Culture and sensitivity is not routinely recommended and should never be done without cytology. A culture is typically only done if systemic therapy is being prescribed. It has been shown that response to topical therapy does not correlated with culture results.[10] If the cytology reveals supplicative inflammation with relatively pure populations of rods or cocci and the animal has not responded to appropriate topical and systemic antibiotic then a culture and sensitivity may be indicated. The lab should also be sent a cytology slide and any information regarding the organisms seen at time of collection so they know if multiple organisms should be identified.

Perpetuating factors

Perpetuating factors are changes in the anatomy and physiology of the ear that occur in response to otitis externa, they occur after ear disease. These factors may be subtle at first but over time can develop into the most severe component of chronic ear disease. These factors are not disease specific and are most commonly seen in chronic cases. Once present, they accentuate or permit the development of secondary causes by providing environments and microscopic niches that favor their persistence. In many cases perpetuating factors prevent the resolution of otitis externa when treatments are only directed at primary and secondary causes. They cause much frustration to clinicians for several reasons. They often result in animals presenting repetitively with different causes present at each subsequent visit. These factors can become self-perpetuating and lead to progressive worsening of disease. They can become severe and end up causing the majority of symptoms exhibited by a pet or be so mild appearing that to many veterinarians as well as owners a pet and its ear canal appear normal. Yet left untreated perpetuating factors, even though primary and secondary causes are controlled or eliminated, result in recrudescence of clinical disease.

In chronic cases often more than one of these factors will be present. Standard treatments of the primary and secondary diseases present often times will not immediately eliminate the perpetuating factors. In early cases, treating the primary cause may be
sufficient in controlling a case, but after the establishment of perpetuating factors treatment may need to be directed at them. The treatment for perpetuating factors is often different that what is required to control primary and secondary causes of otitis externa. Their treatment should be continued until they have resolved which may take months of continuous therapy and in some cases they are permanent and will require life long therapy or a surgical solution.

Perpetuating factors are the most common reasons otitis externa cases require surgery. Perpetuating factors are diagnosed otoscopic examination; repetitive otoscopic examination timed appropriately, tube palpation and other imaging techniques (radiology, CT scans, MRI).

Diagnosis of otitis media can be made when a ruptured tympanic membrane is seen. A technique of tube palpation and flushing can aid in the diagnosis of otitis media. This technique also may reveal false middle ear cavities. The method is greatly enhanced with FOVEO and the ear canal filled with water, which increases magnification by 4/3 thus appearing 25% larger. Also air bubble may be seen coming through some small tears. The soft tube can be used to palpate any material located at the approximate level of the tympanic membrane. Both depth of the canal and location of the tip of the tube are utilized to determine if a false middle ear or otitis media is present. The feeding tube is passed under visualization with a surgical otoscope head down the ear canal to the level where the tympanic membrane is expected to be located.

**Predisposing factors**

Predisposing factors are present prior to the development of ear disease but alone do not cause otitis externa. They increase the risk of development. These factors work in conjunction with either primary causes or secondary causes to become a significant problem. In rare cases a predisposing factor may combine with a secondary cause to create disease even when no primary cause is present. The best example of this is a dog that gets water in its ear that leads to epidermal maceration or damage and then a secondary bacterial or yeast infection occurs. It is possible this is how environment, increased heat and humidity, also contribute to otitis. However in the authors experience these animals often do have a subtle but mild primary disease still present but controlling that disease does not appear to be necessary. Some predisposing factors relate to the normal anatomy of the dog and as such are not something that is cureable unless surgery may alleviate it, such as a stenotic external orifice in a Chinese shar pei. Pendulous pinnae have been shown to be a statistically significant predisposing factor for otitis externa though no studies have adjusted for this finding based on the presence of breed predisposition to other primary causes of otitis[11].

**References**


It is important to be aware of all the different treatment options that are available and their indications (Table 1).

<table>
<thead>
<tr>
<th>Treatment Class</th>
<th>Route Administered</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Analgesics/anesthetics</td>
<td>Systemic</td>
<td>Some cases for examination</td>
</tr>
<tr>
<td></td>
<td>Topical</td>
<td>Chronic proliferative otitis externa/media</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Deep cleaning</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Intralesional therapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ear examine and some cleaning procedures</td>
</tr>
<tr>
<td>Antibiotic (AB)</td>
<td>Topical</td>
<td>Bacterial infection ear canal</td>
</tr>
<tr>
<td></td>
<td>Systemic</td>
<td>Bacterial otitis media or proliferative changes over 50% lumen, topical</td>
</tr>
<tr>
<td></td>
<td></td>
<td>reactions</td>
</tr>
<tr>
<td>Antifungal (AF)</td>
<td>Topical</td>
<td>Yeast overgrowth or when present with inflammatory cells and no bacteria</td>
</tr>
<tr>
<td></td>
<td>Systemic</td>
<td>Otitis media with yeast present from middle ear</td>
</tr>
<tr>
<td>Antiseptic (AS)</td>
<td>Topical</td>
<td>With or following cleaning</td>
</tr>
<tr>
<td></td>
<td></td>
<td>For resistant bacterial infections</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Control of microbial overgrowth</td>
</tr>
<tr>
<td>Cerumenolytics</td>
<td>Topical</td>
<td>Waxy greasy ceruminous exudates in ear canal</td>
</tr>
<tr>
<td>Cleansers</td>
<td>Topical</td>
<td>Control of mild dirty, waxy ears odor</td>
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<tr>
<td></td>
<td></td>
<td>microbial overgrowth</td>
</tr>
<tr>
<td>Glucocorticoids</td>
<td>Topical</td>
<td>Allergy not controlled by cleaning alone</td>
</tr>
<tr>
<td></td>
<td>Systemic</td>
<td>Otitis externa</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pinnal erythema/pruritus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Proliferative otitis greater than 50% of lumen, when exudation not stopped</td>
</tr>
<tr>
<td></td>
<td></td>
<td>with topical therapy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>When cleaning, topical and oral systemic therapy does not improve</td>
</tr>
<tr>
<td></td>
<td></td>
<td>proliferative otitis enough</td>
</tr>
<tr>
<td>Hypoallergenic diets</td>
<td>Oral</td>
<td>Control of adverse food reactions</td>
</tr>
<tr>
<td>Parasiticides</td>
<td>Systemic</td>
<td>Otodectes in adult animals</td>
</tr>
<tr>
<td></td>
<td>Topical</td>
<td>Otodectes in puppies and kittens</td>
</tr>
</tbody>
</table>

Successful treatment outcomes will require that a complete treatment plan is developed the client adheres to the treatment plan. Therefore one of the most important jobs of the veterinarian treating a case of otitis externa is getting good client compliance. This is achieved with client education about the treatment plan and gaining the clients confidence it is a good plan that they can accomplish. The client needs to agree with both what the problem is and the appropriate solutions. It is important that the plan includes the appropriate follow up and that this is explained.

The first step in this process is developing the recheck plans and getting the client to understand their importance and follow through. The client needs to understand clinically the odor, head shaking and discomfort may be gone, but the ear may still be building up debris and not staying cleaned, have proliferative changes, or the tympanum may not have returned. These changes may
evolve and eventually lead to another infection or acute flare up of otitis. The return to a healthy ear canal can only be determined with otoscopic and cytologic examination of the ear canal. Follow up examinations are also important to determine if cleaning is being done effectively and when normal self-cleaning returns. Scheduling the follow up examination is critical and has to be done differently to answer the preceding questions. To determine if home cleaning is effective then the examination should be done within 24 hours of the cleaning procedure. To determine if the interval is to long between cleanings or that self cleaning may have returned the examination needs to occur when the ear has not been cleaned for at least the interval between current cleanings or longer. Clients need to understand there are different types of follow up for chronic ear cases and that multiple visits will be required.

The number one rule of topical therapy is the active ingredient(s) must reach the site to be treated. This means if only one treatment was allowed to manage ear cases then it would definitely be cleaning, as no single topical product is as effective. Cleaning techniques that are most effective occur in the sedated or anesthesized dog and generally that is the preferred initial therapy when there is a lot of proliferation, exudate or otitis media. There are cases where initial therapy will make this more effective or unnecessary but in some cases there will be a poor response without the in clinic cleaning. Deep ear cleaning in clinic also allows for the false middle ear pockets or middle ear to be cleaned. Tube flushing may be an effective non-surgical method for cleaning these deeper sites. It is also the least expensive method. A variety of tubes such as polypropylene tomcat catheters have been recommended for use but my preference is a soft rubber feeding tube (Sovereign® feeding tube and urethral catheter) of several sizes (3.5, 5.0, 8.0 and 10.0 French) though the 5 and 8 are my most commonly used sizes. These may be prepared for use then kept in cold sterilization solutions. They are cut short (5-7 inches in length and the ends are trimmed so that the tube will fit over a syringe hub. A 6-12 cc syringe is attached. Some clinicians prefer to use a three-way valve so that fluids can be run through one port and suction from a separate port. Which action (flush or suction) is being done is determined by the position of the three-way valve. Water or saline may be utilized as the flushing solution. It should be at roughly body temperature. Saline has the advantage of causing less swelling if repetitive flushing is performed. Usually multiple flushes are required and a bowl of flushing solution should be available. Cleansers and antiseptics may be used in the flushing solution though the author rarely does this and utilizes these products only as the final rinse.

The feeding tube is passed down through a surgical otoscope head and attached cone or through a video otoscope. Under visualization the tube is passed down to the level of the middle ear. If possible the tip is then passed ventrally towards the bottom of the tympanic bulla. The objective is to place the tip of the tube at the most ventral aspect so that the exudate and organisms are flushed directly out towards the external ear canal. In other cases the tube may be placed within the exudate, which may be inspissated, and aids in dislodging and removing it. The passing of the tube into the dorsal or middle aspect of the middle ear has a greater risk of damaging the vestibular (oval) or cochlear (round window) that lies within the promontorium. Actual placement in the ventral bulla is difficult due to the boney ridge that separated the ventral from middle parts of the middle ear cavity. Soft tubes are more likely to reach this location due the ability for the tip to bend. Therefore attempts to get the tube below the ridge should be made and is easier when using 5 French or smaller tubes. Trying to bounce the tube off the dorsal aspect of the external acoustic meatus just prior to entering the area of the dilated or ruptured tympanum may help in achieving this. Once the tip is placed in an appropriate location the flushing solution is gently infused into the ear and this will fill the otoscopic cone and any debris is seen floating in the solution. The flush solution is then aspirated out and it along with the aspirated debris is discarded. Flushing by infusing fluid and aspirating is repetitively done until no debris is seen floating up in the solution. Ear cleaning units that combine flushing and suction are very helpful thought not required for tube flushing.

Vestibular syndrome or deafness may occur after ear flushing, even when no ototoxic drugs are utilized. These side effects are uncommon. In one study of 44 cases that had the middle ear flushed no side effects were reported[31]. Another study of 105 otitis ears flushed none had hearing loss and some even improved following cleaning[32].

Home ear cleaning may also be essential, particularly in cases where epithelial migration is not occurring. Generally I do not have clients begin to clean until the dogs ears are not painful and then usually only once weekly. Most often I have clients do an ear wash by filling the ear canal to the opening of the external orifice with a mild antiseptic cleanser. The clients massage the ear both vertical and horizontal ear canal for a few minutes if possible. To effectively massage the annular cartilage the client must be educated about the location and need for deep digital palpation. Following several minutes of massage the material is allowed to be shaken out and then the external orifice and concave pinna is wiped clean with tissue or cotton balls. If they get more than a little debris they should fill and rinse the ear again and repeat until only a small amount of debris is obtained. Do not allow excessive use of cotton tipped applicators down the ear canal as these commonly push debris deeper into the ear canal. Antiseptics are sometimes utilized as an ear rinse daily for some infected ears or following the home cleaning. My favorites contain acetic or other acids or tris edta with 0.15% chlorhexidine which in the US is usually labeled as a flush not ear product.
References
Do a hearing evaluation

It is important to establish if a dog with chronic otitis hears. First this often changes my approach to a case. If hearing loss seems permanent and non reversible then total ear canal ablations and bulla osteotomy become better treatment options. Hearing loss is the main side effect of the procedure and if this were not an issue I would spend less time and expense trying medical therapy. In addition hearing needs to be determined prior to ear flushing and medicating with topical medications when otitis media is likely. It always surprises me how often dogs have fairly apparent hearing loss or deafness and owners are not aware of it. This is especially common when there are multiple pets in the household. It is important to ask questions about response to doors, cars pulling up, being called when outside and localizing the sound, sound sleeping and anything else that will help determine if there is significant hearing loss. Sounds should be made in the exam room when the dog is not paying attention to the veterinarian. It is important to not just see the dog responded to the sound but did it localize where the sound was coming from almost immediately. A problem may occur if a near deaf or deaf dog is not recognized in the examination and then the owner is warned about deafness as a side effect to the deep ear flush and treatment being sent home. After the procedure the client pays attention and recognizes there dog does not hear well then blames the treatment when in fact the dog had been deaf prior to the treatment. Brainstem auditory evoked response (BAER) testing is a more accurate way of assessing the dogs hearing. This allows one to assess hearing threshold, the level of sound that each ear detects and stimulates a brain response. It is being used to assess hearing loss and ototoxicity. Unfortunately it is not readily available.

Dilating the ear for cleaning

With proliferative end stage ears it is difficult to impossible to really get cleansers down the ear. To achieve this when the dog is anesthetized use the 3mm otoscope cone to dilate the ear and force the cone down as far as possible. An ear loop can be passed down the canal just past the tip of the cone and then the cone is filled with the cleanser and slowly pulled out. This will allow a layer of cleanser to be deposited on many of the folds as they fall back in place as the cone is removed.

Glucocorticoids

Topical glucocorticoids are the most common prescription item used in treating ear disease. This makes sense when one considers the most common causes of chronic otitis are allergic diseases such as atopic disease or adverse food reaction, which is likely an allergic reaction. Even ear mites are known to stimulate an allergic reaction. In addition many cases of otitis become secondarily infected with bacteria or Malassezia and glucocorticoids at least topically are believed to improve the response to topical antimicrobial therapy. This has been shown in dogs with Malassezia otitis and is supported by the fact that most topical antibiotic ear products labeled for the treatment of otitis do contain a glucocorticoid.[1] Eliminating or decreasing inflammation in the ear canal is an essential component of treating secondary infections and often is also indicated as it helps control the primary allergic disease as well. What this means is most cases should be treated with some glucocorticoid and so the real question is when to you avoid using them. I really have come to where the only time I do not use glucocorticoids in otitis cases is when 1. Cleaning ears alone is effective, 2. Infections are not responding or 3. Ulcers are not healing even though the infections appear to be controlled.

Glucocorticoids available for topical use in veterinary products are, from generally the weakest to more potent, 1% hydrocortisone, 0.1% or 0.015% triamcinolone, 0.1% betamethasone, 0.1% dexamethasone, 0.1% fluocinolone acetonide and 0.1% mometasone furoate. The initial therapy or during acute exacerbations a potent topical glucocorticoid may be required, but once the inflammation or allergic reaction is controlled prophylactic or long term therapy should utilize the least potent topical glucocorticoid possible. Long-term therapy is safer with products containing 1.0% or .5% hydrocortisone. A topical triamcinolone product (0.015% triamcinolone spray (Genesis®, Virbac) that has reduced systemic absorption has been useful, particularly for pinnal inflammation associated with allergic otitis. In cases of atopy or food allergy induced otitis externa, the pinna is frequently affected and should also be treated. Low dose dexamethasone 0.01 to 0.05% has also been formulated in hospital and used effectively for long-term control of allergic otitis or Malassezia otitis.

Combination therapy the key to killing organisms

Combinations are the key to eliminating resistant bacteria. Three different topical agents, antiseptics, synergistic agents and topical antibiotics, may be used for the purpose of killing the resistant bacteria. When 16 Pseudomonas cases were treated empirically, 90% reported resistant responded to an topical containing the antibiotic the organism was supposedly resistant to and 83% responded when the empiric treatment was reported used for a sensitive strain.[2] The favorable response regardless of what the sensitivity says may have been due to the combination approach and use of the synergist Tris EDTA as well as the high concentration we achieve when...
using topical antibiotics. Topical antiseptics include such ingredients as certain acids (acetic, boric, citric, lactic), alcohols, aluminum hydroxide, chlorhexidine (0.25% or lower concentration), povidone iodine, silver sulfadiazine and sodium chlorite. Micronized silver is the newest addition to our topical antibacterial solutions. Antiseptics kill organisms by methods other than antibiotics, generally are inexpensive ingredients and can work in conjunction with antibiotics. Resistance is generally not a problem though this may be changing which is another reason to employ combination therapy. Some ingredients that look promising for destroying biofilms are chlorhexidine, acetic acid, and tris EDTA, N-acetyl-L-cysteine and sulphydryl compounds. In cases resistant to all antibiotics antiseptics may end up being the treatment of choice. The drawback to using antiseptics is they often need to have contact time in clean ears and be used multiple times a day for a good effect. Some are also irritating which limits their use. The antiseptic should be left in the ear canal for 5 minutes. In difficult cases that are being cleaned under sedation/anesthesia then I may leave acetic/boric acid in the ear canal for five minutes then follow with a five-minute soak with Tris edta/chlorhexidine. When antiseptics are the only topical antibacterial used then they often should be applied 4-6 times a day.

Synergistic agents improve the killing effect of what they are mixed with in a way that is more than the additive effect of the two ingredients. Tromethamine-ethylenediaminetetra acetic acid (Tris edta) is the synergist used the most in veterinary otitis cases. It has been shown to enhance the effects of antibiotics as well as the low safe concentration antiseptic chlorhexidine (0.15%).\[3, 4\] Has been shown to be synergistic with tris EDTA.\[3, 4\] A very interesting agent is polymyxin as it is not only an antibiotic but also a synergistic agent. Polymyxin has a cationic detergent effect and similar to tris EDTA disrupts the outer membrane of bacteria, particularly gram-negative bacteria. It is synergistic with some other antibiotics but also has a synergistic effect with miconazole. When polymyxin is mixed with miconazole it is synergistic for killing Malassezia but also highly synergistic for the killing of Pseudomonas.\[5\] By combining synergistic agents with antibiotics even resistant strains of Pseudomonas are killed.

Repetitive ear flushes in clinic
Since many chronic end stage ear cases will require multiple ear flushes in clinic it is common to encounter clients reluctant to do general anesthesia. Instead it is common to use sedatives and pain medication to allow some of the follow up ear flushes. In these cases even though the laryngeal reflex may be present it can be suppressed enough that care must be taken to prevent inhalation pneumonia. Those resistant Pseudomonas and MR Staphylococcus do not do well in the lungs. Remember any time an ear, with access to the middle ear, is being flushed in a sedated dog and an endotracheal tube is not in place the head should be angled down. We have the racks on the wet table raised at one end with the dog lying in lateral recumbency and the nose at the low end of the rack.

Malassezia in ears
When dealing with possible resistant Malassezia then Posaconazole is reported to be more effective though it was not as potent as some papers described in one recent study. Miconazole is most often found at 1% but when dealing with difficult cases should higher concentrations such as the 2.3 percent or 1.7% would be more effective. Also polymyxin is synergistic with miconazole for killing Malassezia.

Follow up cytology
Antiseptics, antibiotics or anti yeast topical therapy is not discontinued until reasonably normal self cleaning has returned and cytology shows no inflammatory cells or DNA strands. It is common for practitioners to discontinue therapy to early, especially if the ear looks reasonably good and there is no obvious odor or discharge. I see many cases when I think it is time to quit but based on cytology I do not. This is something else it is wise to warn owners to expect and if it does not happen they will be pleased and think you or they did a better job than usual.

References
Recognizing the components of otitis requires an understanding of the normal anatomy and physiology of the external and middle ear, which has been reviewed. Otoscopic examination and cytology are critical in recognizing pathologic findings and for these to be performed well the veterinarian needs to have adequate equipment and training.

The external ear is formed from two pieces of cartilage and a bony canal that are covered by skin, which ends at a specialized epithelial structure the tympanic membrane. The external ear canal is variable in length (5-10cm) and classically divided into the vertical and horizontal portions. As one proceeds down the vertical canal there is another ridge or fold in the cartilage that is called the auricular projection. It creates the “corner” around which one must proceed to allow access down the canal and when otitis is present the lumen ridge is often inflamed and when pushed against by otoscope cones, especially the edge of the cone, may result in pain and the dog resisting examination. The smaller second cartilage is the annular cartilage. It overlaps with the external acoustic meatus. The external acoustic meatus varies but in mid size dogs is about 1 cm long. The skin lining the acoustic meatus lies on bone and therefore is not subject to movement and massage as the skin lining the cartilaginous canal. The medial ring of the acoustic meatus is the location of the tympanic membrane. Often there are larger primary hairs located in the skin adjacent to the tympanum and this is more often seen on the ventral wall of the lumen, a helpful landmark for locating the ventral tympanum with diseased ears.

The skin and adnexa are constantly producing exfoliating corneocytes, intercellular material and glandular secretions. This material forms the ear wax and cerumen that is believed to play some protective role. This cerumen is constantly being produced throughout the ear canal. If this material were to build up blockage could result. However there is a normal clearing mechanism. The material produced in the ear canal is cleaned or cleared out by the movement of the epidermis, epithelial migration. The surface of the skin of the tympanum and ear canal is constantly moving from the tympanic membrane laterally to the external orifice of the ear canal. This process starts on the tympanum and this was shown to occur in dogs.[1] The tympanic membrane is an epithelial structure that separates the external ear laterally from the middle ear cavity located medially. The tympanic membrane of the dog is made up of the pars flaccida and pars tensa. The pars flaccida is a small area of the dorsal to anterior-dorsal aspect of the tympanum, which is relatively flaccid and quite vascular. The majority of what is seen of the tympanum when it is examined through the otoscope is the large pars tensa. A normal pars tensa is translucent, with striations seen extending from the manubrium of the malleus outward to the periphery. A whitish appearing discoloration can sometimes be seen through the lower to mid section of the tympanum. This whitish structure is the bony ridge that separates the tympanic cavity from the tympanic bulla. The manubrium of the malleus is “C” shaped with the open end of the “C” pointing toward the nose. It is located over the anterior-medial aspect of the tympanum.

The middle ear consists of the tympanic cavity and the medial wall of the tympanic membrane, the auditory ossicles and associated ligaments, muscles and nerves (chorda tympani and other smaller nerves), and the auditory tube. The tympanic cavity is divided into three parts: dorsal, middle, and ventral. The dorso-medial surface of this is primarily made up of the barrel shaped, cochlear promontory. The promontory is situated opposite to about the mid dorsal aspect of the tympanum. At the caudal end of the promontory is the cochlear window, which communicates with the bony labyrinth of the cochlea. This is the structure one must avoid when doing a myringotomy and flushing the middle ear. The ventral portion is the tympanic bulla and is the largest portion. The tympanic bulla is somewhat egg-shaped, with the dorsal aspect open to communicate with the middle part. It is separated dorsally from the tympanic cavity by the septum bulla, which is most prominent over the medial and anterior aspects of the bulla and responsible for making passing tubes into the ventral bullae very difficult. It may have many bony ossicles or projections along it lateral free edge in the lumen of the bulla.

**Microscopic anatomy of ear canal cerumen**

Ear samples are routinely collected from abnormal ears for cytologic examination and sometimes for culture and sensitivity testing. The samples should reflect the material exudate from the skin of the ear canal or the middle ear cavity. A technique, which will get a deep sample, is to pass a soft rubber tube down the canal and aspirate once the tip is deep into the canal. Cytologic examination of discharge usually does not establish a definitive diagnosis, but it is valuable in determining what infectious agents, if any, are present. With waxy discharges heat the author has preferred fixation though two studies suggest it may not be necessary. Modified wright's stain (Wright's Dip Stat) is a rapid method that adequately stains specimens and has two colors to help differentiate stained items. Cytologic evaluation is the preferred method to ascertain the role of Malassezia and probably bacteria. Two published studies specifically evaluated cytology in normal dog and cat ears and one study in comparison to otitis externa cases but at 400x.[2, 3] Though they did not have that similar results one important observation they made is normal ears never had inflammatory cells. The Tater study did not find rods and Ginel was not able to separate rods and cocci as 400x. An unpublished study at 1000x is the basis of
what I use. Normal dogs and cats then greater than 3 yeast per oil immersion field is considered highly suspect and for bacteria greater than 5 cocci or 1 rod per oil immersion field would be very suspect. But as or more important is the presence of inflammatory cells which is highly suggestive that secondary infection is present.

Cytology allows evaluation of the cellular make-up of the discharge as well as microbial agents present. The degree of wax, lipids, keratin (nucleated corneocytes) can also be determined. Ceruminous otitis externa is seen with endocrinopathies and seborrhea; the discharge in this condition is keratin and glandular secretions. Eosinophils may be seen with parasitic disease, topical drug reactions and some food allergic animals. Cytology determines what secondary infections or microbial overgrowth is present. In addition the presence of mixed bacterial aggregates that are three dimensional may be a way to evaluate for biofilm infections. Biofilm formation has been identified as a common problem in human otitis media and may play a role in some otitis externa cases. Canine ear isolates have been shown capable of forming biofilms.[4-6] Toxic neutrophils indicate that the ear canal must be flushed to remove the toxins. The presence of white blood cells as well as phagocytosis of bacteria indicates that the body is responding to the infection and treatment for the bacteria is warranted. The presence of blue staining nuclear strands indicates that some inflammatory cells are present even though intact cells may not be identified. If any neutrophils or nuclear strands are found then it is likely there is still a bacterial component to the disease even if bacteria are not found.

Cytologic evaluation is the preferred method to ascertain the role of *Malassezia* in a particular case for two reasons. In one study by the author 18% of the cases that had *Malassezia* detected by cytology were sterile on culture by a commercial laboratory culturing specifically for *Malassezia* at 37 degree C.

**Magnifying the ear canal**

Otoscopes must have a strong light and power source combined with at least 10x magnification that allows focusing within the normal length of the ear canal. If any of these components is not present otoscopic examinations may not be totally effective. We have borrowed this equipment from human medicine where there are two main types of otoscope heads the diagnostic or medical and the surgical. They differ in the size of the magnifying lens that one looks through as well as the shape of the cone holders. Many practitioners purchase the diagnostic otoscope head. In general we prefer the surgical otoscope head, which allows more manipulation and angulations as well as easier use with cleaning and therapeutic procedures that require passing instruments or tubes into the ear canal with concurrent visualization. One of the most common mistakes made in practice is the use of hand help battery operated otoscopes that no longer have enough power to adequately light the deep ear canal. In general every clinic should have at least one plug in otoscope, which is not dependent of having fresh fully charged batteries. The battery operated is valuable for being readily moveable to different locations in the practice but for abnormal ears that require work a strong well-lighted otoscope is preferred.

Various sizes of otoscope cones are needed to be able to examine the different size and breeds of dogs and cats seen in practice. This equipment is essential to practice and even if the newer fiberoptic video enhanced otoscopes are available the traditional otoscopes are still necessary. These allow larger instruments and tubes to be passed into the ear canal and allow much faster deep ear cleaning. Smaller 3mm cones are fine for routine examinations but when working on ears it is important to use the largest diameter cone that you can get down the ear canal. This will improve visualization and allow more room for manipulating instruments and tubes. A clean cone, which is at least 10minute soaking in cold sterilization fluids, should be used in each ear for examination and performing procedures. At least 10minute soaking in cold sterilization fluids

The advent of fiber optics, improved lighting and miniaturization of video cameras combined with a rigid endoscope has led to the development of Fiberoptic Video Enhanced Otoscopy (FOVEO). This equipment can be connected to a video monitor and printer, digital recorder or video camera. The fiber optic tip with camera also magnifies and with a focal length of several centimeters can improve the visualization of the ear canal. Besides improving visualization it allows permanent recordings of what is present as well as allowing clients or other veterinarians to see the pathology of the ear canal. In some cases small tears of the tympanic membrane not readily seen with the normal 10x magnified otoscope will be apparent with FOVEO. In addition filling the ear canal with water or saline is sometimes used with FOVEO as it further enhances magnification and keeps the tip of the camera lens from fogging. This cannot be done with normal otoscopes. With water or saline in the ear canal, perforations not even visible with FOVEO will sometimes be found and are recognized by the air bubbles coming from the middle ear cavity. This equipment is relatively expensive but considering the improved diagnostics and more importantly the client education and benefits on gaining client support for recommended procedures makes this a worthwhile investment in a busy practice. The fiberoptic scopes also have made assessment of the abnormal tympanic membrane more effective.

The technique for doing proper otoscopic examination is one that allows complete as visualization as possible with minimal pair or trauma. Many dogs or cats will allow a carefully done otoscopic exam but resist or make it impossible to complete an examination if the technique is not optimum. Examinations are best done on a table to allow for appropriate orientation of the scope. Though large breed dogs may be able to be done on the floor is the head is held high enough and the operator is kneeling on the floor. The head should be high enough to allow the observed to move the otoscope into a more horizontal position. Occasionally it is easier to examine an ear of a dog lying in lateral recumbence on a table. The muzzle should be directed slightly towards the thoracic inlet. It may also
be necessary to have someone else hold the dog or cat's muzzle as the natural tendency is for the head to be tilted as the examination starts. This will redirect the cone tip resulting in more pain. The pinna should be pulled up and out from the base of the skull, which helps to straighten the ear canal and minimize the blocking of the lumen by the cartilage fold that occurs near the junction of the vertical and horizontal canal. In addition, the cone is passed down the lumen of the ear canal while the operator is visualizing the canal through the otoscope cone. Attempting to insert the cone without visualization is a sure way to “hit” the canal epithelium, which can be painful even in a normal ear. The cone is then moved slowly into the vertical canal, visualizing as you go, then the otoscope handle is rotated downward so the cone approaches a horizontal position. The movement is best accomplished when the ear is also pulled up and out over the tip of the cone so that the two processes happen simultaneously. Proper placement at the junction often allows visualization into the horizontal canal and if necessary advancement into the horizontal canal. Deep penetration into the horizontal canal is only done if necessary to visualize the tympanum. One problem often encountered in practice is the extremely painful ulcerated swollen ear that one cannot adequately examine. Even with anesthesia, these cases may not be adequately examined. It may be necessary to treat the animal and reduce the swelling and inflammation and have the patient return in 4-7 days so that an otoscopic exam can be properly performed.

References
Food allergy important clinical findings

Canine atopic dermatitis is a clinical diagnosis and it can be caused by foods or environmental allergens or a combination.[1]

Generally the cases with food allergy have perennial signs. It has also been shown that AFR cases are more glucocorticoid-resistant[2, 3]. Some cases with food allergy are responsive to glucocorticoids, cyclosporine or oclacitinib but when CAD cases are not responsive food allergy is more likely than environmental allergy. That has been shown is studies for glucocorticoids and cyclosporine though the studies were not really designed to answer this question specifically.[4, 5]. Other cutaneous signs may be seen and if present in a dog with CAD are strong indicators food may be a problem. These cutaneous manifestations include lesions associated with urticaria, vasculitis (more often eosinophilic), erythema multiforme, otitis, onychodystrophy, and perianal fistula.[6-9].

AFR may cause a wide variety of non-cutaneous signs that most commonly involve the gastrointestinal and cutaneous organs. In addition: behavioral change, neurologic, urologic, respiratory, hematologic disorders, pseudo lymphoma, malaise, and fever have been reported [8, 10-12]. Despite our focus on the skin, another area that must be seriously considered is the gastrointestinal system. A significant percentage and up to half of the CAD cases from food have gastrointestinal disorders [12-14], although they are often mild and not severe enough for the owners to even note them as abnormal. Vomiting and diarrhea are seen in less than 15% of the cases. The most common sign is an increased number of bowel movements. Based on unpublished surveys, three a day is suspect but still can be normal, whereas four or more per day should be considered abnormal. Two studies that specifically questioned owners regarding gastrointestinal signs, including number of bowel movements, reported abnormal responses in 60% and 65% of the cases with confirmed AFR [14, 15]. One study that confirmed my impression reported that AFR dogs had 3.1 bowel movements per day and dogs with nonseasonal pruritus that did not have AFR had 2.1 bowel movements per day. When all the dogs were on the ZD Ultra diet (Hill's), the average number decreased overall to 1.6 but was lower in dogs that had AFR [15]. More important, the number of bowel movements in AFR dogs not only decreased on the elimination diet but also increased on provocation. The cause of the increased bowel movements may relate to alterations in colonic transport function. Dogs with nonspecific dietary sensitivity are particularly susceptible to diet-induced changes in absorptive function that are associated with damage to colonic microstructure and disrupted electrolyte transport [16]. It is also very important to get a good gastrointestinal (gi) history, as many food induced atopic dogs will have abnormal gi signs. Stetina et al in an article accepted by Vet Derm studied the normal incidences of some gi signs. Table 1

<table>
<thead>
<tr>
<th>GI Sign</th>
<th>Frequency</th>
<th>N= 314</th>
<th>%</th>
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<tr>
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<td>27</td>
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</tr>
<tr>
<td></td>
<td>2</td>
<td>205</td>
<td>65.3</td>
</tr>
<tr>
<td></td>
<td>3*</td>
<td>70</td>
<td>22.3</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>11</td>
<td>3.5</td>
</tr>
<tr>
<td></td>
<td>≥ 5</td>
<td>1</td>
<td>0.3</td>
</tr>
<tr>
<td>FCS (1-7)</td>
<td>1</td>
<td>3</td>
<td>1.0</td>
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<tr>
<td></td>
<td>2**</td>
<td>227</td>
<td>72.3</td>
</tr>
<tr>
<td></td>
<td>3**</td>
<td>71</td>
<td>22.6</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>5</td>
<td>1.6</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>8</td>
<td>2.6</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Belching* (0-5)</td>
<td>Never</td>
<td>108</td>
<td>34.4</td>
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<tr>
<td></td>
<td>Only after eating/drinking**</td>
<td>45</td>
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<tr>
<td></td>
<td>A few times/year</td>
<td>73</td>
<td>23.3</td>
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<tr>
<td></td>
<td>A few times/month</td>
<td>43</td>
<td>13.7</td>
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<td>Multiple times/day</td>
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<td>Flatulence (0-5)</td>
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<td>72</td>
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<td>29.0</td>
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<tr>
<td></td>
<td>A few times/month</td>
<td>74</td>
<td>23.6</td>
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</table>
Recognizing all the signs is critical for doing diet trials effectively, particularly when cases have both environmental and food induced CAD. Clinicians and owners often only grade pruritus and skin disease and as a result may miss the improvement from an effective diet trial. Also since GI signs typically improve faster (2-4 weeks) than skin lesions observing these other signs allows one to assess the effectiveness of the diet sooner than in dogs with just skin disease as those signs may take longer (4-8 weeks) to improve. In some cases improvement of the skin will not be recognized until both the environmental and food allergens are both being treated at the same time.

**Diagnosis of AFR**

Diagnosis of AFR is often based on history. It may then be further suggested by doing an elimination diet trial (EDT) and showing lack of signs when foods are avoided. It can be even more strongly confirmed through provocation tests with suspect foods. Performing diet trials correctly is not easy. In one study, owners who intended to complete a home cooked diet trial had a 36% withdrawal rate [17]. In another study of 63 dogs with suspected AFR pruritic dogs, 27% failed to correctly complete a commercial diet trial with 13% having known exposure to other food [13]. Some have suggested that the dropout rate is higher with home-prepared diets; however, one study comparing home-prepared with commercial diets did not find a significant difference in completion rate [18]. We do not know how many cases fail to complete a diet trial or how many other times cases ate non diet items that the owners did not report or were not aware of. One study showed that improved client education and the use of diagrams and emphasis on the role of diet in allergic dogs is valuable in improving client compliance [19]. These facts mean we often cannot be 100% sure that an AFR has been ruled out and educating the client about the many potential pitfalls is important.

Failure to recognize that an AFR is a significant contributor to signs means that the pet is destined to long-term drug therapy that is often associated with poorer responses and frequent flares with secondary infections [5].

**Phases of a diet trial**

A diet trial performed correctly has several phases. Putting the pet on a new diet—referred to as the elimination diet—is the first step. During this phase, clients observe the pet for changes, generally the resolution or reduction in signs. (see Client education below) Once changes are noted or the specified end point of the trial is reached, then the pet is reevaluated. After all signs and symptoms are assessed is again fed the diet it was on before the elimination diet. This is the initial challenge phase. Some clients want to avoid this phase and go immediately to the ingredient challenges. Any recurrence of signs with any challenge is a positive provocation and the first step toward a tentative diagnosis. In my opinion, the most important confirmation of the diagnosis is when signs remain resolved in the second challenge. Absolute confirmation requires ingredient-provocation testing, which involves multiple episodes of positive provocation evidenced by exacerbation of signs when the offending ingredient is added and resolution of signs when it is withdrawn. Ingredient-provocation testing is how to determine which diets, commercial or home-cooked, are options for long-term management. The diet trial does require a committed owner and family. When one completes all three phases the dog and client will have invested at least 3 and often 4-6 months. This is not something to take lightly.

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<table>
<thead>
<tr>
<th>Frequency</th>
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<thead>
<tr>
<th>Frequency</th>
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</tr>
</thead>
<tbody>
<tr>
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<td>227</td>
<td>72.3</td>
</tr>
<tr>
<td>A few times/year*</td>
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<tr>
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<tr>
<td>Multiple times/day</td>
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<table>
<thead>
<tr>
<th>Frequency</th>
<th>Count</th>
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<tr>
<td>Rarely, ≤ once/year</td>
<td>197</td>
<td>62.7</td>
</tr>
<tr>
<td>A few times/year*</td>
<td>105</td>
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<tr>
<td>A few times/month</td>
<td>8</td>
<td>2.6</td>
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<tr>
<td>A few times/week</td>
<td>3</td>
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<tr>
<td>Multiple times/day</td>
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The elimination diet
The elimination diet should ideally comprise no ingredients that the pet has been exposed to. However, this is usually impossible and the concern of cross-reactivity also impacts how diet decisions should be made. Cross-reacting allergens do occur, although the true extent is unknown. A study suggested that the high incidence of reactions to a venison diet in a country where venison is rarely fed may be due to cross-reactivity [20]. Cross-reactivity can occur to more than other foods. A dog with atopic dermatitis (AD) that developed oral allergy syndrome to tomato was shown to cross-react with the Japanese cedar pollen [21].

Since proteins are the most common offending allergen, the primary goal is to feed a protein and carbohydrate source that the pet has not been routinely exposed to. Pure carbohydrates are not of primary concern, except that most carbohydrate sources do have low levels of protein in them that may be allergenic. Even cornstarch, which is commonly found in medication and other tablets, has a low level of protein. Fat supplements may also be contaminated with protein. This may be one reason that three studies that have looked at diet contamination have shown this is a serious problem and the hydrolyzed diets appear to be better choices to avoid contamination.[22-24] What is not known is how often a low level of contamination will cause a failure in a diet trial.

There are three main sources for the hydrolyzed diets: Hills, Purina, and Royal Canin. These diets have lower average molecular weights than nonhydrolyzed diets and these smaller proteins do decrease but not eliminate reactions to those proteins. The theory behind these diets is that food allergy is generally due to large complex proteins or glycoproteins. Hydrolyzing reduces the molecular weight so they are no longer allergenic. Human evidence has yielded some evidence to support this theory. The use of these diets has been reviewed in veterinary medicine and the diets are not totally effective in eliminating reactions.[25] However the diets did work for some dogs sensitive to the parent ingredient.

Because of the difficulty doing diets, long time needed to complete multiple trials, potential for cross-reactions, problems with contamination and difficulty in balancing home made diets it is better to do diet trials with the high quality commercial hydrolyzed diets. They are also expensive which is an advantage when it comes time get clients to do ingredient challenges, as that is the way they can find a less expensive high quality diet they can feed for the rest of the pets life. The presence of gi signs is valuable because they can be assessed at four weeks and if not improving an alternative diet be selected. If all the hydrolyzed diets are ineffective in resolving the gi signs the a home make diet such as pumpkin and pinto beans may be utilized but is not a balanced diet and this needs to be discussed with the owner. Home cooking is not be done in growing dogs and should be only done for the 8 weeks then supplements added to balance the diet.

Client education
Key points need to be emphasized to owners before starting a diet trial. Establish baseline symptom scores before the trial is started because this provides the comparison for future responses and exacerbations. It is preferable to establish these scores without concurrent microbial disease. Therefore, baseline signs are often determined at a recheck when the pet is on other medications, such as antibiotics and ant yeast medicine. Symptom scores should record the extent and the pattern of pruritus as well as what gastrointestinal and other signs are present. The Hill visual analog score is helpful, but it is important to pay attention to the extent of pruritus in all affected areas. Some areas may change when the overall pruritus score does not in cases of canine AD with both food and environmental components. Grade at least lesions and pruritus of the paws, perineum, dorsal trunk, and ears. For example, the dog may still have grade-10 disease at the end of the trial even though the pruritus of the ear or dorsal lumbar have totally resolved; such cases often indicate that the dog has a combination of allergies. Clients must be educated on how to recognize a response in their pet, and this can only be done if they pay close attention during the challenge phase. Owners of nonresponsive cases must always be counseled that though they do not think the diet has helped they need to see whether any changes occur after reintroduction of the old diet.

An important but often difficult aspect to control is other sources of foods the animal may ingest. Preventing consumption of other foods often means keeping animals confined indoors with outside exposure controlled, such as on a leash. I have also had cases that require a muzzle to prevent inappropriate food consumption. The owners must be aware that the dog should consume nothing but what is in the diet on a regular basis, so that precludes other pets’ food, treats, medication wrapped in food and even alone, chewable forms of dog vitamins, and supplements. It takes very little for signs to flare, as was shown in a study where 12 dogs that were allergic to soy were challenged with one tablet of Interceptor Flavor Tabs, which contain pork liver, soy, and 2.3 mg milbemycin. Clinical scores increased significantly in 10 of 12 dogs, with peak scores seen 2 days after challenge in five dogs and 5 days after challenge in five dogs [26]. So dogs eating inappropriate foods weekly may not respond to the diet trial. This does mean a monthly flavored heartworm or flea control product is okay, but the owner needs to pay close attention at the monthly application times, as this is essentially a challenge with that ingredient. The fluralaner flea product is only given every three months and contains hydrolyzed pork protein allowing a diet trial to be completed without the challenge. The whole family must be aware of the dietary requirements. Dogs need to be prevented from cleaning floors of crumbs. The presence of young children in a household often precludes any chance of controlling a diet in an indoor pet. Coprophagia must also be prevented. There is a report that a food-allergic dog that ate cat feces did not respond until the housecat was also put on a similar hypoallergenic diet.

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Challenge and specific provocation testing

True confirmation of AFR occurs when feeding the offending diet induces signs (challenge phase), which resolve on the elimination diet with no other changes in concurrent therapies. Many clients are resistant to this proposal until I explain its value. The first is the best, money. The limited ingredient hydrolyzed diets are generally expensive so most owner will be motivated to find a new food, especially once it is explained the cost is not for a extra high quality diet but just a highly processed diet. This is a big reason I use hydrolyzed diets and describe their expense as the cost of a test. Some pets will develop new allergies and by doing multiple challenges the client will not have to start from scratch to determine what else the pet can eat. In addition, knowing what foods the pet is not sensitive increases feeding options. This is particularly helpful for the long-term management, especially in multiple-pet households.

How the challenge is done can vary depending on the client. Some like to try and prove exactly what the dog is allergic to. For these we do ingredient challenges. One ingredient at a time is added to the elimination diet for up to a week. The other is new commercial food challenges with different ingredients. Here I generally pick a less expensive limited ingredient diet and switch to that. If the dog does not react then we have either found another diet it can eat or it was not food allergic. So I also then try a treat that contains lots of ingredients so we hopefully can confirm the food allergy is present but maybe not the exact ingredients. With either approach there are some rules to follow. The client keeps a diary in which ingredients cause reactions. They should watch for how long and what signs or signs are seen with each ingredient. After signs have improved significantly or have resolved completely, the pet should be challenged with the diet being fed before the diet trial. If there is no increase in signs, then all other treats, etc. should be fed. Each challenge should be given only until a recurrence is obvious to the client or for 7 days. If there is no recurrence after 7 days, that food is not likely to be the problem. When signs recur, it is usually just an increase in pruritus. This will usually occur rapidly if the exacerbation is noted in the first 2 or 3 days on the challenge. With true allergy, signs recur rapidly in my experience, most well-confirmed food allergies are worse in 1 to 2 days. If this occurs, then the elimination diet is again fed until the signs resolve. The sooner a client observes a sign of disease occurring and goes back on the elimination diet, the sooner the pet will respond. Fortunately, when they only get one to several meals of the offending diet the response is usually rapid again and often does not need a treatment to resolve it.

References

Pruritus is an uncomfortable sensation of the skin that provokes the desire to rub or scratch, the popular term for this action is itching. Pruritus is a primary neurologic sensation that is a symptom associated with many diseases. The diseases result in the production of pruritic mediators that stimulate itch specific C fiber nerve receptors that are found in the epidermis and dermis. The classic pruritus mediator that has been studied the most is histamine. The discovery of a fourth histamine receptor (H4) has stimulated a new evaluation. There is evidence the H4 receptor is important in both TH2 helper cell type 2 (TH2) inflammation and pruritus. H4 has been shown to occur in dogs but its role is just being investigated. However there are many other mediators believed more important in the dog. There is a long list of pruritic mediators that come from a variety of classes such as neuropeptides, peptides, proteases, cytokines and leukotrienes. We have known for a long time that mast cells contain many pruritic mediators but sensory nerves, lymphocytes and endothelial cells are also sources as is the keratinocyte. Keratinocytes can produce proteases, cytokines and neuropeptides, especially acetylcholine now considered an important mediator of itch. Work in dogs has shown that serum IL-31 is elevated in over half of atopic dermatitis dogs but not in normal, flea allergic or experimentally induced house dust mite allergic beagles.[1] IL-31 is produced by canine TH2 lymphocytes and this production is increased when house dust sensitized T cells are co-stimulated with Staphylococcus enterotoxin B.[2] It is also important to note that two different groups have found IL-31 receptors in the dorsal root ganglia of dogs.[2-4] Pruritus is induced in dogs with exposure to IL-31 and with this model pruritus can be reduced with treatment with prednisolone or the Janus kinase inhibitor, oclacitinib.[1, 5]

Oclacitinib maleate is a new synthetic drug that that has been developed for the treatment of allergic diseases in dogs. It is a member of a relatively new class of drugs called Janus kinase (JAK) inhibitors. Janus kinases are a group of 4 enzymes (Janus kinase 1-3 and tyrosine kinase) that function by facilitating transmission of signals form cell membrane receptors intracellular. They function in pairs with certain cytokine receptors being acted on by various combinations of paired enzymes. Oclacitinib mainly acts on JAK 1 and at higher serum levels on JAK 2. The Cmax does relate to the dose and at 0.6mg/kg daily for 168 days is 273-406 ng/ml. Cmax at 0.4mg/kg was around 200ng/ml for beagle and mongrel dogs after a single dose.[6] Oclacitinib is considered an immune modulating drug because it suppresses cytokine function, particularly IL-31 and to some extent IL 2.

Efficacy of oclacitinib has been shown for pruritus associated with allergic disease.[7] A blinded placebo controlled study evaluated oclacitinib in 436 dogs with a variety of allergic diseases. Pruritus scores decreased from 7.39 to 2.59 and 7.58 to 5.54 in the oclacitinib and placebo treated groups respectively. The response in the treated group was significant and significantly better than the placebo group. Another blinded placebo study done by board certified veterinary dermatologists studied 299 AD dogs.[8] Pruritus scores decreased from 7.8 to 2.6 and from 7.7 to 7.4 in at the 14 days scoring in the oclacitinib and placebo treated groups respectively. This was very significant difference between groups. Following 14 to 28 days all dogs were allowed to go into an open label study and at the end of 112 days the pruritus score averaged 3.2. The skin lesions as graded by the canine atopic dermatitis extent and severity index (CADESI) had also dropped from a pre treatment score of 62 to 32 and 58 to 57 in the oclacitinib and placebo treated groups respectively. When all dogs finished the open label phase the CADESI was 26 at day 112. Another study showed efficacy in flea allergy dermatitis.[9] Apoquel was also shown to decrease pruritus as fast as glucocorticoid therapy and in IL 31 pruritus model even better than glucocorticoids.[10, 11]

There is one 84-day randomized controlled trial comparing Apoquel® (oclacitinib) to Atopica® (cyclosporine) in 226 dogs. Veterinary dermatology specialists performed this study with client owned dogs in Australia. Dogs were evaluated for PVAS and CADESI-02 scoring on days 1,2,7, 14, 28, 56 and 84 days. Differences were significant at all time points up to day 28 regarding PVAS scoring. By day 56, cyclosporine treated dogs had a similar PVAS scoring to Apoquel treated dogs. As expected the Apoquel treated dogs had much quicker onset of activity regarding the pruritus reduction (See Graph below). More adverse events were found in the cyclosporine treated group which was largely gastrointestinal (vomiting and diarrhea Atopica group (44 and 15%) vs. Apoquel group (14 and 4%)[12] (See table below comparing side effects). Apoquel is FDA approved to be used with low dose prednisolone and a recent study showed no increase in adverse events when combined with low dose prednisolone therapy during the first 3 weeks of therapy. Combination therapy expedited the reduction of pruritus during the first 3 weeks during Atopica induction.[13]

Initial results at the Animal Dermatology Clinic in San Diego were evaluated in August 2014. Apoquel was prescribed for 107 dogs, 13 (12%) of 107 stopped the drug because of poor efficacy, 2 stop for the development of masses, one for UTI, 11 went off for alternative therapy and 9 was because ASIT was working. 3 cases were deceased. One at 9-year age with lymphoma, one at 14year age and was reported weak prior to expiring and one with a Histiocytic sarcoma. We had followed up on 47 dogs treated with16mg tabs and 30 (64%) were still on therapy, 43 dogs on 5.4mg and 26 (60%) still on therapy and 17 dogs on 3.6mg with 12 (71%) still on therapy.
In dogs pruritus is manifested by a variety of behaviors though most classic is scratching but also includes: biting, chewing, dragging body parts, licking, rolling, rubbing against objects, scooting, and shaking. Clients may indicate that a dog is not able to itch a part of its body but in reality any area can be itched. However the location partly determines which one of the described methods is utilized. Unfortunately these methods of itching are behaviors that may be seen to some degree in normal animals or animals experiencing another sensation such as pain. Determining that pruritus is abnormal is typically based on a number of criteria such as severity, intensity, duration, induction of skin lesions, or not being able to be distracted from the behavior. Pruritus may occur without visible cutaneous changes, may be associated with a rash that caused the pruritus, or have skin changes present that have resulted from the pruritus. So complete recognition of pruritus and where a dog is pruritic can only be determined by a good history from an observant dog owner. This leads to a problem when trying to assess all pruritic locations as some may not be as affected and therefore the behavior considered normal. For example when surveyed in groups I find there are some veterinarians who believe a dog observed to lick its paws once or twice daily is normal but all agree that 100 times a day is abnormal. Coming to a consensus between those two numbers is difficult. Based on an unpublished survey it is very infrequent for an owner of a dog that they consider normal and has never been treated for skin or ear disease to answer that question with daily or more! Recently Stetina et al completed a study in 314 apparently healthy dogs. The results have been presented at the 2015 NAVDF and the paper accepted by Veterinary Dermatology. This study has revealed that the following behaviors regarding pruritic behaviors. Table 1

<table>
<thead>
<tr>
<th>Pruritic Behavior</th>
<th>Frequency</th>
<th>N= 314</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paw licking/chewing</td>
<td>Never</td>
<td>106</td>
<td>33.8</td>
</tr>
<tr>
<td></td>
<td>Daily*</td>
<td>24</td>
<td>7.6</td>
</tr>
<tr>
<td></td>
<td>Multiple times/day</td>
<td>8</td>
<td>2.6</td>
</tr>
<tr>
<td>Facial/muzzle rubbing</td>
<td>Never</td>
<td>121</td>
<td>38.5</td>
</tr>
<tr>
<td></td>
<td>Daily*</td>
<td>29</td>
<td>9.2</td>
</tr>
<tr>
<td></td>
<td>Multiple times/day</td>
<td>6</td>
<td>1.9</td>
</tr>
<tr>
<td>Head shaking</td>
<td>Never</td>
<td>102</td>
<td>32.5</td>
</tr>
<tr>
<td></td>
<td>Multiple times/day*</td>
<td>15</td>
<td>4.8</td>
</tr>
<tr>
<td>Sneezing</td>
<td>Never</td>
<td>73</td>
<td>23.3</td>
</tr>
<tr>
<td></td>
<td>Daily*</td>
<td>17</td>
<td>5.4</td>
</tr>
<tr>
<td></td>
<td>Multiple times/day</td>
<td>4</td>
<td>1.3</td>
</tr>
</tbody>
</table>

A visual analog scale utilizing those behaviors has been developed and validated for assessing pruritus by owners of dogs.[14] This scale was evaluated in 305 dogs that were either healthy or had non cutaneous disease and 408 dogs with skin disease.[15] In the non-skin disease dogs the median pruritus sore was zero, which was recorded by 214 (70.2%) owners with 228 (75%) of the dogs having a score ≤ 0.5. Ninety dogs (29.5%) had scores above 0. The median score in the skin disease group was 5.5 and only 26 (6.4%) of 408 with skin disease had a score of 0. Stetina study showed a lower level though similar results for 0 scores in normal dogs and there was a positive correlation between higher scores and increased frequency of many pruritic behaviors. Stetina et al found 60.2% scored 0 and 92.1% were 2 or less and only 9 dogs (2.8%) scored > than 3.

Fleas are also known to cause pruritus particularly in flea allergy dermatitis. A recently study has also shown fleas are very important in non-allergic dogs as well. When dogs were identified to have at least ten fleas on them 100% were given PVAS scores above 0 and most were above what is considered normal.[16] Effective flea control with fast killing Spinosad was able to decrease pruritus dramatically but improvement was taking up to 90 days to be seen.

References


Pododermatitis is often defined as inflammation of the skin of the foot. However, several dictionaries actually use the term related to only inflammation of the dermal tissue underlying the horny layers of the hoof and generally are referring to diseases most often seen in cattle. If one uses the broader definition often applied to dogs then any foot (paw) epidermal or dermal tissue that is inflamed would be a form of pododermatitis. This would include interdigital spaces, footpads, nail folds (paronychia), and claws. The diseases that may affect any of these structures would include most of the diseases that affect dog skin, which results in an extremely long and not very helpful differential diagnosis. Therefore another approach is to separate the disorders based on more specific anatomic regions as well as to those diseases that may affect the paws along with other body areas from those diseases that are limited to the paws. Even in this context there are diseases that tend to affect only one paw or even one digit versus diseases that typically affect all or at least most paws and digits. When one narrows the presenting features based on this approach then the differential diagnosis is much more limited.

The author uses definitions based on these more specific anatomic sites and therefore different differentials. Paronychia is those diseases that are limited to the skin of the claw folds of the digits. Any involvements of the claw are superficial and from deposition of exudate or debris from the claw fold accumulating or contacting the adjacent claw. Pad diseases are those that affect the pads, which are located on the palmar/plantar surface of each digit, and under the metacarpal- and metatarsal-phalangeal joints, and the carpus of dogs and cats. The skin of the pad is non-haired, thickened, tough, and rough surfaced. It is most often hyperpigmented and the hypodermis contains large amounts of adipose tissue, as most pads are weight-bearing surfaces. Claw diseases are those that result in changes in the claws and can include the dermal or deep structures of P3. That leaves the rest of the digital and interdigital hair skin, as the last anatomic region of the paw which when inflamed is what this author defines as pododermatitis. We can then take this one more level and that is disorders that affect the hair follicles of the interdigital haired skin, podofolliculodermatitis.

Chronic interdigital pododermatitis has been described for years. Though it is often idiopathic it has been proposed that friction, scarring and trauma may predispose or cause follicular damage and lead to infection and inflammation. Podofolliculitis is one form of pododermatitis, which is defined as follicular disease (most often hyperkeratosis) with perifolliculitis and or folliculitis or furunculosis. These cases may involve one or multiple paws. Once there is follicular involvement in multi paw symmetrical disease then the most common differentials are secondary bacterial podofolliculitis, demodex and follicular hyperkeratosis and furuncular granulomatosis.

Pododemodicosis is most common in young dogs with generalized demodectic mange. Occasionally cases are seen that following resolution of generalized demodex will have persistent pododemodiecosis or podofolliculitis and sterile furuncular granulomatosis. These cases are generally very apparent with the history of generalized demodex prior to the pododermatitis. Rarely a case of adult onset demodecosis or iatrogenic demodexis from long term immune suppressive therapy will present with lesions confined to the paws. It is important to look close as perioral disease is often seen with the pododemodiecosis in these cases. Pododemodicosis is tentatively ruled out with properly performed skin scrapings and hair plucks. In rare cases demodex pododemodicosis will only be diagnosed with a skin biopsy. Treatment of pododemodicosis is systemic ivermectin 450-600ug/kg q 48-24 hours. Some difficult cases may respond better to ivermectin twice weekly combined with weekly or twice weekly amitraz paw soaks.

Bacterial podofolliculitis may be seen secondarily to most diseases that affect the paws, including demodex pododemodicosis. It also has been described as occurring as an idiopathic disease. Many cases likely described as idiopathic likely occur secondary to conformational disease. Two syndromes have been described that likely reflect the same or similar syndrome. Canine interdigital has been described as occurring as an idiopathic disease. Many cases likely described as idiopathic likely occur secondary to cases may respond better to ivermectin twice weekly combined with weekly or twice weekly amitraz paw soaks.
“flat footedness”. In others it is possible to see the digital pads projecting anterior. What is also interesting some dogs and even affected dogs with some lesions may develop effective calluses or even modified pad tissue that does not result in perifolliculitis and granulomatous furunculosis. What determines the development of that response is unknown.

What complicates the diagnosis of these disorders is that they can occur secondary to other diseases that result in pododermatitis, pain and altered weight bearing. Even chronic infections lead to follicular hyperkeratosis therefore these syndromes can be associated with other diseases or occur with no predisposing condition other than conformational changes or apparently be truly idiopathic though this is very infrequent in the author experience. Another complicating factor is some dogs with deeply recessed folds in the palmar plantar skin will develop infections related to the fold dermatitis, often aggravated by concurrent allergic dermatitis. Diagnosis thus may be limited to the presence of interdigital palmar plantar comedone and follicular cysts and IrR-LPP or they may be associated with another disease in which case maybe the diagnosis of that name is not appropriate. However once present treating the primary disease will not resolve the pododermatitis. The primary causes that need to be ruled out are the potential causes for bacterial podofolliculitis, such as allergy, hormonal, parasitic, keratinization, metabolic and immune mediated disorders. Once all those are ruled out then it may be appropriate to diagnose IPPFCf or IrR-LPP if there is follicular disease and appropriate histopathology. Certainly a conformational component needs to be addressed as an underlying cause because when present medical therapy is rarely successful without long term anti-inflammatory therapy.[4, 9] Once conformational disease is diagnosed then the treatment of choice is surgical removal of the diseased tissue and creating non-haired weight bearing surfaces. Both syndromes may present with secondary infection but eliminating the infection does not result in complete resolution of the lesions. All drainage, fistulous tracts and pain may resolve with antibiotics leading some owners and even veterinarians to believe the lesions are healed, only to recur following the discontinuation of antibiotic therapy. Even successful removal of the diseased tissue has had recurrence if the dog ends up weight bearing on haired skin that is sutured into the defect. For localized lesions focal surgical excision or laser therapy may be successful. The key is to remove all foreign hair and epithelial debris and then allow the lesion to granulate in so there is no haired skin brought back into the weight bearing area. Cases with generalized pododermatitis may respond best to a complete podoplasty.[10, 11]

References
Skin infections with bacteria are often found in dogs secondary to other diseases such as seborrhea, endocrine diseases and allergic diseases. Many of these cases have abnormalities in skin barrier function or desquamation. When the primary disease is controlled if this defect is not corrected the dog may still be prone to recurrent infections though episodes may be less severe or less frequent. In chronic or recurrent infections other factors may develop which are referred to as perpetuating factors. The most common bacteria to cause skin infections in dogs is *Staphylococcus pseudintermedius* though occasionally other bacteria such as *Staphylococcus aureus* or *schleiferi*, *Enterococcus*, *Corynebacteria*, *E. coli*, and *Pseudomonas* may be pathogenic. The emergence of methicillin resistant *Staphylococcus* including *pseudintermedius* in dogs is now recognized around the world. Prior antibiotic therapy generally has been shown to be a risk factor for its occurrence though this was not the case in a recent study in Germany.[1] The Staph pseudintermedius associated with infections has very similar virulence factors with the only difference shown was increased protein A in dogs with pyoderma.

The diagnosis of pyoderma requires a skin lesion that has neutrophils with bacteria present that is preferably found intracellular within inflammatory cells. The classic primary lesions of pyoderma are: Pustules, furuncles, and fistula. Other lesions suggestive or compatible with pyoderma include: Crusts, papules, nodules, and lichenification. The spreading ring of scale (epidermal collarette) associated with some erythema, exudate or crusting is also very typical of pyoderma. If cocci are seen then most commonly the pyoderma is due to *Staphylococcus* though definitive identification requires a culture. Based on the simplest definition of a pyoderma I prefer to diagnose bacterial overgrowth when no inflammatory cells are present but bacteria are present in abnormally high numbers. High is greater than one cocci or 0.5 rods per OIF (1,000X) based on unpublished work by Dr Colombo. It has also been proposed that 5 cocci may be an appropriate number to use. Further work evaluating this is indicated and should look at various sites commonly involved with pyoderma. Histopathology is also helpful in diagnosing pyoderma though bacteria are not often seen. Histopathology is also used to identify primary diseases as well as perpetuating factors. Most suppurative folliculitis and perifolliculitis occur because of pyoderma. The presence of bacteria in a crust or the stratum corneum is also significant. Determination of resistance does require sensitivity testing and should be performed whenever cases have not responded to empiric therapy.

Predisposing and perpetuating factors
Since pyoderma is most often secondary successful long-term management will require that underlying primary diseases are identified and managed, but it is also important to realize other aspects of the dog may predispose such as inappropriate friction or alteration in skin microenvironment from things such as skin folds. Both friction and skin folds may be associated with genetically selected traits or obesity. Chronic trauma to the skin results in changes of the affected hair follicles. This is best exemplified by the formation of a callus. In some cases this response can predispose to pyoderma.

The role of chronic skin disease and the development of recurrent and also resistant pyoderma are well accepted. What is not often discussed is what role does the pyoderma have on causing recurrent pyoderma. Does the presence of a pyoderma result in changes that may perpetuate the development of chronic inflammation and more pyoderma. There are some clinical observations that support this but studies are needed to answer this question. These perpetuating factors occur because the pyoderma has damaged cutaneous structures. The histopathology of chronic pyoderma cases will often have follicular hyperkeratosis. What has not been studied is what causes the follicular hyperkeratosis, is it always just the primary disease or is it the pyoderma? Many atopic dogs that have had chronic pyoderma will have follicular hyperkeratosis, but that is not a classic lesion of atopic dermatitis. It is common for a dog with deep pyoderma to have a history of chronic superficial pyoderma that eventually progresses to a case with both superficial and deep lesions. Why does this occur? Other aspects than just the primary disease may be involved. In some cases maybe drugs the dog is on contribute. How do corticosteroids impact chronic pyoderma cases? Folliculitis often results in foci of alopecia. The loss of hair now exposes the skin to ultraviolet radiation and in some dogs they do not have the ability to pigment the skin. What role does the ultraviolet radiation have on the local immune response or even the hair follicle structure or cutaneous inflammation? When an infected hair follicle does rupture it releases keratin and hair shafts into the dermis. That material also stimulates inflammation and in some cases fibrosis and scarring. Though normally this material is broken down and eventually eliminated some cases develop persistent hair shaft sequestrum that appears to be associated with chronic or recurrent cases. In others it may not be hair shafts but remnants of corneocytes are found in the center of microabcesses or scars and the possibility of cocci that may adhere to corneocytes being protected inside a folded or rolled up corneocyte is another possible site for sequestering bacteria and protecting them from tissue levels of antibiotics or the body’s immune defenses. Abscess or granuloma formation may alter the ability of some antimicrobials to effectively reach or kill the microorganisms. Another pathologic change that may be less apparent is fibrosis unless
it occurs grossly. Fibrosis more often occurs at the microscopic and not the gross level. The fibrosis may be perifollicular or more diffuse throughout the dermis. Certain breeds (Doberman pinscher, bull and Staffordshire terriers, Rottweiler) seem more predisposed to excessive scarring that appears to make resolution of the pyoderma more difficult.

Clinically cases occur that the primary disease is well controlled or eliminated yet recurrent infections may continue for some time. One could argue in the atopic dog that this is because the barrier defect that was present even before the atopic disease is not really controlled. How does one explain in the testicular tumor dog that still gets recurrent pyoderma after the testicular tumor is removed? Studies evaluating causes of chronic recurrent pyoderma other than primary diseases are needed. If perpetuating factors are important then how we manage these cases may need to change. If we can prevent infections from causing perpetuating factors or find ways to reverse perpetuating factors we may improve the chances of eliminating recurrent infections.

Treatment
Success treating skin infections requires appropriate antimicrobial therapy and systemic antibiotic therapy has been the main emphasis of veterinarians for many years. Topical therapy though considered helpful can actually be essential to successful therapy and in some cases with resistant bacteria such as methicillin resistant Staph (MRS) may become the main or sole method to eliminate the infection. Even following therapy is it common to find Staphylococcus either persisting on the skin or in carriage sites and often these will still be resistant strains though fluctuations in this pattern are seen.

Additionally any pathologic changes in the normal anatomy or physiology of the skin that occur because of the inflammation from the infection need to be reversed or controlled. If any part of these components is not addressed then more antimicrobial therapy will be required and success will be limited. Some treatments may need to be directed at reversing pathologic changes or long-term therapy may be required until the body naturally remodels or reverses those changes. In others surgical correction or removal of localized fibrotic or granulomatous lesions can be an effective and cost saving procedure. Long-term pentoxifylline may help to reverse scarring in some cases with widespread lesions not amenable to surgical therapy. Glucocorticoids have been used in some cases with residual granulomas but this should only be done after antibiotic therapy has eliminated the bacteria and the granulomas are sterile based on culture of ground up tissue samples.

Cleaning the skin promotes desquamation, which removes surface bacteria and yeast as well as irritants and allergens. In some cases ingredients may be used to normalize keratinization or improve barrier function. Inflammation may be decreased by addition of anti-inflammatory ingredients or just the use of cool water. This along with moisturizing and cooling the skin will also decrease pruritus. Cleansing the skin is most readily accomplished by bathing the pet and is also the most effective way to topically treat large body areas. Bathing also lends itself to the use of rinses after the bath that may contain topical antimicrobials. In general the more frequent the bathing the better and in some cases 2-3 times a week is very effective in preventing recurrent pyoderma and bacterial overgrowth. Daily is required in some cases to get complete resolution then less frequent may maintain remission.

Antiseptics are often incorporated into shampoos and other topical therapies (leave on conditioners and gels, lotions, sprays and wipes) used to treat pyoderma. These are particularly useful for more localized areas such as the chin, paws and fold areas. Similar to antibiotics one might expect natural selection to eventually favor the development of resistant strains of bacteria. A group of gene mutations have been recognized that confer some resistance to a wide variety of lipophilic cationic compounds including quaternary ammonium compounds which is what the genes have been named after (QACs) though many other antiseptics are also seeing resistance due to these genes.[2] So the problem with resistance is not just to antibiotics but also antiseptics. These have not yet been found in canine S pseudintermedius.[3] Strategies for reducing resistance and mitigating the problems it can present have been described for parasites for a number of years. Integrated pest control is a process of using multiple different types of anti parasitic agents and rotating and or combining there use. Apparently this is a strategy that we should incorporate into out approach to canine recurrent pyoderma. This approach has been more used for years in dealing with chronic otitis cases and now that we see some similarities between chronic recurrent pyoderma chronic recurrent otitis we should be incorporating a similar approach.

The most common active antimicrobial ingredients used in veterinary medicine are: benzoyl peroxide, chlorhexidine, ethyl lactate, mupirocin, neomycin, polymyxin, phytosphingosine, salicylic acid, sulfur and triclosan. Multiple studies have shown chlorhexidine and benzoyl peroxide to be particularly effective though some have show benefit with other antiseptic ingredients. Based on how we approach ear cases it is preferable to use synergists or combinations of antiseptics as long as their effects are not antagonistic. In addition using systemic antimicrobials that target the bacteria by pathways that do not share the same gene mutations for resistance will be more similar to how integrated pest control is done, we should consider integrated antibacterial therapy as a way to try and minimize the risk of or slow down the development of even more resistant strains.

References

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