The focus of this two part lecture is to increase your familiarity with common auto-immune skin diseases, the diagnostic tests required to identify them definitively, and common treatment modalities. We will start with a review of diagnostic tests required when dealing with auto-immune skin disease.

The first test is cytology. Cytology is simple to perform but there are many common pitfalls. First, the clinician must consider whether the sample tissue is appropriate to use a glass slide or a piece of clear packing tape to collect the sample. Slides can be easily pressed onto moist or gooey lesions. Slides can also be used to lift the edge of a crust and slide underneath. Tape is most helpful in areas two small for the glass slide and lesions that are dry. The next step is staining your sample. Tape should not be flamed and does not require dipping in fixative. Lastly, you must evaluate the cytology. If you have a dilapidated microscope then you are going to have more trouble and achieve poor results. The more cytology you perform the more comfortable you will become with the test.

Next on our list is the basic CBC and Chemistry that we all know. These tests may not seem particularly related to the skin disaster standing on your exam table. Especially when the dog is happy and energetic. However, these tests are important for ruling out underlying metabolic problems that could cause the skin disease. More often you will use these tests to guide the medications you choose to treat the animal.

Biopsy is the ultimate test for dermatology. However, performing a biopsy is not always going to get you a straight answer. There are some simple things you can do to get better biopsy results. First, collect multiple samples. In most cases try for 4-6 pieces of tissue. Second, center your biopsy punch on the lesion. Do not send normal tissue to a pathologist. If you send in the margin of a lesion and include normal tissue there is a risk that the lab technician will not “cut in” the diseased tissue for examination. Third, if you see infection on cytology then you should consider resolving infection before collecting biopsy specimens. Infection can obscure the primary disease and make the pathologist’s job much more difficult. Fourth, send a good history along with your samples. Fifth, include clinical photographs with the samples when possible. Lastly, send your tissue samples to a dermatopathologist. Who you send your samples to could make the difference between the right answer and a wrong answer or no answer at all.

Pemphigus foliaceus

Pemphigus foliaceus is one of the most common auto-immune skin diseases seen in dogs and cats. This disease is characterized by pustules and honey-colored crusts. This condition is typically idiopathic but it can develop secondary to drug exposure. Pemphigus foliaceus is often seen in patients previously diagnosed with allergic dermatitis; however, no link between the two has been proven.

In pemphigus foliaceus the immune system is attacking a particular protein in the complex structure (called a desmosome) that links keratinocytes together. Destroying the bonds between keratinocytes is termed acantholysis and results in acantholytic cells. Acantholytic cells are typically plump and round because they are no longer connected to their neighbors. They stain darkly and have a clearly visible nucleus. Different forms of pemphigus exist and one of the primary differences between them is what layer of the skin this acantholysis occurs. For pemphigus foliaceus the damage occurs in the two uppermost layers (the stratum corneum and the stratum granulosum). More serious forms of pemphigus affect deeper layers of the skin and cause significantly more damage. As acantholysis occurs, vesicles and sterile pustules are formed. These are fragile and easily damaged because they are located in the uppermost layers of the epidermis. Depending on the intensity of the immune response, pustules can develop and rupture in under an hour or over the course of days. For comparison, pyoderma pustules develop more slowly and are more resilient (more difficult to break). In addition, pyoderma pustules are typically centered around a hair follicle. Both pemphigus pustules and pyoderma pustules will contain neutrophils but intact pemphigus pustules will not contain bacteria.

As already mentioned, the classic lesions of pemphigus foliaceus are pustules and crusts. These lesions can occur anywhere on the body but are commonly found on the face and trunk. Pustules can develop inside the aural opening resulting in serum leakage and crust debris falling into the ear canals. The result is typically a wicked otitis externa. In many cases the nasal planum is also abnormal. The planum typically becomes dry, thick, and crusted. Ulcers of the nasal planum can occur secondary to crust being traumatically removed. However, pemphigus foliaceus does not cause ulceration of the oral cavity or mucus membranes. The paw pads may be affected as well. Discrete pustules may be seen on the pads but more often the pads are thickened, dry, and crusted. Some dogs will be reluctant to walk but this is uncommon with pemphigus (much more common with hepatocutaneous syndrome).

Diagnosis is via biopsy. Intact pustules are preferred because they offer the clearest picture of the disease process. However, crusts are also very useful biopsy specimens. When collecting biopsies for potential pemphigus foliaceus it is critical not to scrub the skin. In most cases it is advised to avoid shaving the animal’s fur as well. Even the slightest disturbance to the skin can damage the fragile pustules seen with this condition. In the event that no pustules are present, the proof of pemphigus might be in the crust on top
of the skin rather than in the skin sample itself. Consequently, always include crust debris in the formalin jar and request the crust be processed when you biopsy for pemphigus.

Treatment, which is really to say management, is almost always successful but required life-long. Some cases of drug induced pemphigus foliaceus will remain in “remission” even when immune suppressive therapy is discontinued. However, it is often difficult to prove which cases are drug induced which makes predicting which patients will be able to stop therapy nearly impossible. Initial therapy requires steroid administration. Oral daily prednisolone/prednisone dosages of 2mg/kg to 6mg/kg are often required. Steroid therapy often yields dramatic improvement in two to four weeks when dosed adequately. Some patients will respond better to other steroids such as dexamethasone or triamcinolone. Recheck examinations every two to four weeks are critical to assess response to therapy and tailor drug therapy. Secondary bacterial infection is common in pemphigus and your clients will not be able to discern the difference between a pyoderma pustule (which needs antibiotics) and pemphigus pustule (which would cause you to evaluate your immune suppressive plan). In general, the goal is to slowly taper steroid therapy once clinical “remission” has been achieved. Over the course of three to four months some dogs will achieve good clinical response and can be maintained with every other day steroid therapy. However, the majority of patients will experience significant steroid side effects (such as weight gain, polyuria, polydipsia, polyphagia, behavioral abnormalities). Because of steroid side effects and the fact that most patients require life-long immune suppressive therapy it is typically necessary to add another medication as a steroid sparing agent. First line drugs for this purpose are cyclosporine and azathioprine. Second line drugs include mycophenolate and leflunomide. In most cases, I will start a steroid and a steroid sparing drug at the beginning of treatment. All of the above listed steroid sparing drugs have a delay of four to eight weeks until they become clinically effective. By starting both types of drugs at the same time I am able to reduce steroid therapy sooner.

**Discoid lupus erythematosus**

Discoid lupus erythematosus (DLE) is sometimes referred to as cutaneous lupus erythematosus. DLE is a relatively benign auto-immune skin disease which does not affect other organ systems. Histologically there is no difference between DLE and systemic lupus erythematosus (SLE) which is why a good clinical history and blood analysis are important.

**Mechanism**

The first sign of DLE is typically depigmentation of the nasal planum. Often the planum becomes grey, white, or even slightly bluish in color. The nasal planum will then typically lose its cobblestone architecture. Erythema and scaling typically follow. In severe cases erosions, ulcerations, and crusting eventually develop. Lesions may also be seen around the eyes and on the pinnae. In rare cases lesions can also occur on the distal limbs, foot pads, and perianal region.

Cytology may reveal pyogranulomatous inflammation but secondary infection is uncommon. CBC and Chemistry are typically normal. ANA testing is usually negative. Biopsy samples should be collected from hypopigmented areas or intact crusts. Ulcers and erosions should not be biopsied.

Differential diagnoses include: Pemphigus erythematosus, pemphigus foliaceus, mucocutaneous pyoderma, dermatomyositis, uveodermatologic syndrome, contact dermatitis, and SLE.

DLE typically responds well to low-level immune suppressive therapy. Specifically, it is estimated that 50-70% of DLE cases will respond to combination therapy with Tetracycline and Niacinamide. (Doxycycline and minocycline have both been effectively substituted for tetracycline.) However, tetracycline/niacinamide therapy is slow to take effect and the full benefit may not be seen for 8 weeks. Oral steroids can be used to provide initial relief while waiting for tetracycline/niacinamide to take effect. Another option which is often utilized is topical 0.1% Tacrolimus cream. Tacrolimus is applied once to twice daily until full effect and then tapered to the lowest effective dose. Life-long therapy is usually needed. The intensity of therapy may vary over time. DLE is aggravated by sun exposure so some dogs will experience a worsening of symptoms in the summer. Pediatric sunscreen can be used to help avoid sun exposure.

**Mucocutaneous pyoderma**

Mucocutaneous pyoderma (MCP) is not an auto-immune disease. However, I have included it in this lecture because it mimics DLE and is often a source of speculation and confusion. The first sign of MCP is typically edema and erythema of the lip margins. The commissures are especially susceptible. Over time exudate and crusting may develop. Depigmentation may occur as well. Similar lesions may develop on the eyelids, nares, vulva, prepuce, and anus.

The primary differential diagnosis is DLE; however, zinc responsive dermatosis, PF, PE, adverse drug reaction and uveodermatologic syndrome can all appear similar to MCP. Biopsy reveals changes similar to DLE except that the dermal-epidermal junction is not obscured and hydropic degeneration is minimal or absent. Unfortunately, the presence of ulcers and secondary infection can interfere with the pathologist’s ability to evaluate the dermal-epidermal junction. I have seen many patients referred to me after being biopsied with a diagnosis of either DLE or MCP. Choose your biopsy sites wisely and try to eliminate or at least reduce infection first.

MCP is a pseudo auto-immune disease caused by bacterial infection. In some cases topical cleaning and frequent use of a chlorhexidine wipe is sufficient. However, many cases need oral antibiotic therapy for 3-4 weeks. Topical therapy with Mupirocin
ointment either as sole therapy or in addition to oral antibiotic therapy is typically very effective. MCP is a chronic relapsing condition. Lesions may respond well to oral antibiotic therapy and then not return for several weeks or months. Other cases require daily topical antiseptic cleaning life-long.

**Uveodermatologic syndrome**

This syndrome is sometimes referred to as VKH-like disease because of its similarity to VKH in humans. It is characterized by concurrent granulomatous uveitis and depigmenting dermatitis. In humans and Akitas there is a genetic basis for the disease. However, any dog breed can be affected. I most often associate this disease with Huskies, Malamutes, Samoyeds and their related breeds. The mechanism of this disease is the formation anti-melanocyte antibodies which result in immune mediated destruction of melanocytes. Most textbooks describe ocular lesions (acute bilateral uveitis) occurring first with dermal lesions occurring concurrently or at some later time. However, I have seen many cases where depigmentation was the first symptom.

Because ocular lesions usually occur first the initial clinical signs typically relate to uveitis. Clients may observe include photophobia, blepharospasm, excess lacrimation, or blindness. Depigmentation usually begins on the nasal planum, lip margins, or eyelid margins. Some dogs will demonstrate diffuse depigmentation of the hair coat, the paw pads, the scrotum, the anus, or the hard palate. The depigmentation is typically well demarcated and without erythema or scale. In some cases erosion, ulceration, and crusting will develop.

Immediate biopsy is recommended. The best biopsy samples are from areas recently depigmented. Collecting tissue samples from erosions and ulcers is not recommended. Crusted lesions should be sampled if present. Histopathology is relatively straightforward and shows pronounced pigmented incontinence. Lichenoid interface granulomatous dermatitis is also present.

Rapid consultation with an ophthalmologist is strongly recommended. The ophthalmologist should be advised that you suspect uveodermatologic syndrome and that you have collected tissue samples for histopathology. In general, the epidermal lesions associated with this disease are mild but the ocular changes are severe and may be irreversible. Without timely aggressive therapy blindness will occur.

Treatment usually requires the combination of oral steroids along with an additional immune suppressive agent such as azathioprine or cyclosporine. Ocular treatments for uveitis are also indicated. Life-long therapy is required but blindness can be avoided. The status of the skin lesions cannot be used to estimate the status of the ocular lesions.

**Erythema multiforme (EM)**

There is some debate regarding the relationship between erythema multiforme, Stevens-Johnson syndrome and Toxic epidermal necrolysis. For the purpose of this lecture we are going to use a rather broad description of erythema multiforme as the previously mentioned debate is not critically important in a clinical setting.

The clinical features of erythema multiforme can be diverse. “Target” lesions are considered the classic representation of this disease but are only reported in 38% of cases. Coalescing erosions and ulcers which form an “ink blot” appearance are common in more advanced forms of the disease. Both target lesions and coalescing ulcers are most often seen on the caudal ventral abdomen. Other, less specific clinical features include acute development of symmetrical macules, papules, plaques, vesicles, and bullae which might result in ulceration. Lesions are occasionally painful but usually not pruritic.

There are numerous differential diagnoses for erythema multiforme due to the variety of potential clinical signs. Mild forms of erythema multiforme may look similar to urticarial allergic reactions, superficial spreading pyoderma, bacterial folliculitis, dermatophytosis, and demodicosis. Other, slightly more severe cases may resemble sterile neutrophilic dermatosis (Sweet’s syndrome). Severe cases of erythema multiforme must be differentiated from burns, lupus erythematosus, vasculitis, hepatocutaneous syndrome and zinc responsive dermatosis.

Individual keratinocyte apoptosis (death) with lymphocyte satellitosis in all levels of the epidermis is the most characteristic histopathologic feature of Erythema Multiforme. However, it is still important to have the tissue sample evaluated by a dermatopathologist so that this key feature is not overlooked. Other non-specific changes include interface dermatitis and mild inflammation which may affect hair follicles. Pigmentary incontinence is variable and also non-specific.

Erythema Multiforme often has an underlying trigger. Potential triggers include: drugs, bacterial infection, viral infection, and neoplasia. Many cases are considered idiopathic but this should not be assumed without thorough investigation. The diagnostic work-up should include thoracic and abdominal imaging as well as CBC, Chemistry, and Urinalysis. The owners should be questioned about any medications or supplements they gave prior to the development of lesions.

An “old dog” form of Erythema Multiforme also exists. Unlike classic EM, “old dog EM” usually produces lesions which are more exudative and proliferative (rather than ulcerative). In addition, the lesions are usually focused on the face and ears instead of the ventrum. An underlying trigger is rarely found in cases of “Old dog EM.”
Treatment involves immune modulatory therapy. Steroids are often the first line of therapy but Atopica and Azathioprine are also used frequently. Higher doses are often necessary initially to gain control over the disease. Life-long therapy, potentially at lower dosages, is usually required.

**Cutaneous adverse drug eruption/reaction**

An adverse drug reaction is most generically described as any un-intended effect of a prescribed medication. Cutaneous adverse drug reactions in dogs and cats are considered uncommon although the true incidence is unknown. Any drug may be implicated in adverse drug reactions but those most commonly involved are: sulfonamides, penicillins, cephalosporins, levamisole, and diethylcarbamazine. Reactions may occur the first time a drug is administered or after a long, previously uneventful course of administration. In other cases, reactions develop during subsequent courses of the same medication. No age or sex predilection is reported; however, drug reactions are more likely to develop closely following vaccination.

Cutaneous adverse drug reactions can demonstrate multiple clinical presentations and mimic almost any other dermatosis. However, the most common clinic presentations are: contact dermatitis, exfoliative dermatitis, pustular dermatitis, pruritus resulting in self-inflicted lesions, maculopapular eruptions and erythema multiforme.

Biopsy is critical for diagnosis but so is a thorough history. Any potential drug triggers should be stopped as quickly as possible. In many cases, stopping the offending drug will result in clinical resolution of skin lesions in 7-14 days. Prognosis is usually good unless internal organ involvement has occurred, another auto-immune disease has been triggered (pemphigus foliaceus, erythema multiforme), extensive skin sloughing has occurred, or a resistant bacterial infection has developed.

Most cases will benefit from immune modulatory therapy. This is usually achieved with steroid therapy because a quick response is needed. Patients with severe ulceration or pruritus will be prone to secondary bacterial infection. This can be a clinical challenge as one tries to avoid adding drugs which could further stimulate the adverse reaction. Topical antimicrobial therapy should be used whenever possible. Systemic fluoroquinolones are typically the least offensive antibiotic option. However, reactions have been documented to all classes of antibiotics. The inciting medication and related compounds should be avoided in the future.

**Cutaneous vasculitis**

At the most basic level, cutaneous vasculitis involves inflammation which targets blood vessel walls. Inflammation narrows the vessel lumen and interferes with blood flow. Peripheral vessels which are very small and locations with poor collateral circulation are most commonly affected. Lesions are also commonly seen in areas of “wear and tear” such as elbows, hocks, paw pads, and the muzzle. It should be noted that vasculitis can occur without an immune component in situations such as burns and trauma.

It is important to realize that vasculitis is actually a reaction pattern and not a specific diagnosis. Multiple diseases can result in vasculitis. Investigating for the underlying cause of the vasculitis is critical to long term treatment success. Drug reactions and infections are considered the most common triggers. However, other possible causes include: infections, dietary hypersensitivity, insect bites, neoplasia, certain drugs, and connective tissue disorders. Even with intensive testing some cases of vasculitis are considered idiopathic.

Biopsy is required to identify vasculitis. However, confirming the diagnosis can be difficult. Definitively diagnosing vasculitis requires finding the precise area of the blood vessel wall which is being targeted by inflammation. Considering the vast network of vessels in the dermis and epidermis this can be like looking for a needle in a haystack. In addition, the pathologist has to differentiate from inflammatory cells that are simply passing through the vasculature and into the tissue verses inflammatory cells targeting the vessel wall. To add even more confusion, there is a category of vasculitis described as “cell poor” which demonstrates far more subtle changes to the vascular walls. As such, pathologists often use clues found elsewhere in the biopsy to make the diagnosis. Those clues include: pale staining collagen, atrophy of hair follicles, and a cell poor interface dermatitis.

Diascopy is a very useful, rapid, in-clinic test in cutaneous vasculitis. Diascopy involves gently but firmly pressing a clear glass slide against the skin in an area of erythema/urticaria. Erythema associated with vasculitis will not blanch with diascopy because the blood is outside the vessels. Erythema associated with allergy, for example, will blanch with diascopy.

Clinical signs of vasculitis vary based on the severity of the inflammation and the length of time that passes between when the disease develops and when the owner brings the animal to you for examination. Acute cases will often demonstrate palpable purpura, pitting edema and the formation of bullae, eschar, and ulcers. Papules, plaques, pustules, and urticaria may also be seen. More commonly, vasculitis is seen as a chronic disease. Pinnal lesions are often alopecic, dry, and crusted. Lesions on the pinnae usually effect the apex or concave surface. Severe vasculitis on the margin of the pinnae can result in a jagged or “cut out” shape. Scabs and frequent bleeding may also be features of pinnal lesions. Paw pad lesions typically involve a “punched out” defect in the center of the pad. In less severe cases the center of the affected pad may demonstrate a shallow circular crater or hypopigmented macule. It is important to note that cases of vaccine induced vasculitis typically demonstrate a lesion at the site of vaccine administration as well as lesions elsewhere on the body. However, the vaccination site lesion may be very minor.
Treatment typically involves modulating the immune response with steroids, cyclosporine, azathioprine or other similar drugs. Pentoxifylline is an alternative treatment option which often helps milder cases. Pentoxifylline is a phosphodiesterase inhibitor which can increase the flexibility of red blood cells making it easier for them to pass through narrow vessels. Pentoxifylline also has the ability (mildly) to reduce inflammation in the epidermis. Additionally, topical therapy can be helpful for small lesions. Tacrolimus 0.1% (brand name = Protopic) or a steroid ointment such as fluocinonide 0.05% are commonly used. Some dogs will only need treatment for 4-6 months. Other patients will require life-long therapy; however, over time the drug dosages and frequency of administration can usually be reduced.
We will start with a basic overview of atopic dermatitis. Atopic dermatitis is a life-long condition which usually requires life-long therapy. Achieving a true clinical cure for allergic dermatitis is possible but rare. Atopic dermatitis typically manifests as pruritus and erythema. However, some animals may develop recurrent pyoderma or otitis externa instead. While it is difficult to estimate, the current assessment is that 10-15% of the canine population suffers from atopic dermatitis. (Many suspect the number is considerably higher.) In technical terms, atopic dermatitis is a genetic predisposition to hyper-react to allergens in the environment. Unlike what many of us were taught in Veterinary School, allergen exposure occurs mainly through the skin. True inhalant (only) allergic dermatitis is rare. Respiratory symptoms that occur along with allergic dermatitis may represent irritation caused by debris rather than a true allergic process. Allergen exposure is enhanced by defects in the epidermal barrier. One of the many functions of the epidermis is to “keep the outside out and the inside in.” Animals that are genetically predisposed to allergic dermatitis have genetically programmed defects in their epidermal barrier. These defects result in increased allergen exposure. It is important to realize, and communicate, that allergic inflammation causes more than just the itching we can observe in the exam room. Allergies increase transepidermal water loss, dernal and epidermal inflammation, and the risk of secondary infection.

The first step of treating an allergy patient is achieving an appropriate diagnosis. This begins with a good physical exam. Many allergy patients demonstrate erythema on the ventral aspects of the front paws and in the ear canals. Typically the pinnae themselves are not primarily affected. Pinnal lesions should raise concern for Sarcoptes scabiei and extension of infection from otitis externa. Dogs with environmental allergies are also known for not having lesions on their dorsal lumbar area. This is a location more commonly associated with flea allergy dermatitis. Superficial pyoderma, malassezia dermatitis, alopecia, and seborrhea are common with all types of allergy so observing these symptoms should trigger you to look at common allergy affected areas. Of course, the other crucial part of examining a dog is questioning the owner. Not every owner is observant or adept at communicating but it is our job to tease out as many important details as possible. Important allergy related questions to ask are: “At what age did your dog start having skin/ear problems?” “When did this episode begin?” “Have you observed any change with the weather or seasons?” “Do you know anything about your dog’s parents or siblings?” “Are there any other pets in the house?” “If so, are the other pets affected?” The last part of a good allergy exam is client education. Education is critical because allergies are chronic and frustrating. It is best to have educational information available in multiple formats. Paper hand-outs, informational emails, in-office videos, and internet resources are all readily available. Controlling where your clients obtain their information will not only save you frustration later but also convey your commitment and knowledge to your clients. You can find many useful handouts at [www.animaldermatology.com](http://www.animaldermatology.com).

Now that you have collected a good history and performed a thorough physical exam the next step is working down the diagnostic pathway of allergic dermatitis. Unfortunately, there is not one single test that can diagnose allergies. Atopic dermatitis is a diagnosis of exclusion. This often needs to be explained to our clients. Proper diagnosis of atopy requires appropriate history, consistent clinical signs, and proof that the pruritus and skin disease are not caused by infections, parasites, metabolic disease, and endocrine disease. There are times when your diagnostic work-up is actually quite simple. Sometimes your client will bring you a pruritic dog that receives regular flea prevention, has a history of seasonal variation, and does not have active skin lesions. If you are very lucky they might even know that a parent or sibling is also affected in a similar way. In this situation you might go straight to talking about treatment options. However, in many instances, the allergy patient isn’t so obvious. Allergy patients often suffer from alopecia, seborrhea, pyoderma, and otitis. In addition, many clients cannot remember when the symptoms began, or worst yet, you might have a husband and wife who vehemently disagree about the history. In these situations you must start at the beginning and rule out infections, parasites, and metabolic/endocrine disease. Cytology from the ears and skin is the first step. Cytology is almost always indicated. Cytology allows you to quickly identify yeast and bacteria and provides a semi-quantitative method of monitoring progress. A dry microscope slide can be pressed on moist lesions, scraped under crusts, or used to break pustules. Another useful method of collecting cytology is with clear packing tape. Packing tape is most helpful for dry lesions, folds, and nail beds. When using tape you do not need to “heat fix” the sample or use the fixative step of your three step staining protocol. Skin scrape sample collection is often indicated. Cytology allows you to quickly identify yeast and bacteria and provides a semi-quantitative method of monitoring progress. We all know the basics of skin scraping. But here are a few tips to improve your success. First, shave the area you intend to scrape. Second, apply mineral oil to the sample site and pinch the area firmly. Third, scrape until you obtain capillary bleeding. You should observe red blood cells on the slide when you look at it under the microscope. Lastly, it helps to have mineral oil waiting on your slide so that all the debris you remove from the skin surface stays where you can view it. The last of our skin related tests is DTM culture. DTM cultures can be particularly frustrating for veterinarians and technicians so perhaps the best tip is to send them to an outside lab (such as Purdue ADDL or IDEXX) if you don’t enjoy checking them yourself. When collecting your samples for DTM culture it is best to collect samples from the edge of lesions. Broken hairs are especially
helpful. It is also useful to use a fresh tooth brush to pick up dander, debris, and hair from the entire surface of the animal. If you choose to perform DTM culture in house please remember: 1) Use plate type media not jars or test tubes. 2) Do not close the culture tightly. 3) Keep the culture in a dark area with approximately 30% humidity and at 86 degrees farenheit. 4) Color change does not confirm diagnosis of a dermatophyte. Many contaminants can cause the medium to change from orange to red so microscopic examination of the fungal growth is essential to confirm dermatophytosis.

The one very obvious diagnostic that we have not discussed yet is allergy testing. At some point in time most pet owners who are dealing with allergy problems will inquire about allergy testing. It is important to have the facts about allergy testing so that you can guide your clients accurately. First and foremost, allergy testing is not a tool to diagnose allergies. In other words, it is not a screening tool. Rather, allergy testing is used to define the allergy more precisely, predict flares, direct environmental modification, and formulate immunotherapy. Allergy testing is not a screening tool because positive results don’t immediately prove that allergy is the cause of the skin symptoms. Rather, you must have a supportive history and clinical signs along with evidence that you have eliminated other causes of skin disease. In regards to allergy testing specifically, there are two accepted and peer-reviewed methods: serum testing and intradermal testing. Serum testing only requires the collection of a blood sample. This type of test is quick and easy for the general practitioner and does not require any special equipment. Serum allergy testing is generally touted as not being affected by drug therapy such as steroids or antihistamines. However, these drugs can contribute to poor results in some dogs. In addition, serum allergy test results will be affected by season of the year. Within the past ten years numerous companies have begun offering serum allergy testing. I caution you not to choose an allergy testing company solely on cost. While all serum allergy companies use a similar testing model there are unique differences that can be quite important. Lastly, a paper published last year highlighted the difficulty with this testing method by sending samples from the same patient to multiple labs. Agreement between the labs was very poor.3 Intradermal allergy testing is typically only performed by veterinary dermatologists because of the need to keep expensive antigens in stock for testing and because of the learning curve necessary to read an intradermal allergy test accurately. Intradermal allergy testing also requires sedating the pet and shaving a patch of hair on the side of the thorax. Perhaps the most confusing factor in recommending intradermal allergy testing is knowing the drug withdrawal times required prior to the test. In general, the withdrawal time for oral steroids and antihistamines is two weeks. For injectable steroids like triamcinolone or dexamethasone the withdrawal time is 2-3 weeks. For Depo-Medrol, the withdrawal time is three months. Topical steroids should be stopped 48 hours prior to the test. Fortunately, there is NO withdrawal time for Atopica or Apoquel. There are many unique benefits to intradermal allergy testing. First, this test is not affected by season. Second, it allows a veterinarian to test the organ affected and observe the true intensity of an allergic reaction. Lastly, and perhaps most importantly, every intradermal allergy test has a built in scale. These are positive and negative reactions designed into every skin test. This helps us adjust for inevitable patient to patient variation.

Before you can develop a good allergy treatment plan you must realize that no single therapy is 100% effective. It is also important to understand that no two patients are exactly the same and that it is easier to prevent rather than suppress flares. Multimodal therapy is recommended because it allows intervention of allergic inflammation at multiple points in the disease process. It is easier to think of allergy therapy as core and supportive treatments. Most patients need a core therapy and one or two supportive therapies. However, severe patients need multiple core therapies and supportive therapies.

For ease of discussion we will consider five core allergy therapies: 1) antihistamines, 2) steroids, 3) Atopica, 4) Apoquel, and 5) Immunotherapy. We will focus on Immunotherapy, Atopica, and Apoquel today. Immunotherapy is still considered the “gold standard” of allergy therapy. Immunotherapy allows us to modulate the allergic response without drugs. This occurs via multiple mechanisms including the development of IgG blocking antibodies, a decrease in allergen specific IgE and an increase in the number of regulatory T cells. Consequently, immunotherapy provides many unique benefits that drug therapy cannot. Immunotherapy may also prevent new allergies from developing and is the only therapy that could potentially result in a clinical cure.1 Because immunotherapy is not a drug there are no major side effects or drug interactions. Anaphylaxis can occur during immunotherapy but this is rare. Immunotherapy is tailored to each individual so animals at higher risk for anaphylaxis can be induced more gradually. Risk for anaphylaxis is based on breed and the intensity of the allergy test reactions. Immunotherapy has classically been administered as subcutaneous injections. However, within the past three years, sublingual immunotherapy drops have become available for pets. Both routes of administration can be effective. Early publications suggested that oral immunotherapy would be more efficacious but my experience has been that the two forms are equally successful. Multiple schedules for administering these products are available based on the laboratory used and the dermatologist involved. When discussing immunotherapy with clients it is important to clearly communicate that immunotherapy is not a fast acting treatment with many dogs not showing significant benefit for 6-12 months. As a general rule, animals should receive immunotherapy for at least a year before deciding whether it is effective and worth continuing. Because of the slow onset, many patients need additional therapy in the beginning. This might include antihistamines, steroids, Atopica or Apoquel. While immunotherapy can provide a clinical cure, it is rare and most dogs require immunotherapy for life. As a general rule immunotherapy is considered approximately 70% successful with 45-50% of those dogs requiring some type of additional supportive therapy long term.
Fortunately, we have two safe and effective drug options for treating allergy symptoms. Atopica (modified cyclosporine) became available commercially for dogs more than ten years ago. Atopica works via suppression of IL-2, T-helper, and T-suppressor cells.4 By far the most common side effects of Atopica are vomiting and diarrhea. Usually these are mild and do not require specific therapy or cessation of therapy. Another side effect that sometimes occurs is gingival hyperplasia. Obviously gingival hyperplasia is not a life threatening side effect. It is typically seen only in patients receiving high doses of cyclosporine or after many years of therapy. In most cases gingival hyperplasia resolves when Atopica is discontinued. Atopica is a very useful drug but there are a few items to keep in mind. First, because Atopica may take 4-6 weeks to see full effect it is not helpful for immediate control of flares. I typically recommend a 30 day recheck so that I can evaluate the patient’s progress. To help prevent vomiting you can freeze the capsules, give the medication with a small meal, divide the dose throughout the day or start with a low dose and ramp up to your target dose over two weeks. Lastly, you will commonly want to combine Atopica with a steroid during the first two to three weeks of treatment. The steroid provides immediate relief while the Atopica ramps up.2

Apoquel is the newer drug on the market. Apoquel was released in January 2014 and then quickly went on backorder. Apoquel become more widely available this April although production and distribution are still less than ideal. Apoquel is a completely different medication than Atopica and it works via an extremely different mechanism. Apoquel (Oclacitinib) works via blocking IL-31 at the JAK-STAT pathway. IL-31 is the cytokine linked to the feeling of itch. By blocking IL-31 there is also suppression of Epithelial Langerhans cells and T-cells. Because of overlap in the Jak-Stat pathways Apoquel also suppresses IL-2, IL-4, IL-6, and IL-13 which are also involved in allergy. Apoquel’s serious side effects are linked to this overlap as well. The most concerning side effect to watch for is decreased hematopoiesis. One of the benefits of Apoquel is the speed on action. Most dogs will improve in 24-48 hours but I have had a few patients not respond until 5-7 days. Vomiting is far less common with Apoquel (as compared to Atopica) but it can occur and it can be severe.5

Another new product has recently achieved conditional release. Canine Atopic Dermatitis Immunotherapeutic is currently available through most dermatologists and some general practitioners. CADI is a once a month injection of a monoclonal antibody designed to target IL-31. Side effects are extremely uncommon. This product can be given to puppies and dogs with other health problems.

With all of the products available for treating atopy in dogs you might think it would be an easy task. However, every patient has different allergies, different primary signs, and different secondary problems. Consequently, you need to have a consistent treatment strategy.

Step one of this strategy is to eliminate current infections. Eliminating infections reduces pruritus and inflammation while also improving the patient’s odor and appearance. The relief that a patient derives from resolving infections may be dramatic.1 This is also the time to impress upon the client the importance of secondary infections. In many cases our clients may ignore or be oblivious to the signs of infection. When present, infections can negate the improvement obtained by the actual allergy treatment. Another major problem of recurrent secondary infections is antibiotic resistance. For this reason it is imperative to prescribe an appropriate antibiotic for an appropriate length of time. It is also important to consider topical antimicrobial therapy. Topical therapy can provide immediate relief for the pet. More importantly topical therapy also works synergistically with the oral antibiotic / antifungal medication to reduce the risk of resistance. Of course, dealing with infections includes dealing with ear infections. Otoscopy is always a useful part of the allergy exam. Remember that otic cytology is important any time you suspect an ear infection. Cytology helps you determine which ears are inflamed due to allergy and which ears have infection. Cytology also helps you track the progress of your therapy. When managing otitis externa remember to choose both your ear wash and ear medication carefully.

Improving the epidermal barrier is step two. The epidermal barrier is composed of lipids and corneocytes in the stratum corneum. The dominant lipids in the stratum corneum are called ceramides. Free fatty acids and cholesterol are also found in the lipid portion of the stratum corneum. However, ceramides play a crucial role by helping align the other lipids. When intact, the lipid portion prevents water loss as well as allergen and antimicrobial penetration. Consequently there is less allergen exposure, less risk of infection and less pruritus. Ceramides are now available in multiple forms. You will find ceramides in shampoo, sprays, conditioners, and spot-on products.

Conscientiously choosing a core treatment is step three. In order to make a good recommendation to your client you must consider the patient’s underlying medical conditions, the severity of the allergy, the primary symptoms, and the limitations of the dog and owner. You also want to steer your clients to the safest therapy for long term use. This entails considering Immunotherapy, Atopica, Apoquel, and CADI.

Step four is adding supportive therapy as needed. What you add is based on what the patient requires. Supportive therapies include: antibacterial and antipruritic shampoos, wipes, and sprays as well as oral antihistamines, oral essential fatty acids, and topical ceramides.
Clinical Update on Dermatophytosis:
Better Ways to Fight the Fungus Among Us
Darin Dell, DVM, DACVD
Animal Dermatology Clinic
Indianapolis, IN

Review of clinical signs
Perhaps the most critical task in discussing the clinical signs of dermatophytosis in cats is to highlight the fact that feline dermatophytosis looks very different from human dermatophytosis. In fact, dermatophytosis in animals can cause a wide variety of clinical signs. Often, dermatophytosis in cats appears as one or more irregular patches of alopecia. Affected and surrounding hairs may appear broken or frayed. Alopecia may be localized or diffuse. Erythema, scale, crust, and papules may or may not be present. Pruritus is uncommon but may occur. Dermatophytosis may look very similar to stud tail, chin acne, milliary dermatitis, pemphigus foliaceus, or cutaneous lymphoma. Onychomycosis (infection of the nails) and kerions (deep nodules) can occur secondary to dermatophytosis but are uncommon. Due to the widely variable presentation of dermatophytosis in the feline patient, a DTM culture is indicated in most cases of feline skin disease.

Science of the details
Numerous species of dermatophytes are known to exist. In our companion animal species the majority of disease is caused by: Microsporum canis, Microsporum gypseum, and Trichophyton mentagrophytes. Of these three, Microsporum canis is the most common. Transmission occurs by contact with infected hair or scales. Fungal elements in the environment, on fomites or animals can cause infections as well. The source of M. canis is usually an infected cat. In comparison, M. gypseum is usually contracted from contaminated soil and T. mentagrophytes from rodents or rodent dens.

The infective portion of the dermatophyte organism is the arthrospore. Arthrospores can be carried on dust, air currents, fomites, and ectoparasites like fleas. Physical damage to the stratum corneum is important to facilitate invasion of arthrospores. Taking this into consideration one can easily understand the heightened concern for secondary dermatophytosis infection in patients suffering from allergies or flea infestation.

It is helpful to have an understanding of the cycle of an “average” dermatophyte infection when treating patients and advising clients. For this example we will consider M. canis. Lesions typically develop seven to ten days after inoculation. For the next six to eight weeks the lesions typically enlarge. Finally, lesions may self-resolve by twelve to fourteen weeks after initial exposure. Upon exposure to viable arthrospores hair shafts are in both endothrix and ectothrix infection. Fungal hyphae are formed and migrate downward to the hair bulb. This process continues until the fungus reaches the keratogenous zone (Adamson fringe). Because the fungus needs keratin it cannot proceed down past the area of the hair shaft where keratin is formed. In an actively growing hair (anagen phase) the fungus and hair might remain in equilibrium. In a resting hair (telogen phase) new keratin is not being formed and the fungus must stop growing. Eventually the fungus is expelled when the hair is shed. This situation is also important when considering Wood’s lamp examination (discussed below). Dermatophytes which are not actively growing will not fluoresce. Thus, only infected anagen hairs will glow.

Diagnosis
As with any dermatologic problem, an accurate history and thorough physical exam are important first steps. However, because dermatophytosis can mimic many other diseases we need to review the diagnostic options.

First, the trichogram can be a quick and helpful diagnostic test. Hairs from the lesion and the surrounding area should be collected. The hairs are placed on a slide along with mineral oil. A cover slip is added and the slide is gently heated for 15-20 seconds. Most dermatophyte infected hair with display ectothrix lesions. When looking through the microscope it is recommended to concentrate on fragmented pieces of hair that are larger in diameter than other hairs present. In addition, it is usually most rewarding to look near the hair bulbs. Infected hairs often appear fuzzy or swollen. One must remember that dermatophytes do NOT form macroconidia on tissue. Thus, any macroconidia retrieved from the hair coat represent contamination. A positive trichogram might guide your initial therapy but does not negate the need for further testing.

Second, the Wood’s lamp is simple, easy, and quick. However, the sensitivity and specificity of this test are both quite low. The wood’s lamp is basically a black light but to describe it scientifically it is a UV light with a wavelength of 253.7 nm that is filtered through a cobalt or nickel filter. Hairs invaded by actively growing M. canis will fluoresce bright yellow-green. It has been widely accepted for years that the Wood’s lamp needs to warm up prior to use. However, that is actually not necessary. What is necessary is exposing the hair to the light for three to five minutes. Infected hairs glow because of tryptophan metabolites produced by the fungus. Thus, only anagen hairs will glow because those are the only ones which contain actively growing fungus. One must realize that many other things will fluoresce such as soap residue, dander, carpet fibers and even certain bacteria.
Third, fungal culture is well known and commonly used. Most fungal cultures contain Sabourand dextrose agar or dermatophyte test media or both. Dermatophyte test media is basically Sabourand dextrose agar with cyclohexamide, gentamicin, and chlorotetacycline added to inhibit contamination by bacteria and other fungi. The pH indicator phenol red is also added. However, I often feel the red color change is more of a hindrance than a benefit. Dermatophytes use the protein in the growth media first and produce alkaline metabolites. These alkaline metabolites cause the media to change from yellow to red. Once the proteins are exhausted the dermatophytes use carbohydrates which yield acidic metabolites and turn the agar back to yellow. Many other fungi (contaminants) use carbohydrates first and proteins later. Such fungi result in a color change that occurs 10-14 days after the culture is started. This is one reason why fungal cultures need to be visually examined daily. The color of the agar as well as the color and morphology of the colonies should be noted on a daily log sheet. Color is important to note because dermatophyte colonies are not pigmented. They can be white, off white or buff color. When a suitable colony forms and causes color change at the appropriate time it must be identified. Usually macroconidia are not produced prior to 7-10 days of growth. Sampling the colony for macroconidia involves gently applying the sticky side of strip of clear packing tape onto the surface. The tape is then placed on top of a slide which already contains several drops of lactophenol cotton blue. A cover slip is then applied and the sample can be easily examined for macroconidia. If you find macroconidia but cannot identify them or if you fail to find macroconidia but have a suggestive white colony you must simply wait and repeat the microscopic examine in a few days. Microsporum canis typically produces white fluffy colonies. Over time the center may become depressed. The macroconidia of M. canis are spindle shaped with thick walls and six or more cells/segments. The terminal end has spines which give a knob like structure. Microsporum gypseum colonies are flat and buff to cinnamon in color. Macroconidia are spindle shaped with thin walls and less than six cells/segments. Trichophyton mentagrophytes colonies are white to cream colored with a powdery surface. The macroconidia cigar shaped with thin, smooth walls. Macroconidia may occur in clusters like grapes.

Fourth, PCR testing has recently become commercially available through Idexx labs (spring 2015). The Idexx PCR includes Microsporum spp, Microsporum canis, and Trichophyton spp. According to Idexx the PCR test has a 95% sensitivity and 99% specificity. Results are available in 1-3 days. You can also request the lab perform a DTM culture to further identify the dermatophyte if the PCR is positive. Submitting a sample for PCR testing is similar to the process for collecting samples for in-house culture. A clean, sterile toothbrush can be combed over the entire pet and placed in a clean, new Ziploc plastic bag. Hairs can be plucked and placed into an empty red-top tube. Nail clippings can be submitted in a red-top tube. Specimens should be refrigerated once collected. The clinical usefulness of this test is yet to be discovered but it could be immensely helpful.

Fifth, dermatophytes are sometimes accidently and sometimes intentionally found on tissue biopsy. Biopsy is very helpful in the diagnosis of dermatophytes which infect the stratum corneum instead of the hair shafts. Kerions are another example of a dermatophyte infection which warrants biopsy. The success of diagnosing dermatophytosis with biopsy is difficult to pinpoint because it varies greatly upon the quality of the sample submitted. However, dermatophytes can be highlighted in tissue specimens using PAS stains. In addition, the presence of fungal organisms in the hair follicle or shaft is typically easily identified.

**Treatment**

Treatment is typically divided into topical and systemic modalities. No discussion on topical dermatophyte therapy would be complete without discussing shaving. Many veterinarians advocate shaving cats who have cultured positive for dermatophytosis. The purpose is obvious. Because the fungus lives within the hair shafts, removal of the hair shafts results in removal of a large amount of infective material. Shaving also allows more effective topical therapy with lotions, sprays, or shampoos. The three main problems with shaving cats with dermatophytosis are: 1) The act of shaving can produce micro-trauma to the skin and thus facilitate new lesions. 2) Who is going to shave the cat and where is it going to happen? Shaving introduces infective spores into the air and contaminates the environment. 3) What cat enjoys being shaved? And are you willing/able to sedate the cat for shaving? As a general rule I don’t recommend shaving cats infected with dermatophytes. Next we must discuss topical antifungal ointments. Multiple products are available over-the-counter and are a favorite of clients who like to self-diagnose and self-treat. When using ointments it is important to apply the product to the lesion and a wide margin around the lesion that appears normal (6 cm). Ointments should be applied every 12 hours. In general, I find ointments only marginally helpful in cats. However, I will recommend an ointment as adjunct therapy if the owner “needs” something to do. I also recommend ointments if there are immune compromised people in the house. Antifungal shampoos and sprays are also available. I find these more helpful than ointments as adjunct therapy because the entire animal can be treated. Even if we are not hastening resolution of the infection we are reducing contagion in the environment. Some clinicians caution against antifungal shampoos and sprays because of the risk of breaking fragile hairs and spreading spores around the animal’s body. The last category of topical therapy is antifungal dips. This category includes Lime sulfur and Enilconazole. Enilconazole dips are not available in the United States. Lime sulfur dips are administered once or twice weekly and are extremely effective. However, Lime sulfur is foul smelling and stains most items. Proper personal protective gear is essential to avoiding human side effects. This is a treatment best performed in the veterinary hospital. One final note on Lime sulfur. The dip
is not rinsed off and instead must be allowed to dry on the animal. Many cats require an e-collar during this drying period to prevent ingestion of Lime sulfur.

Systemic therapy is typically the core treatment for dermatophytosis. Five antifungal drugs are commonly available but two yield the best results. Drug choices include: 1) Itraconazole, 2) Terbinafine, 3) Fluconazole, 4) Griseofulvin, 5) Ketoconazole. Many years ago Lufenuron was claimed to have antifungal activity; however, critical studies of the drug’s effects indicate it does not. Itraconazole is highly effective and has a low incidence of side effects. The dose is 5-10mg/kg once daily with food. Terbinafine is also highly effective and demonstrates low risk of side effects. The dose is 20-30 mg/kg once daily. Terbinafine is available in 250mg tablets at most pharmacies. Most cats will receive ¼ or ½ tablet once daily making this medication very cost effective. Fluconazole is in the same family as Itraconazole and Ketoconazole. However, it is the least effective of the three against dermatophytosis. It does penetrate the blood brain barrier and is excreted in high concentrations in urine. Thus there are certain specific situations where Fluconazole might be indicated. Generally, however, it is not used for dermatophytosis. Griseofulvin is an older antifungal drug. It is effective but has the highest risk for side effects including GI upset and myelosuppression. Persians, Siamese, and Abyssinians may be more prone to Griseofulvin side effects. Griseofulvin should not be used in breeding animals. Ketoconazole is effective against dermatophytes but generally less so than Itraconazole. Ketoconazole as has a higher incidence of causing vomiting, diarrhea, and hepatotoxicity in cats. Of course, using an appropriate drug is only half of the story when treating dermatophytosis. Treatment protocol and duration are also important. I recommend daily therapy with Itraconazole or Terbinafine until 2 weeks after the second negative DTM culture. DTM cultures are repeated every 2-4 weeks depending on the situation. At the time of diagnosis I explain to clients that their cat will likely receive antifungal medication for at least 3 months. It is also important to explain to clients at the beginning that their cat will appear healed long before it is actually free of the fungus. Stopping therapy too soon is the most common cause of “recurring” dermatophyte infection. In truth many of these represent a case that did not achieve complete resolution the first time.

**Decontamination**

Physical removal of hair and dander are essential for environmental decontamination. Hair shafts containing infectious arthrospores which are left in the environment can remain a source of infection for months or even years. (18 months for M. canis.) Environmental decontamination comprises three steps: 1) Mechanical removal of infective material. 2) General cleaning with detergent or soap until area appears clean. 3) Application of a disinfectant to kill any remaining spores. Steps one and two are fairly simple. However, care should be taken to disinfect vacuum cleaners as well as other cleaning tools which could spread the spores. Dilute bleach solution has classically been recommended for disinfection. Using dilute bleach is complicated by the fact that commercially available bleach is available in different concentrations and clients are expected to produce an appropriate dilution themselves. Dilute bleach is also considered unstable and needs to be made fresh daily. Bleach can irritate the skin and cause respiratory difficulties if not appropriately handled. Lastly, bleach is known to discolor fabrics and is thus only a good option for hard surfaces. In 2013, Karen Moriello published an article in Vet Derm evaluating the efficacy of commercial disinfectants against Microsporum canis and Trichophyton spores on textile surfaces. Eight products were evaluated. Surfaces received either 1 spray (1ml) or 5 sprays (5ml) and were left to dry for 10 minutes. Results were similar for both organisms and are summarized in the table below.

<table>
<thead>
<tr>
<th>Product</th>
<th>Growth after 1 spray</th>
<th>Growth after 5 sprays</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>Too numerous to count</td>
<td>Too numerous to count</td>
</tr>
<tr>
<td>Dilute bleach</td>
<td>No growth</td>
<td>No growth</td>
</tr>
<tr>
<td>Formula 409</td>
<td>No growth</td>
<td>No growth</td>
</tr>
<tr>
<td>Chlorox Clean-up</td>
<td>No growth</td>
<td>No growth</td>
</tr>
<tr>
<td>Lysol</td>
<td>No growth</td>
<td>No growth</td>
</tr>
<tr>
<td>Accel TB</td>
<td>No growth</td>
<td>No growth</td>
</tr>
<tr>
<td>Chlorox Anywhere</td>
<td>Too numerous to count</td>
<td>No growth</td>
</tr>
<tr>
<td>Simple Green</td>
<td>Too numerous to count</td>
<td>No growth</td>
</tr>
<tr>
<td>Fantastik</td>
<td>Some inhibition against M. canis but not Trichophyton</td>
<td>No growth</td>
</tr>
<tr>
<td>Trifectant</td>
<td>Some inhibition against M. canis but not Trichophyton</td>
<td>No growth</td>
</tr>
</tbody>
</table>

*Adapted from: Moriello, Efficacy of eight commercial disinfectants against Microsporum canis and Trichophyton spp. infective spores on an experimentally contaminated textile surface. Vet Dermatol 2013; 24:621-e152.

Quarantining infected animals is recommended to reduce the amount of cleaning required. It is ideal to wear dedicated clothing when in the quarantine area to prevent accidental spread around the house.
Patients with otitis externa generally present for head shaking, ear scratching, and odor from their ears. Pet owners may also notice purulent material coming from the ear canal(s), changes in their dog’s behavior, or whining and discomfort. Otoscopic exam typically reveals varying degrees of erythema, edema and debris. These changes can make visualizing the tympanic membrane very difficult or even impossible. Unless the patient is aggressive/dangerous you should try your best to see every tympanic membrane that enters your exam room.

Key points
1. Otitis externa is most often a clinical sign of underlying skin disease, not a diagnosis in and of itself.
2. Identifying and resolving / controlling the underlying cause is essential to long term success in otitis externa.
3. Allergy is the most common ear disease in the canine
4. Topical therapy is the most effective therapy for treating otitis externa
5. Cytology (clean) – Plan (persuade, purge) – Recheck (re-engage)

Identifying the underlying cause of otitis externa can be difficult. The PSPP system can help you work through the potential causes and also make it easier to discuss otitis with your clients. PSPP stands for Primary, Secondary, Predisposing, Perpetuating. The Primary category includes things that can cause disease in a normal ear. The list includes: allergy, auto-immune disease, foreign objects, mass/polyps, endocrine dysfunction, immune mediated disease, and parasites. The most common primary problem I see is allergy, but in general practice you probably see a fair amount of ear mites and foreign bodies too. Whatever the primary factor, it has to be resolved or controlled before you are going to achieve lasting success. The Secondary category includes things that create disease in an abnormal ear. The secondary list includes: bacteria, yeast (malassezia), fungi, medication reactions, and over-cleaning. Because of the way we commonly communicate about otitis externa it is easy for our clients to misunderstand and think that bacteria or yeast are primary causes of otitis. Sometimes it helps to point out that ear canals are not sterile. There is a normal flora in the ear canal just like on the skin. Infections must be resolved but they are not the root cause. Predisposing factors are fairly simple to understand and are typically what most clients blame for ear disease. Predisposing factors are present prior to otitis but cannot by themselves cause otitis. This list includes: conformation, excess moisture, obstruction, systemic disease, and treatment effects. Sometimes it helps to reassure our clients that there are Cocker Spaniels without ear disease despite their floppy ears and Poodles without ear disease despite their excess ear hair. The last category, Perpetuating, is the one most often neglected in veterinary practice. Perpetuating factors occur as a result of the otitis and increase the likelihood of another infection. These factors are: excess cerumen production, altered epithelial migration, edema of the ear canal, rupture of the tympanic membrane, and otitis media. I believe that the first three issues in the perpetuating category are most overlooked and least understood in private practice. Excess cerumen production occurs any time there is inflammation in the ear canal. The body’s response is to make more cerumen in an attempt to push out whatever is happening. Unfortunately, this excess cerumen can be a great growth medium for yeast and bacteria. Cerumen production can continue to be excessive for several weeks after the infectious component of the otitis initially resolves. For this reason, it is beneficial to continue ear cleaning even after ear infection has resolved. Altered epithelial migration also develops during otitis externa. Normal otic epithelial migration starts at the tympanic membrane and marches distally out the aural orifice. This too is designed to help move debris out of the ear canals. However, inflammation within the canal disrupts this process resulting in build-up of debris in the canal. Altered epithelial migration is another reason why stenotic ears and cobblestone ears demonstrate wax build-up. Again, it is necessary to continue ear cleaning until this process is re-established. Edema in the ear canal is at least a problem you can see through the otoscope. But, the importance of edema is often underestimated. Edema will also trap cerumen which can potentially lead to a better environment for bacteria or yeast growth. Edema can also cause discomfort and pain which could result in ear pruritus and trauma.

Treatment for otitis externa starts with the PSPP system. In most cases, you can run through the PSPP list in your mind just like you would a check list for any other disease. In most cases you can quickly rule out ear mites, foreign objects, and polyps. You might need to perform blood tests to look for endocrine disease if other suggestive signs are present. Similarly, you might need to perform skin biopsy to look for auto-immune or immune mediated disease if other supportive lesions are present. In the majority of cases you are not going to find any of the problems listed above in this paragraph. The majority of otitis externa in the canine is secondary to allergic dermatitis. In that case, the first question to ask yourself is whether the allergy is controlled or not. If the allergy is generally well controlled and the otitis externa is due to a flare or a dietary indiscretion then resolving the problem will be easier. Well controlled allergy patients may still have one or two episodes of otitis externa each year. If the allergy is unknown or un-treated then
you will have more work to do. Not the least of which will be convincing the owner that their dog has allergies. Still, you may choose to focus initially on the otitis and address the allergy in two to four weeks.

The first step toward treatment is otoscopic exam. You need to assess pain, pruritus, edema, erythema, constriction, and exudate as well as the tympanic membrane. Next you will need to perform ear swab cytology. It is best to collect exudate from both the horizontal and vertical portions of the ear canal. Obviously you are checking for *Malassezia*, coccoid bacteria and rod shaped bacteria. But you are also looking for nuclear streaming, white blood cells, red blood cells, and evidence of biofilm. Bacterial culture from the ear canal may also be necessary depending on the situation. Ear cultures are not universally helpful for two reasons. First, you might culture normal flora. Second, MIC’s are usually based on serum levels of antibiotics. In the ear we are concerned about topical / direct exposure to the antibiotic. The essence is of the problem is that some antibiotics to which the bacteria are listed as “Resistant” will actually be “Sensitive.”

Now that you have performed an exam and evaluated cytology you have to choose a therapeutic plan. I want to stress that there isn’t one universal plan for otitis externa. We can’t group treatment into levels such as easy, moderate, and severe either. However, asking yourself the following six questions can help you make better treatment decisions.

1. Is there an allergy and are you treating it now?
2. How much debris is in the ear canal?
3. How is the conformation of the ear canal
4. What type of infection is present?
5. How much edema and erythema are present?
6. How much pain and anxiety are present?

Now, in more detail

1. **Is there an allergy and are you treating it now?** You may not treat allergy at the first visit for otitis externa. But, you should at least start the conversation about allergy.

2. **How much debris is in the ear canal?** This will help you decide what type of cleaner to use and how often. For thick sticky wax you will probably want a micellar solution or one with squalene. For mucoid exudate you will probably want a Triz EDTA product with Chlorhexidine.

3. **How is the conformation of the ear canal?** Is it constricted? Cobblestoned? This too will help you decide what type of ear wash to use and whether to use a topical medication that is a gel, ointment, or liquid. The more the canal is constricted the more you need a wash that is better at dissolving cerumen. Ointments are less likely to travel deep into a constricted or cobblestoned ear canal so you probably want a liquid medication.

4. **What type of infection is present?** This will help you pick a topical treatment. The side note is that YOU have to know what drugs are in the products on your shelf. Infection with rod shaped bacteria will also encourage you to use an ear wash with Triz EDTA. Most rod shaped bacteria are gram negative. Triz EDTA damages the gram negative membrane and forms channels which allow antimicrobials into the bacteria.

5. **How much edema and erythema are present?** This will tell you what strength of steroid to use. Topical steroid therapy may be sufficient or you might need oral steroid therapy as well. If the ear canals are completely constricted then you will definitely need help from an oral steroid. Again, you have to know what ingredients are in the products on your shelf! Common steroid ingredients in otic medications, in order of potency are as follows:
   a. Prednisolone
   b. Betamethasone
   c. Mometasone

6. **How much pain and anxiety are present?** This will tell you if you need to prescribe additional pain relief or anti-anxiety medications. These medications are short term but can really help both the dog and the owner. This might require a prescription of Tramadol, Rimadyl or Xanax. Don’t underestimate the pain or anxiety related to ear infection! How many clients have told you that their dog runs away when they see the ear wash bottle or tube or ear ointment?
Cutaneous adverse food reaction
The incidence of cutaneous adverse food reaction (food allergy) in cats is difficult to pinpoint.

One study of 61 pruritic cats found that 16% had cutaneous adverse food reaction. Interestingly, 42% of the cats with cutaneous adverse food reaction also had a history of vomiting or diarrhea. It is estimated that only approximately 50% of cats with adverse food reaction respond to glucocorticoids.

Unfortunately, the cause and pathogenesis of cutaneous adverse food reaction are unknown. It is known that Toxocara cati infection can enhance IgE response to orally administered antigens.

Researchers suspect that multiple factors are important.

No age or sex predilection has been reliably reported in cats. However, multiple reports suggest that Siamese cats are predisposed. The most common clinical sign is pruritus. The pruritus is nonseasonal and typically severe. Pruritus is typically focused on the face, ears and neck but can be generalized. Eosinophilic granuloma complex, miliary dermatitis, otitis externa, angioedema, urticaria, and conjunctivitis can all be seen as a result of cutaneous adverse food reaction as well.

Diagnosis of cutaneous adverse food reaction requires eliminating other potential diseases by collecting a minimum database. In feline dermatology the minimum database includes: cytology. Skin scraping, dermatophyte culture. and Wood's lamp investigation. If gastrointestinal signs are present as well then baseline biochemistry tests and fecal analysis are also recommended. Once the appropriate tests have been performed then a dietary trial can be initiated. At this time, dietary trials are the only accurate means of diagnosing cutaneous adverse food reaction. The goal of a dietary trial is to observe whether avoiding ingredients that a cat previously ingested will result in clinical improvement. As such, it is important to have at least some basic knowledge of the patient's previous diets. Prescription novel protein or hydrolyzed protein diets are recommended because of their increased consistency and reduced risk of cross contamination during processing. Home cooked diets remain a good choice for capable clients. The trial food is continued for at least 12 to 16 weeks before assessing its potential benefit. Consistent application of a quality flea control product is recommended during the entire trial to avoid fleas as a potential flare factor. Obviously, cat treats and human food are not allowed during the diet trial. It is also important to avoid flavored medications, pill pockets, and hunting. I recommend using metal or ceramic bowls because they are more easily cleaned and plastic bowls can cause reactions in and of themselves.

Flea bite hypersensitivity (flea allergy dermatitis)
Depending on your location in the country, flea bite hypersensitivity may be extremely common or completely non-existent. Experimental models have shown that intermittent exposure to fleas results in more severe hypersensitivity reactions. This is consistent with clinical experience. While animals with high flea loads can develop hypersensitivity, it is usually the patient who has relatively rare or low intensity exposure that becomes allergic. It is also useful to note that non-allergic animals who are chronically exposed to fleas usually develop partial or complete tolerance to flea saliva antigens. On the other hand, fleas are a known flare factor for animals with any type of allergy.

Flea bite hypersensitivity can develop at any age. Pruritus is typically focused on the dorsal lumbar region, flanks, tail base, perineum and tail. Clinical signs include barbered hair, papules, and erythema. While flea burden, and thus flea bite hypersensitivity, often spikes in the spring and fall, this syndrome can be a non-seasonal problem. The pruritus caused by the flea can persist for many weeks after the flea has died.

Diagnosis of flea bite hypersensitivity is usually based on appropriate clinical signs and suggestive history. Fleas, flea dirt, and/or tapeworms are sometimes found but are not required for diagnosis. Allergy testing, either serum or intradermal, can be performed; however, a positive allergy test result does not prove flea bite hypersensitivity. The results must be correlated with the history and clinical signs.

Treatment for flea bite hypersensitivity focuses on aggressive flea control. This requires both environmental measures and cat-related treatments. For treatment of the patient I recommend combining a topical and an oral flea preventative. This allows you to use two different modes of administration and two (or more) active ingredients. When using two products it is ideal to space out the products so that they are administered two weeks apart. This way each product is still administered at a monthly interval. The other benefit of this type of protocol is that the patient is always within the first two weeks of any flea treatment. In general, flea prevention products are most effective during the first two weeks. Environmental products are plentiful and easy to find either via an exterminator or at a local home improvement store. If possible, keeping all cats in the household indoors is also helpful. Multiple investigators have attempted to desensitize cats to flea saliva via immunotherapy over the past several decades; however, all attempts have failed.
Feline atopy

It is probably not a surprise to learn that atopic dermatitis (or feline allergic dermatitis) is a poorly understood disease. Most of what we know about feline atopy is extrapolated from canines and humans. As we were all told in veterinary school, cats are not small dogs! As such, expect our understanding of feline atopy to evolve over the coming decades.

The majority of cats with atopy develop clinical signs between 6 and 24 months of age. As with atopy in other veterinary species, pruritus is the most common clinical sign. Pruritus is often focused on the face and neck; however, the ventral abdomen, groin, lateral thorax, and rear legs are commonly affected as well. Pruritus often results in closely "barbered" hair or complete alopecia. Macules, papules, and crusts can develop as well. Lesions can appear identical to those of adverse food reaction and flea bite hypersensitivity. In addition, two or more allergic conditions can occur in the same patient. In general, cats are less likely to develop secondary pyoderma than atopic dogs. However, cytology is still important because *Malassezia* spp. overgrowth can occur.

Non-dermatological symptoms may develop as well. Such symptoms can include sneezing, coughing, asthma, and conjunctivitis. When other body systems are affected it is important to expand your minimum database to rule out other diseases which might coexist with atopy.

Allergy testing, either serum based or intradermal is a useful test for feline patients with appropriate clinical signs. Admittedly, allergy testing is performed less often in cats because many cat owners are not willing or able to give antigen injections at home. Other treatment options include antihistamines, steroids, and cyclosporine. Antihistamines are generally not effective enough to control clinical signs of atopy in cats. However, they are safe and inexpensive. Some owners prefer to start with antihistamine therapy before proceeding with other more aggressive options. My two favorite antihistamines in cats are Chlorpheniramine (1-2 mg twice daily) and Amitriptyline (5-10mg once or twice daily). Antihistamines should be given consistently for at least 14 days before assessing the patient for response. Steroids are undeniably the fall back for allergy treatment. In some cases they are even the best choice. But, we need to be smart about steroid therapy. In general I recommend oral steroid therapy over injectable steroid therapy. Oral therapy allows you to adjust the dose more effectively over time. Oral therapy can also be stopped quickly if side effects are observed or another unrelated problem develops. Remember that Prednisolone is more effective than Prednisone at least in terms of treating dermatologic problems. However, my favorite oral steroid for cats is Triamcinolone. You can roughly translate your typical prednisolone dose to a triamcinolone dose by remembering that 5mg of Prednisolone is similar to 0.5mg of Triamcinolone. Often, Triamcinolone can be tapered to every 2-3 days whereas this is uncommon when using Prednisolone. This brings us to an important point about steroid therapy. The dose, duration, and frequency of steroid administration are all important in the development of side effects. Oral therapy allows for every other or every third day dosing which reduces risk to the patient. No discussion on steroid therapy would be complete without mention of Depo-Medrol. For some cats and some owners Depo-medrol may be your only reasonable choice. However, please keep in mind that Depo-medrol remains in the body for three months regardless of how effectively it controls the allergy symptoms. This means that when symptoms return a month after the Depo-medrol injection it is not because the steroid "wore off but rather because the patient is becoming less responsive to methylprednisolone. In cats the primary concerns with steroid therapy is the development of overt diabetes, congestive heart failure, or hyperadrenocorticism. Cats can demonstrate other symptoms such as poor hair coat, alopecia, seborrhea, and thinning of the skin. The last oral therapy for atopic dermatitis in cats is Atopica® (modified cyclosporine). Both Atopica liquid and capsules can be given to cats. However, it should be noted that the feline dose for Atopica is 7mg/kg/day verses 5mg/kg/day for dogs. Cats are generally less likely to experience vomiting or diarrhea when starting Atopica®. In addition, cats can receive Atopica with or without a meal. Studies examining the long term effects of Atopica® on CBC and Chemistry analyses indicate that abnormalities are uncommon. However, it is recommended to collect a blood sample prior to starting Atopica® so that you have a baseline. Included in these tests should be CBC, Chemistry, FeLV, FIV, and a fecal float. I also typically perform testing for Toxoplasmosis although studies have shown that the label dose of Atopica® is unlikely to activate a dormant Toxoplasmosis infection. Repeat monitoring of these tests is recommended every six months depending on the patient's condition and Atopica® dose. In my experience most cats require daily Atopica® therapy to remain complete control of allergy symptoms. However, some owners may willingly trade less perfect allergy control if the result is that they can medicate their cat less frequently. Regardless of the treatment chosen, life-long therapy is almost always necessary.

Eosinophilic granuloma complex

Eosinophilic granuloma complex includes indolent ulcers, eosinophilic plaques and eosinophilic (linear) granulomas. These terms are used to describe a clinical sign, not a final diagnosis. An allergic condition usually underpins the development of these lesions. Possible causes include inhalant allergies, environmental allergies, food allergies, and insect hypersensitivities. Bacterial and viral infections can be a factor but are rarely the primary cause. It is suspected that some cats are genetically predisposed to this syndrome without having classical signs of allergic dermatitis.

What must be remembered is that these lesions usually coincide with an underlying allergy. In certain circumstances, observing one of these lesions can narrow your differential list. For example, if you are examining a cat that has been over-grooming its...
abdomen and you notice that it also has a swollen lip or chin you should think allergic disease instead of a pain related condition or behavioral overgrooming. When speaking to clients it is important to mention the potential of an underlying allergy. If allergy is present then it will need long term control in order to keep the lesions from returning. So, when you observe one of these lesions you should have “the allergy talk” and consider: 1) What is the animal's flea prevention status? 2) Is a dietary trial feasible? 3) Is allergy testing feasible/useful? 4) Is Atopica® a good solution for this cat? 5) Is chronic steroid therapy the best solution in this situation?

A few additional practice tips
1. Always check a cat's lip margins and chin for lesions. “Fat chin” cats are displaying a form of eosinophilic granuloma which is likely secondary to some type of allergy.
2. Plaques, linear granulomas, and rodent ulcers almost always return because the underlying allergy does not self-cure.
3. Some lesions need to be biopsied to rule out neoplasia and infectious disease. Consider biopsy when lesions don't respond well to steroids, lesions cover a large surface area, the patient is older, or the patient is allowed outdoors.
4. While not part of the eosinophilic syndrome, milliary dermatitis can be thought of in much the same way. It is a unique reaction pattern in the feline that occurs most often secondary to some form of allergy. Milliary dermatitis develops without self-trauma (licking or scratching) caused by the patient.

Otitis externa
Thankfully, otitis externa is uncommon in cats. When present, otitis externa in cats is usually secondary to allergies, ear mites, or polyps/tumors. Obviously, cytology and otoscopic examination are critical to helping you identify infection, ear mites, and masses in the ear canal. We are going to focus on allergy related otitis externa because it is often overlooked. Allergy related otitis externa can result in bacterial otitis, malassezia otitis, excess cerumen production or simply otic pruritus. Allergic otitis can occur with or without other allergy symptoms. Or the symptoms may be mild enough that the owner doesn't mention them to you. As usual, a thorough examination and thoughtful questioning are important. In many ways, treating feline otitis is the same as treating canine otitis. However, here are some useful tips to remember:
1. Cats typically don't arrow deep ear cleaning unless sedated
2. Few medications are labelled in the United States for treating otitis in cats.
3. I typically use Posatex® because of once daily application. Posatex® is also less likely to cause deafness than gentamicin products.
4. If an underlying allergy is present it needs to be treated or you will "fight" the otitis forever.
How to Win Friends and Influence People with Topical Therapy
Darin Dell, DVM, DACVD
Animal Dermatology Clinic
Indianapolis, IN

Shampoo therapy is an important treatment modality for veterinary patients with dermatologic issues. Unfortunately, shampoo therapy is often neglected by the busy practitioner and pet owner. There are many reasons why veterinarians should have at least a basic understanding of shampoo therapy. First, many of our clients are curious about shampoo therapy. This provides the veterinarian with an opportunity to educate the client and provide better patient care. With the rise of the internet and the mega-box store environment, our clients are exposed to an ever expanding pool of information. Just like in other facet of veterinary medicine, the information that our clients receive about shampoo via marketing or the internet is often misleading or downright wrong. Taking this opportunity to educate the client reinforces the veterinarian's position in the client's life and as part of their pet's health care team.

Being able to quickly and confidently answer the most common shampoo questions will help both you and your staff. The most common question I am asked is, "How often should I bathe my dog?" The best answer to this question is that the frequency of bathing depends both on the dog's health status (taking into account the hair condition, skin condition, and internal health) as well as the shampoo being used. When using medicated shampoos to treat a specific skin problem you should plan to bathe at least weekly to observe a benefit. Twice weekly or every other day bathing is even more helpful. The second most common question I am asked is, "Can I just use my shampoo?" The answer to this question is more straightforward, "No." Dog skin has a normal pH of 7 and human skin has a normal pH of 5. Human shampoo may seem to effectively clean the dog's hair but it is not ideal for the skin underneath.

Now that you have educated the client and convinced them that bathing their pet is a good idea you need to make sure they know how to bathe their dog properly. This is often assumed by our profession but it should not be. The first tip in discussing proper bathing is the water. The water should be cool to tepid because hot water will increase pruritus. In addition, a study confirmed that soft water allows the active ingredients in your shampoo to work better. Prewashing is another helpful tip that can reduce the amount of medicated shampoo your client uses per bath. Another big factor in the effectiveness of the shampoo you prescribe is the contact time. Having 10-15 minutes of contact time is critical for proper activity of medicated shampoos. Suggestions to make 10-15 minutes pass more quickly include: playing 3-4 of your favorite songs in the bathroom while waiting, taking your dog for a walk while it is soaped up, and wrapping your dog in a towel and watching television with them while they are soaped up. Once the bath is over it is important to encourage your clients to avoid using hair dryers. Even on the cool setting hair dryers will dry out the skin.

In order to confidently recommend medicated shampoo you need to understand why it is important. The two most common conditions for which you will prescribe medicated shampoo are allergic dermatitis and pyoderma. Shampoo therapy can act synergistically with oral medications to help eliminate infection, improve moisture in the skin, and reduce pruritus. Adding a shampoo might allow you to use a shorter course of oral antimicrobial therapy or a lower dose of steroid. In addition, topical treatments work quickly to remove bacteria and inflammatory mediators thus helping provide an immediate response. Lastly, using topical antibacterial products will help avoid antibiotic resistance.

Next, you need to have a basic understand of shampoo ingredients. It is beyond the scope of this lecture to discuss every possible shampoo ingredient. Consequently, we are going to focus on the most common and most useful active ingredients in three categories. The categories we will discuss today are: antimicrobial, antiseborrheal, and antipruritic.

The first ingredient we will discuss in the antimicrobial section is chlorhexidine. Chlorhexidine is a common antimicrobial agent in many veterinary products so most veterinarians feel comfortable and familiar with this ingredient. But there are many benefits of chlorhexidine worth mentioning. A study published in 2013 showed that chlorhexidine bathed hairs retained an antibacterial quality for several days after bathing. Thus, the antibacterial benefit of chlorhexidine extends for days even after the bath is over. Another study, this one published in 2012, indicated that chlorhexidine was bactericidal at lower concentrations than other ingredients. The study went on to show that chlorhexidine was also the fastest acting bactericidal ingredient. Second, we will talk about miconazole and Ketoconazole. Many of us are familiar with these ingredients for their antifungal properties. However, studies have shown that combining miconazole with chlorhexidine provides even more antibacterial activity. It is worth noting at this time that miconazole and ketoconazole shampoos are not effective as sole therapy for dermatophytosis. Enilconazole and lime sulfur dips remain the best choices for topical therapy of dermatophytosis. The next ingredient to know is ethyl lactate. Ethyl lactate is a useful antibacterial agent that also has degreasing action. The last antimicrobial ingredient to be familiar with is benzoyl peroxide. Benzoyl peroxide has a several useful properties in addition to its antimicrobial effects including: flushing follicular, reducing comedones, and reducing seborrhea. In some cases you will find it helpful to alternate between antibacterial shampoos such as Chlorhexidine and Benzoyl Peroxide. You may also find patients who are extremely sensitive to Chlorhexidine and thus require an alternative antimicrobial agent.

Antiseborrhea agents are easily the most confusing group of active ingredients. Two terms that are frequently used when talking about antiseborrhea shampoos are: keratolytic and keratoplastic. Keratolytic means that the ingredient breaks the bonds between corneocytes in the stratum corneum (the upper most layer of the epidermis). Keratoplastic means that the ingredient alters the
replication characteristics of the dividing cells in the stratum basale (the bottom most layer of the epidermis). These terms are not very helpful in general practice and in reality many of the active ingredients are both keratolytic and keratoplastic. From weakest to strongest the ingredients are: zinc gluconate, benzoyl peroxide, selenium sulfide, salicylic acid, sulfur, and coal tar. At this time you cannot purchase a veterinary prescription shampoo with zinc gluconate or selenium sulfide. Selenium is classically considered the ingredient in Selsun Blue®. This is not a shampoo I recommend for several reasons. First, there are many Selsun Blue® products and not all of them contain selenium. In addition, we want to discourage the use of human shampoo. So we'll talk about benzoyl peroxide first. It is important to remember that benzoyl peroxide can be an effective antibacterial agent as well as an antiseborrhea product. Benzoyl peroxide is also very drying so many shampoos will also include moisturizing agents. Salicylic acid can be found alone, or more commonly, combined with other active ingredients. Salicylic acid is a very effective keratolytic ingredient Sulfur is the strongest anti-seborrhea agent that you will find in a prescription shampoo. The effects of sulfur are directly related to the concentration used. This makes sense if you consider Lime Sulfur dip at most powerful end of the sulfur spectrum. Sulfur can be keratolytic and keratoplastic as well as antimicrobial. The last anti-seborrhea agent is tar. Tar is no longer available in a prescription shampoo but it needs to be mentioned because OTC tar shampoos can be easily purchased. Tar is an extremely potent antiseborrhea agent. However, part of the way it accomplishes this is by being severely keratoplastic. Remember that tar is a carcinogen! Tar is toxic to cats and also very drying. I do not recommend using tar shampoos except under special circumstances and under the supervision of a veterinarian.

Our next group of shampoo ingredients are aimed at reducing pruritus. This group includes diphenhydramine, pramoxine, and hydrocortisone. Diphenhydramine (Benadryl®) has week topical activity in dogs and cats. Pramoxine is a topical numbing agent that dulls the nerve endings in the skin thus reducing the sense of itch. Some animals respond very well to Pramoxine. Hydrocortisone is a common ingredient in anti-pruritic shampoos and it can be effective in some patients. It is important to remember that hydrocortisone is the weakest of the synthetic steroids so you can't expect a topical hydrocortisone product to resolve all of your patient's itching.

Lastly, one note about inactive ingredients. The quality and blending of the inactive ingredients is important for factors like fragrance, lather-ability, and rinse-ability. These factors should not be overlooked because these are things that our clients notice. To make the shampoo dilemma more complicated, inactive ingredients can also affect the efficacy of the active ingredients. This underscores the importance of using a reliable brand of shampoo.

Next I want to review relevant shampoo technology. This includes Novasomes™ by Vetoquinol®, Spherulites™ by Virbac®, Triz EDTA from Dechra®, and ceramides. Novasomes™ are microscopic droplets with an outer lipid membrane and an inner water core. These droplets stick to the hair shafts electrostatically during bathing and then degrade slowly over time. This provides a slow release of moisture to the skin. Spherulites™ are somewhat similar. However, Spherulites™ have multiple layers of active ingredient and water. During bathing the Spherulites™ adhere to the hair and then degrade slowly over time providing both further activity and moisture. Triz EDTA is an ingredient that many veterinarians are familiar with because of ear rinse solutions. Triz EDTA is helpful in the fight against gram negative bacteria because this agent is able to form pores through the lipopolysaccharide membrane. Active ingredients including antiseptics and antibiotics can then pass through the gram negative membrane to kill the bacteria. Ceramides are a group of natural oils that comprise the major component of the lipid layer in the stratum corneum. Cholesterol and free fatty acids make up the rest of the lipid layer. Studies in humans have shown that damaged skin and allergic skin have reduced ceramide levels. Ceramide levels also decline after a certain age (30 years old in people). Ceramides are important for a number of reasons. First, low ceramide levels cause dry skin and dry skin is itchy Second, low ceramide levels allow penetration of bacteria and yeast into the deeper layers of the epidermis and dermis. This is one reason why bacterial infections develop rapidly and spread quickly in allergic patients. Lastly, ceramides are important for limiting antigen exposure. Over the past couple years we have learned that most allergen exposure in our companion animal species occurs via cutaneous absorption. This is one more way that allergies predispose our patients to an ever worsening cycle of skin disease. The genetic predisposition for allergic dermatitis equates to lower ceramide levels in the skin. Lower ceramide levels allow more antigen penetration which results in allergy related inflammation. That inflammation further lowers ceramide levels and allows more allergen penetration.

Before we finish shampoo therapy I want to offer my suggestions for the types of shampoo you should have in practice. There are many good companies selling quality veterinary shampoos. But, you don't need every shampoo that a company produces. You might also not have just one brand of shampoo. I suggest you try them for yourself or have a couple of your best clients try them and give you their opinions. I do recommend that you keep your shampoo inventory as lean as possible. This will avoid confusion among technicians and lay-staff when reinforcing your recommendations. The three types of shampoo that you absolutely need are: 1) An antimicrobial shampoo. I prefer a shampoo with Chlorhexidine, Miconazole, and ceramides because you can use such a product for any skin infection. 2) A benzoyl peroxide shampoo. You will use this ingredient most commonly in patients with demodicosis but it will also serve as a back-up for bacterial pyoderma. Benzoyl peroxide will also handle mild seborrhea cases. 3) A moisturizing general cleaning shampoo. Having a quality shampoo you can feel good about recommending will help keep your clients out of the shampoo isle at the pet store. If the shampoo you choose is packed with moisturizers then it will be good for some of your dry flaky dogs too.

We are fortunate to now have topical therapy options beyond the scope of shampoo therapy.
This includes medicated wipes, sprays, lotions, and mousse products. The most common situations to use these products are for infections and moisturizing. Just like with shampoos, many different companies offer good products. The benefits are similar to shampoo therapy with added convenience (which translates into improved compliance). Medicated wipes are great for small areas of infection (skin folds especially) and easily allow twice daily treatment. Sprays and mousse products are great for larger areas! I recommend using these products twice daily to help resolve infection then tapering for long term control of problem areas.
Calcinosis cutis
Calcinosis cutis describes the deposition of calcium salts into dermal tissue (usually calcium phosphate or calcium carbonate). Four types are recognized in humans: Iatrogenic, Idiopathic, Dystrophic, and Metastatic. There is overlap between categories and these labels are not particularly helpful in veterinary medicine. The most common cause of calcinosis cutis in veterinary species is hyperadrenocorticism. Typically this is either secondary to hyperadrenocorticism (endogenous or exogenous) or steroid administration. Lesions typically develop on the dorsal neck and then spread caudally down the topline. Localized calcinosis cutis can occur secondary to chronic application of topical steroids. This is often apparent on the caudal ventral abdomen secondary to steroid sprays. Less commonly, calcinosis cutis can develop secondary to percutaneous absorption of calcium. Such exposure to calcium can occur when a pet comes in contact with certain floor cleaners, fertilizers, and ice melt products.

Calcinosis cutis can occur in any breed but it is more common in English Bulldogs. It is also more common in patients receiving Depo-Medrol injections. The clinical appearance of calcinosis cutis changes over the progression of the syndrome. Early lesions are chalky white to pink with indistinct margins. More advanced lesions are white, firm, and usually surrounded by intense inflammation. Pruritus is usually present and may be severe. Ulceration is common and secondary infection usually follows.

Diagnosis is easily confirmed with biopsy as the changes are unique and often dramatic. Collect biopsy samples from areas not affected by self-trauma and ulceration. Biopsy reveals diffuse or multifocal calcification of dermal collagen. Epidermal thickening and dermal edema are typically present as well. Calcinosis cutis is one dermatologic condition that can be seen on radiographs. It should be noted that serum calcium levels are not elevated in this syndrome.

Treatment involves eliminating exposure to environmental calcium and discontinuing steroid administration. If neither of these are a factor then cortisol testing is recommended as hyperadrenocorticism is very likely. If the patient does have hyperadrenocorticism then that condition needs to be managed in order to eliminate the calcinosis cutis. Patients without hyperadrenocorticism or exposure to external calcium or steroid containing products may have other severe systemic disease such as renal disease. Alternatively, some cases will develop secondary to repetitive micro-trauma (lesions typically on the pressure points of the limbs).

No treatment directly removes the calcium (aside from surgical excision). DMSO gel can be used to dissolve the calcium deposits. However, DMSO should be applied twice daily and may require weeks to months of treatment. Most owners cannot tolerate the smell of DMSO in their house for that length of time. Without DMSO, the calcium deposits will dissolve in two to twelve months. Patients with a history of calcinosis cutis should not receive steroid therapy in the future.

Hepatocutaneous syndrome
Hepatocutaneous syndrome has also been called: Superficial necrolytic dermatitis (SND), Metabolic epidermal necrosis (MEN), Necrolytic migratory erythema (NME), and Diabetic dermatopathy. I recommend against using the term Diabetic dermatopathy because it is confusing and not descriptive. In addition not every dog with Hepatocutaneous syndrome has diabetes.

The pathogenesis of hepatocutaneous syndrome involves death of keratinocytes in the upper layer of the epidermis due to presumed amino acid starvation. Most affected dogs have a distinctive chronic hepatopathy; but, serum chemistry evaluation may not reveal any abnormalities. Potential causes of the hepatopathy include phenobarbital, primidone, mycotoxin, and gastro-enteritis. In humans this syndrome is almost always associated with glucagonoma. However, Glucagonoma is rare in dogs and accounted for only 8% of cases in one study.

Hepatocutaneous syndrome is generally a disease of older dogs. Only four cases have been reported in cats. Skin lesions are typically the first sign as opposed to more common systemic signs of liver disease. Crusts and erosions occur in areas of trauma I wear. Thus, the paw pads are usually severely affected. The elbows, hocks, and muzzle are frequently affected as well. Many affected patients are often reluctant to walk due to painful erosions and fissures on the paw pads.

Diagnosis requires biopsy of skin lesions with intact crusts. Histopathologically the changes are often described as a "French Flag". Abdominal ultrasound can also be very helpful. A classic Mhoney comb" pattern to liver is present in most cases of Hepatocutaneous syndrome. However, inexperienced ultrasonographers may misinterpret the liver changes. In addition, the degree of change found on ultrasound does not necessarily correlate to severity of skin disease. CBC, serum chemistry, and urinalysis are also recommended. Nonregenerative anemia is common due to chronic disease. As stated before, liver values may or may not be elevated. Hyperglycemia is common and may require insulin therapy. Glucagon levels are elevated in patients with glucagonoma. However, glucagonoma is rare in dogs and cats and glucagon measurement is not readily available.
Management of Hepatocutaneous syndrome is difficult because this disease is a marker of severe internal disease. Consider referring these patients. Affected animals may need both a dermatologist and an internist.

For glucagonoma related disease it is recommended to remove the glucagonoma surgically. Unfortunately, glucagonomas have usually metastasized to the liver and abdominal lymph nodes by the time dermatologic lesions manifest. Cats with glucagonoma may also develop metastasis to the lungs and intestines. Even if metastasis has not occurred, affected patients are typically geriatric and my not be good surgical candidates. Octreotide, a synthetic somatostatin analogue, may be helpful for glucagonoma related disease. Octreotide binds to somatostatin receptors 2 and 5 to inhibit the release of glucagon. Octreotide will not affect the actual tumor but can yield quick and dramatic improvement in skin lesions. Octreotide is given two to four times daily indefinitely until the neoplasm progresses to the point of euthanasia or natural death. Theoretically, Octreotide would also be helpful for hepatic neuroendocrine tumors causing elevated glucagon levels and thus hepatocutaneous syndrome. However, hepatic neuroendocrine tumors are extremely rare with only one case reported in the dog and one in the cat.

A more common therapy is intravenous Aminosyn. Aminosyn can be useful regardless of the underlying cause (glucagonoma or hepatic disease). Aminosyn is the most effective therapy for hepatopathy related disease (which is the most common form). However, Aminosyn does not fix the underlying liver problem. Aminosyn provides nutrition to the starving keratinocytes. Aminosyn injections are typically given once to twice weekly initially and then spread out with injections given every 4-8 weeks long term. Aminosyn can yield a clinical response for up to twenty-two months. Unfortunately, Aminosyn is expensive and the injections must be given over several hours which requires hospitalization. A typical Aminosyn dose is 500mldog or 25mg/kg over 6-8 hours.

Supportive nutritional therapy is always recommended for Hepatocutaneous syndrome.

Nutritional therapy involves increased protein intake via supplementation with egg yolks and cottage cheese, increased fatty acid intake, and Zinc supplementation (zinc methionine 2mg/kg/day). The typical life expectancy with supportive therapy alone is 2 to 5 months.

Steroid therapy can provide temporary improvement of clinical signs. However patients eventually become resistant to steroid effects and steroid administration predisposes to Diabetes Mellitus (remember that many patients are hyperglycemic at presentation).

Topical steroid sprays or ointments may be very useful for focal lesions and carry less risk of inducing Diabetes.

Monitoring for and addressing secondary infection becomes a constant battle in Hepatocutaneous syndrome. Bacterial infection is common due to damage to the epidermal barrier. Malassezia dermatitis may develop as well. Bacterial culture and oral antibiotics may be necessary. Many of these patients do not eat well and it may be difficult for the owner to administer an oral antibiotic.

Consequently, antiseptic sprays and wipes are particularly helpful.

Cutaneous lymphoma
Cutaneous lymphoma is an uncommon malignant neoplasia of the dog and cat. Two types of cutaneous lymphoma are recognized: epitheliotrophic and non-epitheliotrophic. Epitheliotrophic lymphomas are classified T cell lymphomas and include mycosis fungoides, Sezary syndrome, and pategoid reticulosis. Non-epitheliotrophic lymphomas are typically large cell lymphomas and can be either B or T cell in origin. Older animals are usually affected but this disease can occur at any age.

These neoplasms are important even though they are rare because they imitate many other diseases. Non-epitheliotrophic lymphoma typically manifests as single or multiple nodules. Exfoliative erythroderma may occur separately or in addition to nodular disease. Patients with exfoliative erythroderma can easily be misdiagnosed as allergy, scabies, or seborrhea. If the mucus membranes and/or muzzle are affected by non-epitheliotrophic lymphoma it can appear visually indistinct from lupus erythematosus, pemphigus vulgaris, and bullous pemphigoid.

The most common epitheliotrophic lymphoma is mycosis fungoides. This condition displays multiple clinical manifestations. Erythroderma is typically present (same as non-epitheliotrophic). Once again, this erythroderma may appear visually indistinct from allergy, scabies, and seborrhea. Focal lesions progress from patches to plaques to tumors. The final stage involves wide-spread dissemination of tumors with lymph node involvement. Multiple types of lesions can be present at the same time and the speed of progression is not predictable or consistent. Additionally, initial lesions can be very subtle. For example, a client may notice the development of dry flaky seborrhea. During examination you might find a couple small patches of alopecia without inflammation and a nodule which the owner cannot remember.

Diagnosis is relatively straightforward via biopsy. The point of this lecture is merely to encourage you to biopsy older animals or animals with sudden onset of disease more quickly. Cytology is always recommended as well. Occasionally you will find an unusually large population of lymphocytes on cytology when what you expected was neutrophils and cocci.

Therapy depends on the location and the extent of the disease. Consultation with an oncologist should always be recommended. Survival time varies greatly based on aggressiveness of the neoplasia and when the disease is diagnosed. In my clinical experience, most patients survive 2-3 months after diagnosis but this can range from a few weeks up to 18 months. For clients un-interested in oncology referral or classical “chemotherapy” I recommend steroids as monotherapy. Steroid monotherapy can provide 1-3 months of quality time by reducing the intensity of lesions and subsequent discomfort.
**Pemphigus foliaceus**

Pemphigus foliaceus is one of the most common auto-immune skin diseases seen in dogs and cats. This disease is characterized by pustules and honey colored crusts. This condition is typically idiopathic but it can develop secondary to drug exposure. Pemphigus foliaceus is often seen in patients previously diagnosed with allergic dermatitis; however, no link between the two has been proven.

In pemphigus foliaceus the immune system is attacking a particular protein in the complex structure (called a desmosome) that links keratinocytes together. Destroying the bonds between keratinocytes is termed acantholysis and results in acantholytic cells. Acantholytic cells are typically plump and round because they are no longer connected to their neighbors. They stain darkly and have a clearly visible nucleus. Different forms of pemphigus exist and one of the primary differences between them is what layer of the skin this acantholysis occurs. For pemphigus foliaceus the damage occurs in the two uppermost layers (the stratum corneum and the stratum granulosum). More serious forms of pemphigus affect deeper layers of the skin and cause significantly more damage. As acantholysis occurs, vesicles and sterile pustules are formed. These are fragile and easily damaged because they are located in the uppermost layers of the epidermis. Depending on the intensity of the immune response, pustules can develop and rupture in under an hour or over the course of days. For comparison, pyoderma pustules develop more slowly and are more resilient (more difficult to break). In addition, pyoderma pustules are typically centered around a hair follicle. Both pemphigus pustules and pyoderma pustules will contain neutrophils but intact pemphigus pustules will not contain bacteria.

As already mentioned, the classic lesions of pemphigus foliaceus are pustules and crusts. These lesions can occur anywhere on the body but are commonly found on the face and trunk. Pustules can develop inside the aural opening resulting in serum leakage and crust debris falling into the ear canals. The result is typically a wicked otitis externa. In many cases the nasal planum is also abnormal. The planum typically becomes dry, thick, and crusted. Ulcerations of the nasal planum can occur secondary to crust being traumatically removed. However, pemphigus foliaceus does not cause ulceration of the oral cavity or mucus membranes. The paw pads may be affected as well. Discrete pustules may be seen on the pads but more often the pads are thickened, dry, and crusted. Some dogs will be reluctant to walk but that is uncommon with pemphigus (much more common with hepatocutaneous syndrome).

Diagnosis is via biopsy. Intact pustules are preferred because they offer the clearest picture of the disease process. However, crusts are also very useful biopsy specimens. When collecting biopsies for potential pemphigus foliaceus it is critical not to scrub the skin. In most cases it is advised to avoid shaving the animal's fur as well. Even the slightest disturbance to the skin can damage the fragile pustules seen with this condition. In the event that no pustules are present, the proof of pemphigus might be in the crust on top of the skin rather than in the skin sample itself. Consequently, always include crust debris in the formalin jar and request the crust be processed when you biopsy for pemphigus.

Treatment, which is really to say management, is almost always successful but required life-long.

Some cases of drug induced pemphigus foliaceus will remain in remission even when immune suppressive therapy is discontinued. However, it is often difficult to prove which cases are drug induced which makes predicting which patients will be able to stop therapy nearly impossible. Initial therapy requires steroid administration. Oral daily prednisolone/prednisone dosages of 2mg/kg to 6mg/kg are often required. Steroid therapy often yields dramatic improvement in two to four weeks when dosed adequately. Some patients will respond better to other steroids such as dexamethasone or triamcinolone. Recheck examinations every two to four weeks are critical to assess response to therapy and tailor drug therapy. Secondary bacterial infection is common in pemphigus and your clients will not be able to discern the difference between a pyoderma pustule (which needs antibiotics) and pemphigus pustule (which would cause you to evaluate your immune suppressive plan). In general, the goal is to slowly taper steroid therapy once clinical "remission" has been achieved. Over the course of three to four months some dogs will achieve good clinical response and can be maintained with every other day steroid therapy. However, the majority of patients will experience significant steroid side effects (such as weight gain, polyuria, polydipsia, polyphagia, behavioral abnormalities). Because of steroid side effects and the fact that most patients require life-long immune suppressive therapy it is typically necessary to add another medication as a steroid sparing agent. First line drugs for this purpose are cyclosporine and azathioprine. Second line drugs include mycophenolate and leflunomide. In most cases, I will start a steroid and a steroid sparing drug at the beginning of treatment. All of the above listed steroid sparing drugs have a delay of four to eight weeks until they become clinically effective. By starting both types of drugs at the same time I am able to reduce steroid therapy sooner.
Cushing’s Disease in the Derm World
Allison Kirby, DVM, DACVD
Animal Dermatology Clinic
Marina Del Rey, CA

Hypercortisolism is seen when there is an excessive amount of glucocorticoids present in the patient’s body. This increase in steroid levels can either be due to endogenous or exogenous glucocorticoid sources. A similar clinical appearance will be present in both sets of patients no matter the underlying cause of the increased cortisol levels. To make it even more difficult many times these patients present to the dermatology office with no evidence of PU/PD, panting, polyphagia, pot belly and/or liver enzyme elevations to support the diagnosis. Some clinicians believe that unless these systemic signs are present, a diagnosis of hyperadrenocorticism is very unlikely and thus a patient should not be treated. However, many times cutaneous signs can precede systemic signs and one should always screen for this disease if the clinical suspicion is high.

Iatrogenic hyperadrenocorticism
In veterinary dermatology, oral, injectable and topical steroid use is rampant, so sometimes it may be difficult to determine if a particular patient could have natural or iatrogenic cushings. It is very important to get a very accurate medication history from these patients. Clients many times will forget about topical medication administration which can sometimes contain very potent topical steroids. The author has seen two cases where the owners were using so much of a topical steroid powder that they both developed iatrogenic cushings and were misdiagnosed as having addisons disease after both patients experienced gastrointestinal distress due to a completely unrelated issue.

In order to test for iatrogenic cushings the recommended protocol requires the collection of a pre-ACTH serum sample, prior to administration of 5 µg/kg of synthetic cosyntrophin, IV. A post-serum sample is then collected 1 hour later. A dog with iatrogenic HAC should have a flat-line response, generally with both baseline and 1 h post-stimulation values of <1 µg/d. It is important to note that even short courses of glucocorticoids may inhibit the adrenal response to ACTH for up to a month or more.

Calcinosis cutis
Calcinosis cutis is an uncommon occurrence, in which inorganic, insoluble mineral salts are deposited in the dermis, subcutis or, rarely, the epidermis. When related to excess steroids it is considered dystrophic mineralization. Lesions are firm white-pink to yellow firm dermal papules to plaques. Overtime as this calcium remains in the skin the area will start to become ulcerated and create large crusts which can become very pruritic. These changes tend to occur on the dorsal neck, rump and axillary and inguinal regions. These areas can get frequently infected with both bacteria and yeast which can lead to pain. Anytime these changes are seen clinically, or via a biopsy, this patient must be screened for Cushing’s disease and ensure no exogenous steroids are being given. One must remember that this disease will get better before it gets worse. One must also warn the clients that the calcium deposits will continue to appear for some time after diagnosis and treatment for hyperadrenocorticism is started. Controlling the cortisol levels will be the best long term treatment but DMSO has been shown to help resolve the lesions as well. DMSO is generally applied daily to twice daily to the lesions but can have a very strong odor for some clients. I also always warn by owners to wear gloves when applying given the medications ability to help with topical drug absorption. It is recommended with more extended use that serum calcium levels should be monitored to ensure that excess calcium is not entering the blood steam. However, the author has never seen this occur clinically.

Depending on the extent of the calcium deposits sometimes patients will have clinical lesions for years and years and some owners elect to surgically remove the more problematic areas.

Adult onset demodex
Any patient that presents with skin lesions that first develop at a middle to older age should always be skin scraped to ensure demodex mites are not present. In one retrospective study 20% of patients diagnosed with adult onset demodicosis were later diagnosed with hyperadrenocorticism as the underlying disease.

Clinical lesions are similar to those seen in juvenile onset demodicosis. Lesions include erythema, comedones, scaling progressing to partial to complete alopecia with papules, pustules, and hyperpigmentation. Severe cases may be associated with lymphadenopathy, lethargy and fever as well as furunculosis with scales, crusts, exudation and focal ulceration and draining tracts. Pedal demodicosis may be associated with significant interdigital edema and, particularly in larger dogs, may be painful. A secondary bacterial skin infection almost invariably accompanies generalized demodicosis and may lead to pruritus.

Diagnosis will be by multiple skin scrapings, trichograms, and/or biopsy.

Treatment will involve management of secondary infections, control of primary hyperadrenocorticism and appropriate acaricidal medications. Once the cortisol levels have been lowered patients may be able to be cured and not relapse with disease unless cortisol levels raise again.
Dermatophytosis
Dermatophytes are transmitted by contact with infected hair or fungal elements on other animals, on fomites or in the environment. Canines are usually infected with *M. canis* (transmitted from an infected cat), *Trichophyton* spp. (exposure to infected rodents), or *M. gypseum* (from the soil)\(^6\). Typical lesions are collarettes, scales, crusts and/or papules. This is a disease of patients less than one year of age so when present in the mature patient one must determine if there is an underlying condition that is present causing immunosuppression\(^1\).

Adult onset bacterial and yeast infections
This is perhaps the most common reason I screen patients for hyperadrenocorticism. As we know it is not common for a patient, with no previous history of skin disease, to suddenly start presenting with multiple geriatric onset bacterial and yeast skin and ear infections. These adult onset infections can sometimes be very severe and yet some are relatively non-pruritic\(^1\).

These many times will do very well while they are on antibiotics and/or anti-yeast medications and then the infection will return shortly after finishing the treatment course. Patients are screened for cushings disease based on their re-occurrence rate. I generally will not screen patients if the infection resolves quickly and without incident. However, if the infection and pruritus returns in less than 3-4 months I will recommend a low dose dexamethasone suppression test or ACTH test to be performed.

Unless the cortisol levels are managed these infections will continue to occur. This patient will often need extended course of antibiotics rather than the standard 4 weeks since they are immunocompromised until the cortisol levels drop to a normal range.

Hypersensitivity dermatitis
These cases can be the most frustrating for the clinician and the client and there are two main presentations.

One presentation is where patients present at a younger age with pruritic skin disease and then are spot treated, or even placed on long term allergy medications. As this patient ages, gradually their allergies seem to significantly improve through time. Many times owners describe to me that they feel that their animal “has grown out of their allergies”. Then slowly these animals start to have re-occurrence of their secondary infections and pruritus. These patients were essentially self-medicating their allergies with their endogenous production of cortisol. To the owner they feel that the allergies are back when in actuality it is another clinical disease.

The other common presentation is patient that have a long history of mild skin disease and suddenly patients start to get worse and worse clinical lesions as they age. Once their infections are treated they do better for a period of time and then the cycle restarts. These patients will generally have lesions first and then develop pruritus after the rash is present.

Despite the historical presentation both of these patients may slowly start having their pruritus (from their allergies) return once their cortisol levels have dropped to a more normal range. Some clients will see no real clinical change in their patient’s comfort despite medical treatment. Their pet may still get itchy and secondary infections but now it is due to their uncontrolled allergies rather than the hyperadrenocorticism. Educating owners from the start about what to expect is key especially if you know a patient has a history of allergic skin disease. That way they understand that sometimes multiple medications may be needed to keep a patient’s cortisol and allergies at a tolerable level. There have been many times when the author has needed to use more potent allergy medications once treatment for cushings has started. This may also play a role in how low you want their cortisol levels while on therapy. Some clinicians have been known to use lower doses of trilostane and/or mitotane to gather clinical benefit for allergies and sometimes osteoarthritis.

Coat changes
Some of the first signs that astute owners will notice is that gradually the coat loses its luster and becomes a coarser texture. Clients that own dogs with long hair growth cycles (poodle) may also increase the time in between grooming appointments because the hair is no longer growing as fast. This will eventually lead to hypotrichosis and then complete alopecia. The hair on the head and the distal extremities tends to be spared whereas the trunk and tail experience a majority of the changes. However, non-truncal patchy alopecia can occur in up to 13% of patients with HAC\(^8\).

Along with changes in the quality and the quantity of hair the color itself can change as well. Black hairs turn auburn or light brown colored and brown hairs lighten to tan or blonde. This change in pigmentation can occur along the entire length of the hair shaft or only at the distal aspect. In the cases where only the distal tip is affected patients can appear sun bleached.

Skin changes
Other cutaneous signs include: thin skin that can wrinkle very easily, generalized and/or localized hyperpigmentation, with atrophied sebaceous glands and hair follicles. These patients will also easily bruise and create petechiae, ecchymosis and even phlebectasias. Comedones, milia and poor wound healing are also important cutaneous changes that occur in the patient with hyperadrenocorticism\(^1\).
Pruritus
This is perhaps the most unexpected findings in dogs with cushings disease. However, several studies have seen a small number of cases where pruritus (pedal and limb pruritus) was present at the time of diagnosis and resolved once treatment with mitotane was started. It is thought that the pruritus may be associated with neurosis as noted in people with cushings disease.

Treatment and conclusion
Hyperadrenocorticism is a clinical disease that warrants treatment many times in the dermatological setting. Anytime a patient is diagnosed with recurrent adult onset infectious diseases (parasitic/bacterial/fungal) or calcinosis cutis one must screen for the presence of HAC. Once confirmed the cortisol levels must be lowered for those patients to lead a more comfortable life long term. Most patient’s cutaneous signs (resolution of infectious diseases, alopecia, coat changes) will resolve within about 3 months of treatment initiation but calcinosis cutis may take many years, if ever, to resolve.

References
Demodicosis (aka follicular or red mange) is an inflammatory parasitic disease of dogs that continues to pose a challenge in clinical practice, regarding management. In October 2010, an international committee was founded to establish current evidence-based guidelines for treating canine demodicosis. These guidelines, supported by the American College of Veterinary Dermatology in addition to veterinary colleges and societies in Asia, Canada, Europe, and Australia, were published in 2012. Demodex spp. are normal inhabitants of the hair follicles in most species of domestic animals and man. They are host specific and are present in small numbers in healthy individuals. Demodex canis, Demodex injai and Demodex corneti have all been identified in dogs with demodicosis. However, more recent evidence shows that these different forms are may all be different sizes of D. canis. Published data indicate similar efficacy of reported treatments regardless of the Demodex type.

Demodex mites are transmitted from the bitch to nursing pups by direct contact during the first 2-3 days of neonatal life. The host's immune system appears to detect and tolerate the presence of these mites and also has an inhibitory effect on mite proliferation. There is some evidence that mite chitin can be recognized by toll-like receptors from keratinocytes; however, the exact immunological mechanisms that control mite populations in dogs are still unknown. The initial cause of the mite overgrowth in juvenile generalized canine demodicosis is also unknown. It has been hypothesized to have a genetic basis. Once the disease has developed in a dog, indicators of T-cell exhaustion, such as the low production of supportive/stimulatory cytokines (IL-2 and IL-21) and high levels of suppressive cytokines (IL-10 and transforming growth factor-β) along with low numbers of circulating CD4+ lymphocytes have been documented. T-cell exhaustion would also provide a plausible explanation for the lack of relapse of generalized demodicosis after treatment with macrocyclic lactones. In T-cell exhaustion, the decrease in antigenic load, as occurs during the gradual resolution of infection, helps the exhausted T-cell population to regain polyfunctional attributes and more closely match typical memory T-cells. According to this perspective, the main function of acaricidal treatment would be to reduce the parasite load to reverse the T-cell exhaustion and thereby give the host immune system the opportunity to regain control of the mite proliferation.

Demodex canis
Canine demodicosis or demodectic mange is a non-contagious parasitic skin disease seen in dogs. This disease is usually divided into localized and generalized disease. In young animals, endoparasitism, malnutrition, estrus, and debilitation may lead to an immunocompromised state that favors mite proliferation and development of skin disease. In adult animals with demodicosis, disorders such as hypothyroidism, hypercortisolism [naturally occurring or iatrogenic], leishmaniasis, malignant neoplasia [especially indolent lymphoma], and immunosuppressive treatments for cancer or autoimmune diseases have been recognized. In more than 50% of cases no underlying cause was found for the adult onset demodex. However, if initial screening tests (X-rays, thyroid panels, ACTH tests, and abdominal ultrasounds) were normal patients should still be monitored carefully because the primary illness causing the demodicosis may become evident months later.

In many publications, a juvenile-onset and an adult-onset form of the disease are differentiated. However, this differentiation may be difficult in individual cases. It is more important to identify and correct predisposing factors or underlying diseases independent of age, to achieve the best possible outcome.

Localized onset demodicosis occurs where there are only a few (generally less than six) areas of alopecia and scaling in a patient where mites are discovered on skin scraping. These patients generally do not require treatment and will spontaneously resolve.

Generalized demodicosis: Exact definition varies but generally a patient is considered to have generalized demodicosis when that patient has many localized lesions, involvement of an entire body region or has complete involvement of two feet or more. May be severe and a potentially life-threatening disease. Lesions include erythema, comedones, scaling progressing to partial to complete alopecia with pupules, pustules, and hyperpigmentation. Severe cases may be associated with lymphadenopathy, lethargy and fever. Generalized demodicosis is thought to be a hereditary based disease. In addition, there appears to be a Demodex specific T-cell defect that does play a role in severity and this defect is thought to be hereditary.

Diagnosis
Very easily done with simple multiple skin scraping, trichograms or via biopsy.

There are four stages of Demodex canis mites that can be seen on tape cytology and skin scrapings. These stages include fusiform eggs that hatch into six-legged larvae, which mature into eight-legged nymphs and progress to eight-legged adults. If one were to scrape a normal puppy numerous times in areas around the mouth and paws you will probably see a mite or two, however the puppy will not have any clinical lesions.
The skin scrapings have the best yield when primary lesions [e.g. follicular papules, pustules] chosen and skin is squeezed. If one mite is found, additional skin scrapings should be performed. Finding more than one mite is strongly suggestive of clinical demodicosis.

Trichograms are useful in areas that are difficult to scrape, such as periocular and interdigital areas. Negative trichograms should be followed by deep skin scrapings before ruling out demodicosis.1

Skin biopsies may be indicated in Shar-Pei dogs or from very fibrotic lesions (especially interdigital).1

There has been no study that has validated the prognostic value of percentages of immature forms or alive parasites on samples so I look to see if the mites are dead or alive and how many total present as my way of evaluating treatment.

**Therapy**

Localized demodicosis does not require treatment but I highly recommend periodic follow-ups to ensure that the disease is self-resolving and that the patient is not progressing into the generalized form.

For many years, veterinarians relied on a short list of medications for the treatment of generalized demodex however this has recently changed.

**Amitraz:** Traditionally, patients had been treated with dips at concentrations from 0.025% to 0.05% once a week to every other week. It is effective in 50 to 86% of patients and the higher concentration and more frequent dips were probably associated with a higher success rate. Amitraz can be toxic and the use of gloves and one will need a well-ventilated room to perform the treatment. There was a spot-on which included Amitraz that was fairly effective at treating demodex however this medication is currently not being manufactured and was associated with the development of localized and generalized pemphigus.9,10.

**Macrocyclic lactones** (avermectins and milbemycins) are a very common choice for the treatment of demodex.

Ivermectin is an avermectin with a gamma-aminobutyric acid (GABA) agonist activity. Ivermectin is given daily at 0.3 to 0.6 mg/kg until three negative scrapings at one month intervals are obtained. The bovine injectable form of the drug is administered orally as a solution. Ivermectin should not be used in Collies, Shetland sheepdogs, Old English sheepdogs, Australian sheepdogs, and their crossbreds due to the mutation in ABCB1 (formerly MDR-1) gene. Signs of toxicosis include mydriasis, ataxia, weakness, recumbency, coma and even lead to death.

Milbemycin (interceptor®) is a natural fermentation product produced by *Streptomyces hygroscopicus aureolacrimonus*. It is closely related to the avermectins, produced by *Streptomyces avermitilis*, differing only in one position. The anthelmintic activity is believed to result from disruption of invertebrate gamma amino butyric acid (GABA) neurotransmission. Daily doses of 0.5 up to 3.1 mg/kg per day have been shown to have a 60 to 96% cure rate in a few months (up to about 1 year).3

Moxidectin is derived from fermentation products of *Streptomyces cyaneogriseus* subsp. Noncyanogenus. Oral formulation has been used at 0.4mg/kg daily and shown to be effective. There is also a spot application formulation available for dogs which has a 2.5% Moxidectin and 10% imdiclopramide. The product is licensed for application every 4 weeks, but more frequent application (weekly to every other week) is often needed when treating Demodex.

Isoxazoline: Are a novel class of parasiticides that are potent inhibitors of GABA-gated chloride channels and glutamate-gated chloride channels.

Afoxolaner: (NexGard®): Afoxolaner was administered to eight dogs at the recommended dose (at least 2.5 mg/kg) on Days 0, 14, 28 and 56. The topicalical combination of imidacloprid/moxidectin was given at the same intervals at the recommended concentration to eight patients as well. Clinical examinations and deep skin scrapings were performed monthly. The percentage reductions of mite counts were 99.2%, 99.9% and 100% on Days 28, 56 and 84, respectively, in the afoxolaner-treated group, compared to 89.8%, 85.2% and 86.6% on Days 28, 56 and 84 in the imidacloprid/moxidectin-treated group.

Fluralaner: (Bravecto™) Sixteen dogs, all diagnosed with generalized demodectic mange, were randomly allocated to two equal groups. Bravecto™ chewable tablets were administered once orally at a minimum dose of 25 mg fluralaner/kg body weight to one group of dogs, while the second group was treated topically on three occasions at 28-day intervals with Advocate®. Mites were counted in skin scrapings before treatment and at 28-day intervals over a 12-week study period. A single oral administration of Bravecto™ chewable tablets, mite numbers in skin scrapings were reduced by 99.8% on Day 28 and by 100% on Days 56 and 84. Mite numbers in the dogs treated topically on three occasions at 28-day intervals with Advocate® were reduced by 98.0% on Day 28, by 96.5% on Day 56 and by 94.7% on Day 84.

Sarolaner: (Simparica™) Sixteen dogs with generalized demodiosis were randomly assigned to treatment with either sarolaner orally on Days 0, 30 and 60, or topical imidacloprid (10 mg/kg) plus moxidectin (2.5 mg/kg) solution every 7 days from Day 0 to Day 81. For sarolaner-treated dogs, pretreatment mite counts were reduced by 97.1% at 14 days and 99.8% by 29 days after the first dose. Weekly imidacloprid plus moxidectin resulted in 84.4 and 95.6% reduction at these two time points.

Infection control: Generally patients with generalized demodex will also have superficial and/or deep infections. Appropriate systemic antibiotics and antifungals may be necessary for minimum 4 weeks treatment duration. Topical antimicrobial based shampoos should also be implemented to decrease treatment interval.
Glucocorticoids are absolutely contra-indicated, even topically (cutaneous or auricular topicals) even if pruritus is severe\(^1\).

**Monitoring and prognosis**

It is not sufficient to rely on clinical appearance as the end-point of treatment. Clinically normal dogs may still harbor mites on deep skin scrapings. Microscopic cure, defined as multiple negative skin scrapings, in addition to resolution of clinical signs is needed to determine the therapeutic end-point. In general, it is recommended to scrape the three to five most severely affected areas and any new lesions monthly until all scrapings are negative. It is recommended to continue treatment for 1 month after the second negative monthly set of skin scrapings.\(^1\)

The prognosis for canine demodicosis is good, with the majority of cases achieving long-term remission.\(^8\) However, dogs with an incurable or poorly controlled underlying disease may never be cured and may require long-term therapy with the newer generation flea preventatives this is an easier situation than it was even 3 years ago. The current recommendation is to avoid long-term glucocorticoid therapy in dogs with a history of demodicosis.\(^1\)

**Demodex injai**

In 1997, Dr Andrew Hillier presented at the AAVD/ACVD annual meeting in Nashville a canine skin disease due to a novel *Demodex* mite. This mite has a much longer body than *Demodex canis* and in 2003 it was coined demodex injai.

**Clinical features**

Can cause a greasy seborrhea mainly on the dorso-lumbar and facial area. Breeds that are predisposed include the West Highland White, Shih tzu, and Scottish terrier. Mites counts tend to be very low so alopecia may not be evident but patients can sometimes be very pruritic. Excessive glucocorticoid therapy (for allergy and pruritus) and hypothyroidism have been reported as underlying causes\(^3\).

**Diagnosis**

Skin scrapings, trichograms, and a biopsy may be needed in some cases due to scarcity of mites.

**Therapy**

See above

**Demodex cornei**

A short-bodied Demodex mite that may exclusively live in the stratum corneum. It could be a mutant of *D. canis* or a new species. So far the mite is present in cases of simultaneous infestation with *Demodex canis*. Therapy is the same as for *D. canis*.\(^2\)

**References**

4. P B. Variation in size in Demodex canis: from the longest to the shortest forms. *Veterinary Dermatology* 2010;21.
Fleas, Fleas, and More Fleas
Allison Kirby, DVM, DACVD
Animal Dermatology Clinic
Marina Del Rey, CA

There are more than 2,000 species and subspecies of fleas and dogs and cats can be the transient host for any of these species. However, *Ctenocephalides felis felis*, *Ctenocephalides canis*, *Pulex spp.*, and *Echidnophaga gallinacea* are the one ones of medical concern. Overall *Ctenocephalides felis* is the one of most concern in the United States and Worldwide.

**Flea life cycle**
The flea depend on the host for food and protection so they will spend the almost entire adult life of the animal\(^1\). The female flea will lay her eggs on the host usually while the animal rests or sleeps. These eggs quickly fall off the host and contaminant the environment. Flea eggs usually hatch in 36 hours and some make take up to 10 days\(^1\). Low temperatures (\(<0^\circ\text{C}\)) for 24 to 36 hours are lethal to most eggs. The eggs then hatch into larva which move to the dark protected areas like deep into carpets due to their negative phototaxis and positive geotropism. Larva are the most sensitive stage in the flea life cycle and only about 25% will survive in the environment due to lack of food, dryness, and extreme temperatures\(^2\). The third instar of the larva will then form of a cocoon and form a pupa. The pupa is more hardy than all the other stages but will die at the extreme temperatures. The adult flea can remain in the cocoon for as long as 140 days before emerging with proper temperature and humidity. In most households, *C. felis* will take 3 to 4 weeks to complete its life cycle so it is very important for flea infested households to understand that despite starting flea control they may still see fleas that first month or two.

The newly emerged adults require a host for long-term survival. Once on a host, *C. felis* initiates feeding within seconds to minutes. Feeding is so rapid that partially digested blood can be defecated in as little as 2-6 minutes after fleas acquire a host. Mating occurs on the host after feeding and the female *C. felis* begin egg production within 24-36 hours after their first blood meal\(^3\). With peak egg production a single female flea can lay between 40-50 eggs per day.

**Flea control**
Flea are essentially everywhere and depending on the area can either be a seasonal or year round issue for pet owners. All animals are considered at risk and those that frequent grooming facilities, doggie day care, dog parks, have or access to wildlife populations are at even higher risk. Effective treatments used on the animal can eventually eliminate environmental fleas, provided that untreated animals do not reinfest the area\(^4\).

**External environment**
Because flea eggs fall to the ground, the infested pet’s yard can be seeded with fleas by the pet itself or by stray dogs, cats, opossums and raccoons. As discussed earlier flea larva are very sensitive to heat and desiccation and given this fact, adults should not develop on paved areas, on deck surfaces, or in short-cut, un-exposed lawn. The areas that are protected from the direct sun and have some form of shelter are the largest problem areas. This would include area under decks, overgrown brush, and crawl spaces. These are the areas to be concerned about when treating the environment. There are many different products out there that can treat the environment including carbamates or organophosphates that are available in liquid and powders\(^5\). For those families wishing to have a more natural approach there is a company marketing beneficial nematodes (Fleabusters). This product contains harmless nematodes called Steinernema carpocapsae, which kill flea larvae and pupae in the grass and soil\(^6\). The efficacy of this system is not known\(^7\).

**Internal environment**
This is usually the hardest part of flea control and prevention and requires thorough cleaning. Vacuuming will help remove eggs, larva and adults but may also cause adults to emerge. Once must remember to empty the bag or canister after each process. Dog beds and carpets should be washed or replaced.

Hiring a profession may be the best recommendation since they have access to many products that we do not and they are familiar with the proper application. However, many products are available to treat the interior of a house. For the client that has significant issues with the use of these products sodium borate would probably be the best recommendation. The borate compounds have rapid ovicidal and larvicidal activity, which is suspected to be through a dehydrating mechanism. The professionally applied product (Rx for Fleas, Inc.) is guaranteed for 1 year, provided carpets are not cleaned, and has a reported efficacy of greater than 99%\(^8\).

For prevention of re-infestation another good option would be the use of insect growth regulators. These products prevent the larva from transitioning to the pupa stage. If these products are applied in the house before fleas are introduced, infestation should be aborted. Methoprene is degraded by sunlight and should be reapplied at least every 30 weeks. Fenoxycarb and pyriproxyfen are sunlight stable and last 6 to 12 months.
### For use on animals
The following is a table of the most commonly used products that are administered to the patient themselves.3,8,9

<table>
<thead>
<tr>
<th>Key Drug</th>
<th>Drug Class</th>
<th>MoA</th>
<th>Key points</th>
</tr>
</thead>
</table>
| Spinosad       | Macrocyclic lactone | nAChR agonist               | Contraindicated with high dose ivermectin  
GI upset somewhat common                                                   |
| Afoxolaner     | Isoxazole           | GABA and Glutamate antagonists | Effective against demodex and some tick species  
Highly palatable  
Minimal upset stomach  
Fluralaner = effective for 12 weeks                                         |
| Fluralaner     |                     |                             |                                                                             |
| Sarolaner      |                     |                             |                                                                             |
| Selamectin     | Avermectin          | GABA agonist                | Fleas continue to feed during first hour.  
Peak efficacy not seen for 36-42 hours  
Effective against sarcoptic mange when applied q 2 weeks x 3 applications |
| Imidacloprid   | Neonicotinoid       | nAChR agonist               | Efficacy within 6-12 hours  
Fleas stop feeding within 3-5 minutes                                         |
| Fipronil       | Phenylprazole       | Insect GABA receptor agonist | Fleas continue to feed during first hour.  
Toxic to rabbits                                                            |
| Dinotefuran    | Neonicotinoid       | nAChR agonist               | Vectra 3D product contains permethrin, do not use in cats                    |
| Pyriproxyfen   | Insect growth regulator | Juvenile hormone analog    | Mode of action similar to methoprene but not UV sensitive like methoprene |
| Permethrin     | Pyrethroid          | Target voltage gated Na+ and Ca+ channels | Kills ticks, biting flies, and mosquitos  
Toxic to cats  
Repellant action  
Most EPA reports of "major pesticide reactions" involved spot-ons containing pyrethrins |
| Nitenpyram     | Neonicotinoid       | nAChR agonist               | Onset within 30 minutes  
100% efficacy within 4-6 hours  
Little residual activity within 48 hours                                      |

### Therapeutic plan for the flea infested pet
When encountering a patient for the first time with either clinical signs related to flea allergy dermatitis or who is flea infested one must take an accurate history. Determine if that patient frequents areas where fleas could be commonly found (dog parks etc) and also discuss the outdoor environment at home. Question the owner about the possibility of wildlife in the area and if there is a lot shaded areas the patient likes to frequent. Then start prescription flea preventative for all pets in the household. Treat the pruritus and any secondary pyoderma with appropriate medications. Make sure you pick a preventative that fits with the client's preferences (oral vs. topical) any concurrent dz (food allergy, flea allergy, demodex mites), the pet's lifestyle (tick exposure, bathing frequency).

### Advice for clients
Clients many times will say their flea control doesn't work. These clients will need to be educated about the flea lifecycle and feeding behavior. Advise them that while our prescription flea preventatives are highly effective, they take time to kill fleas and do not prevent all feeding. Fleas will need to bite the pet before being killed by the adulticide. It is likely that owners will see live adult
fleas on their pet after having given a flea preventative, but it is highly unlikely they will have an infestation when prescription flea prevention is used on a consistent monthly basis. Remind them that flea preventatives do not create an invisible force field that kills every flea before it jumps onto the pet.

Clients who do not believe fleas are the problem
You do not have to see the flea for the flea to cause a reaction. Use a peanut allergy analogy to help them understand: If a person is allergic to peanuts, one peanut may touch their food and they will have a reaction. They do not have to see the peanut. Repeat the history they gave back to them, wait for them to validate that you have the story straight. Then, present the fact that itching and secondary infections in the back half of the body is textbook for flea allergy. Explain that every flea medication, just like every drug of any kind, wanes in efficacy from the time it is given to the time the next dose is due. A pet on good monthly flea control will never have an infestation, because fleas that infest the pet will die before they have enough time to lay eggs. However, for a pet that is sensitive, a few hours of feeding before the flea dies may be enough to cause a reaction. For this reason, hypersensitive pets do better on bi-monthly flea prevention. Compliment the owner on the cleanliness of their home and their pet, advise them you are sure their pet would never have an infestation. However, remind them that with all the good work they are doing and money they are spending on allergy work-up it would be a shame for a future flea bite to confound analysis of the itch level and potentially lead us astray in our diagnosis.

Clients who are concerned about safety
Flea preventatives exploit a difference in the nervous system between insects and mammals10,11. It is anatomically/physiologically impossible for these products to kill a mammal the same way they kill fleas. Adverse reactions may occur as they can with any oral or topical product of any kind, but the benefits far outweigh the risks. Point out that monthly or bi-monthly flea prevention is a lot safer than repeated courses of steroids and antibiotics to manage the symptoms. Explain that the majority of reported adverse reactions in pets and people are involve topical products containing pyrethrins or older organophosphates and carbamates12,13. These products may or may not have been used appropriately by the owners (e.g. pyrethrins may have been applied to cats). Explain that some topical products such as imidacloprid are not systemically absorbed. While dermal hypersensitivity reactions can occur, point out that this is also true with any soap or lotion we would use on ourselves. Many dermal reactions are related to carrier ingredients rather than the insecticide13. Inform clients of the diseases which can be caused and/or transmitted by fleas2,3. These include iron deficiency anemia, rickettsiosis typhi, rickettsiosis felis, bartonella henselae, mycoplasma haemofelis, yersinia pestis, dipylidium caninum. Educate them that these diseases are worse than flea infestation and may require treatment that is less safe than prescription flea preventatives. Use of the broader term "parasites” can sometimes invoke greater willingness of the owner.

What about 'natural' flea preventatives?
These medications are typically ineffective, this is usually easy especially once you educate them and potentially point out evidence of fleas on their animal. Also 'natural' does not always mean safe, garlic can cause anemia14 and Tea Tree oil (melaleuca) can cause transient hind-limb paresis, hepatotoxicity13 and is commonly implicated in atopic disease. Other ingredients like peppermint, clove, cinnamon, lemongrass and thyme have been links to neurologic signs13.

References
Pruritus in puppies may be one of the most difficult diseases that can present in clinical practice. This is due to many factors including: client frustration, the relative lack of safe treatment recommendations to decrease pruritus, constant changing weight of the patient, and the fact that sometimes a clear diagnosis is not available/obtainable.

**Client education**

Many times owners are already very irritated by the time they make an appointment to be seen. The puppy they just adopted is showing signs of illness and this is not what they expected to be managing at such a young age. In addition, training and housebreaking is a much more challenging experience if the drive to itch is so intense that the puppy cannot focus on the task at hand which can frustrate the client even further. Empathizing with the client’s situation and explaining all the different possibilities/treatments that are available is a must.

**History**

Just because the patients are so young does not mean that your history should be limited. Knowing if the patient came from the shelter and/or a breeder and if any of the littermates are affected can be a valuable pieces of information that can help narrow down the possible differentials. The client should also be questioned about travel history prior and post adoption. In the particular area that I work I have seen numerous dogs flown in as young adults/puppies from Africa, South American, Mexico, Middle east and all through-out the United States. There is some dermatological disease that will be more common in foreign counties than in the US so this may change your differentials.

In addition, I always ask what type of life style does this patient have? With the growing trend of doggie day care, hiking/walking groups, and dog parks canines have much more of a social lifestyle than ever before. This type of interaction can lead to increased flea exposure and other contagious diseases and can give you information about any other animals affected within the same social group.

The client should always be questioned regarding the main areas of the body that the puppy is itching/licking, how severe the pruritus is, and response to any previous medications that have been given.

Despite the patients being seen for pruritus one must always ask about gastrointestinal signs when presenting with a pruritic puppy. If the patient has any history of vomiting, diarrhea, decreased appetite, excess gas, mucous in the stool and how many bowel movements per day can help support the possibility of a food related allergy.

**Physical examination**

Many of the pruritic puppies I have seen have completely normal physical examinations. However, one must always perform a pinnal-pedal reflex in young patients on their first examination. The reflex is assessed by rubbing the tip of an earflap on to the base of the ear for several seconds. This test is considered positive if the ipsilateral hind leg makes a scratching movement. This test has been shown to have a sensitivity of 81.8% and a specificity of 93.8% of dogs in a study of 588 patients. Along with the testing of the pinnal-pedal reflex the patient should be flea combed and one should ensure there is no evidence of flea dirt as well.

**Diagnostics**

1. Superficial skin scrapings should always be performed in all itchy young patients. For the superficial scrapings I will often scrape the pinna and the lateral elbows and hocks and the examine the specimen at 10x. If I am very suspicious of scabies, I will often take numerous scrapings (sometimes more than 5) to see if any mites/eggs/fecal pellets are found.
2. A deep skin scraping is also performed generally at the face, at least one of the paws, and then 1 or 2 other clinically affected areas. The material is placed on separate slides and viewed at 10X to help determine if demodex mites are present and if present is the disease localized or generalized.
3. Surface cytology: Any papules, pustules, crusts or areas of lichenification are sampled and examined at 100x for any signs of bacteria and/or yeast organisms and to evaluate the inflammatory cells present.
4. Fungal culture: Although generally not considered an itchy disease one must consider performing a fungal culture on young puppies that present with lesions consistent with a folliculitis and/or hair loss. I have personally seen extremely itchy dogs that had a primary dermatophyte infection and their pruritus resolved once the dermatophyte was cleared this is mainly seen with Trichophyton and M. persicolor infections in dogs.
Diseases

Sarcoptic mange

Intensely pruritic, contagious disease caused by Sarcoptes scabiei var. canis. This is considered a zoonotic disease and clients should be warned about the potential for transient lesions. In canine mites prefer the skin of the ears, elbows, abdomen and hocks where there tends to be less hair. Patients obtained recently from the shelter and animals that attend dog parks and doggie day care are at increased risk. Patients tend to be mostly itchy at the ears and face and the entire ventral surface with the dorsum essentially spared.

Clinical lesions

Intense pruritus will be the main clinical sign and these dogs will sometimes have to be manually restrained in the exam room. The initial lesions are generally crusted papules that can progress rapidly to alopecia, erythema, and thick yellow crusts. Some patients do not show any lesions at all beyond pruritus. The level of pruritus is directly related to the number of mites present. The pruritus seen is from a hypersensitivity reaction to the mites themselves.

Diagnosis

Can be very difficult to diagnosis since even after numerous scrapings; anywhere between 20-50% of the time the mites, eggs and/or fecal pellets are not found. Many clinicians rely on response to adequate medications as their main way of diagnosing this disease. As we discussed earlier, a positive pinnal-pedal reflex is helpful for screening for potential cases. Fecal flotation can also sometimes find mites due to excessive grooming behavior is affected animals. An ELISA test exists for the diagnosis of scabies and is between 84- 92% sensitive and 90- 96% specific. However, it can take up to 5 weeks for an animal to start producing adequate antibodies to illicit a positive test.

Treatment

At this time there are many ways to treat this disease and choice of medication will depend on patients age and owner’s preference. If patient lives in a multi-dog household all animals must be treated for resolution. 2-4% lime sulfur dip weekly for a period of 4-6 weeks has proven to be effective and does have additional anti-itch properties for the patient. Ivermectin at weekly administration between 0.2-0.4mg/kg has also been used at every two week intervals for three injections or orally once weekly for 6 weeks. Other effective medications include selamectin, imidacloprid/Moxidectin, and milbemycin, and several of the new generation isoxazoline flea medications like sarolaner5.

Pelodera strongyloides

Small nematodes that lives in decaying material in the soil where it normally completes its entire life cycle. However, the third stage larvae are capable of penetrating human and mammalian skin and can cause a severely pruritic dermatitis. Generally, these animals live in the Midwestern United States and have access to damp straw bedding.

Clinical lesions

Creates a pruritic dermatitis that will occur on parts of the body in contact with the damp bedding. Commonly lesions will be on the ventral abdomen, chest, perineum, legs, lateral shoulder and thighs and spares the head and back. This nematode can cause alopecia, erythema and crusted lesions in sites infected.

Diagnosis

You can find these nematodes in skin scrapings and are generally between 600-750 µm in length and 30-40 µm in width. The clinician should ensure that the nematodes found are not a type of hookworm. One can also diagnosis this disease via biopsy where the larva are found inside hair follicles.

Treatment

Complete removal of the contaminated bedding is mandatory to reliably treat these animals. All areas must be washed and sprayed with insecticide. To treat the patient one can use Ivermectin but once the environmental is cleaned patients can undergo spontaneously resolution.

Ancylostoma and uncinaria

Larva are present on grasses and soils during the spring and summer season. They are seen patients that live in large capacity dog kennels and in patients that frequent dog parks that are not properly maintained.

Clinical lesions

Red papules on the skin that come in contact with the soil/grasses. As the disease progresses these areas become thickened and alopecic. The paws can become erythematous and may become swollen and pruritus is variable but always present.

Diagnosis

Positive fecal examination for hookworms and compatible clinical signs can usually lead to a diagnosis. However, if the fecal examination is negative one can perform a biopsy to aid in the diagnosis. Histopathology can reveal a perivascular dermatitis and recent larval migrations tracts can sometimes be seen. Larva are not usually present on biopsy samples.

Treatment and prevention

The widespread use of heartworm preventives that also have anti-helminth activity has minimized this disease. Treatment should emphasize cleaning of the premises, frequent removal of feces. Once can use pyrantel pamoate tablets or fendbendazole for treatment but keep in mind the treatment cycle needs to be repeated in 2-3 weeks to resolve the infection.
Intestinal parasite hypersensitivity
Certain intestinal parasites (ascarids, Coccidia, hookworms, tapeworms, whipworms) can cause severe pruritus in certain canines. It is thought to be a type I hypersensitivity2.

Clinical signs
Can vary but some patients can have papules, crusts, seborrhea, and sometimes even hives related to this disease.

Diagnosis
Positive fecal and/or response to treatment

Treatment
Proper anti-helminth based off of fecal analysis

Flea allergies
Depending on your location flea allergies can be the most common allergic hypersensitivity dermatitis you see or not present at all.

Clinical lesions
Intense pruritus centered around the dorsal L-S region, tail, flanks and inguinal region. One may also see papules in the umbilical area as a primary clinical sign. This leads to alopecia, crusting, papules and pustules and acute moist dermatitis “hot spots”.

Diagnosis
Presence of adult fleas, flea feces or based off the majority of the clinical signs being in back half of the body.

Flea allergies
Depending on your location flea allergies can be the most common allergic hypersensitivity dermatitis you see or not present at all.

Clinical lesions
Intense pruritus centered around the dorsal L-S region, tail, flanks and inguinal region. One may also see papules in the umbilical area as a primary clinical sign. This leads to alopecia, crusting, papules and pustules and acute moist dermatitis “hot spots”.

Diagnosis
Presence of adult fleas, flea feces or based off the majority of the clinical signs being in back half of the body.

Treatment
Client education about the flea life cycle. One must ensure that all animals in the house are on proper, consistent flea medications all year round in some areas. Question owner regarding feral cats and other wildlife that could contribute to the flea burden in their environment and necessitate environmental control as well. Sometimes you need to treat the patient as if it is a flea allergy and then see how patients responds to therapy.

Food allergies
It is noted that 33-50% of all dogs diagnosed with a food allergy are less that 1 year of age. There is no breed or sex predilection7.

Clinical lesions
Some patients do not exhibit any clinical lesions beyond pruritus. Some patients have chronic otitis externa as their only clinical sign of a food allergy. Erythema, papules, macules, excoriations, ulcerations, alopecia, lichenification, and hyperpigmentation can occur on the interdigital region, axillae, groin, perineal area and face. Some patients will also have concurrent GI disease which may include: vomiting, diarrhea, increased bowel movements, flatulence, and fecal mucus.

Diagnosis
Perform a strict 6-12-week diet trial with a hypoallergenic diet approved for growth. This includes Royal Canine Venison and Potato, Royal Canine HP, and Purina HA.

Treatment
Continue to feed the hypoallergenic diet or do individual ingredient re-challenge to determine exactly what patient is allergic to.

Atopy
Typically presents between the ages of six months and three years but clinicians have seen it appear as young as three months. However, many times it will take many months to come to this diagnosis since it is one of exclusion and other allergies and parasitic diseases must be explored.

Clinical signs
Pruritus, erythema, papules, excoriations typically occur, in the axillary region, inguinal, interdigital, muzzle, periocular, pinnae and the medial aspects of the thoracic legs. Patients may be year round or seasonal depending on the allergens they are sensitivity.

Diagnosis
Exclusion of other pruritic disorders. According to Favrot in order for a patient to be considered atopic they must satisfy five of the following criteria8
1. Onset of clinical signs younger than 3 years of age
2. Must live mostly indoors
3. Steroid responsive itchiness
4. Itchiness with no skin lesions
5. Front feet are affected
6. Pinna are affected
7. Ear Margins are not affected
8. Back is not affected

Treatment
Antihistamines, topical therapy, fatty acids, cyclosporine, steroids, immunotherapy, monoclonal antibody.

Idiopathic pruritus of puppies
First documented by Danny Scoot from Cornell University where he described ten puppies that started with pruritus between 2-7 months of age. All puppies had no history of a change in diet or environment and all were properly dewormed.
Clinical lesions
Pruritus with no clinical lesions

Diagnosis
Difficult to diagnosis properly since really a diagnosis by exclusion

Treatment
None in the puppies documented by Scott. The pruritus just resolved between 3 ½ to 5 months after onset.

References
Oclacitinib (Apoquel®)
Oclacitinib is approved by the FDA for the control of pruritus associated with allergic dermatitis and control of atopic dermatitis in dogs at least 12 months of age. Apoquel® is the first selective Janus kinase (JAK) inhibitor developed for the dog. JAKs play a key role in cytokine signaling and the signal transduction of pro-inflammatory, pro-allergic, and pruritogenic cytokines. Although multiple JAKs exist, Apoquel® preferentially inhibits JAK-1, which is involved with the signaling pathways for IL-2, 4, 6, 13, and 31. Apoquel has the greatest affinity for inhibition of JAKs involved with IL-31 signaling, the cytokine recently demonstrated to play a central role in the development of pruritus. Apoquel® is administered at 0.4-0.6mg/kg twice-daily for the initial two weeks and then decreased to 0.4-0.6mg/kg once-daily for long-term use. The medication is available in 3.6mg, 5.4mg and 16mg tablets and it is recommended to administer in full and ½ tablet increments. The absolute bioavailability of oclacitinib maleate was found to be 89% and has been shown to have a rapid onset of action, significantly decreasing pruritus within the first 24 hours of administration.

This medication is not recommended for use in patients with previous history of neoplasia. Side effects seen with this medication over a study period of 4 months include pyoderma, non-specified dermal lumps, otitis, vomiting, diarrhea, histiocytoma, cystitis, anorexia, lethargy, yeast skin infections, pododermatitis, lipoma, polydipsia, lymphadenopathy, nausea, increased appetite, aggression, and weight loss. On average, dogs gained 4% body weight on oclacitinib maleate during one study period. Generalized demodicosis and viral papillomatous have also been seen post-approval and during initial dosing studies. Co-administration of this medication and cyclosporine and/or corticosteroids is not recommended for long term. However, a study was recently published where oclacitinib was administered with cyclosporine for a period of three week in laboratory beagles and there were no adverse events seen. However, long term studies will be needed before it is deemed safe to use these two medications concurrently.

It is off label to use the medication in cats but numerous veterinarians and specialists are experimenting with its role in both feline allergic dermatitis and feline asthma. There has been one published study where 12 suspected atopic cats were treated with a mean dose of 0.47mg/kg twice daily for 14 days and then once daily for another 14 days to judge clinical efficacy. Five of these cases seemed to achieve good improvement in resolution of clinical lesions and decrease in pruritus. The remained seven either dropped out of the study due to poor response or there was no change in clinical lesions or pruritus.

Canine atopic dermatitis immunotherapeutic®
The USDA conditionally licensed product CADI is a caninized anti-IL-31 monoclonal antibody developed by Zoetis. Monoclonal antibody therapy works by one of two mechanisms; either by binding a soluble molecule and preventing it from interacting with a cell surface receptor or by targeting the cell surface receptor directly. CADI works by “soaking up” circulating IL-31 produced by lymphocytes preventing it from activating cell receptors. It is administered as a subcutaneous injection given no more frequently than every 30 days. CADI therapy offers the several advantages in that it is a very targeted therapy whose adverse event profile appears to be very narrow at this time. It can be administered to any age of dog, and may be given with any concurrent medications. Studies at this time reveal administration of CADI significantly reduced pruritus upon IL-31 challenge for up to a month compared to a placebo. These studies also demonstrated that the efficacy was dose dependent with few anti-drug antibodies (ADA) produced. Finally, the efficacy and safety of CADI in field conditions compared to a placebo was evaluated and revealed that treated dogs had a significant reduction in owner assessed pruritus compared to placebo treated dogs. The clinical improvement can be seen within 1-3 days post injection and was effective in around 80% of patients. During initial studies no dogs developed serious adverse reactions, no dogs developed immediate post-injection reactions, and the most commonly reported adverse events were vomiting, diarrhea, and lethargy. Given this is a caninized monoclonal antibody it will not have a place in the treatment of the feline patient. During the study period many patients were also on corticosteroids, cyclosporine, antifungals, antibiotics, immunotherapy, and/or oclacitinib and there were no complications found with administration of these medications together. Laboratory beagles have received 7 monthly subcutaneous injections at 3.3mg/kg and 10mg/kg and no side effects have been reported in this population. CADI is available in 10mg, 20mg, 30mg, and 40mg sterile single-use preservative-free 1 ml vials that need to be kept refrigerated.

Microsilver BG™
Microsilver BG™ is a micronized form of silver that is found in a line of topical products made by Vethbiotek. For a long time, silver has been known for its ability to kill yeast and multi-drug resistant bacterial infections; but it’s main clinical advantage comes from its activity against biofilms. Biofilm organisms have an inherent resistance to antibiotics, disinfectants and germicides. It has been shown that up to 96% of Staphylococcus pseudintermedius isolates from canines have the ability to form biofilms. Unlike planktonic populations, bacterial cells embedded in biofilms exhibit intrinsic resistance to antibiotics due to several specific defense mechanisms conferred by the biofilm environment, including the inactivation of anti-microbial agents by exopolysaccharide (EPS),

265
over expression of stress-responsive genes, oxygen gradients within the biofilm matrix and differentiation of a subpopulation of biofilm cells into resistant dormant cells. The intrinsic resistance of bacterial cells within biofilms to conventional anti-microbials has led to new technology for the treatment of biofilm-associated infections, including the use of silver preparations. Silvers inherit anti-bacterial properties and low toxicity towards cells has made it heavily used in the human field to reduce nosocomial infections.

Vetbiotek has brought this technology into a line of shampoos, sprays, mousses and wipes that contain a silver molecule that is 10 microns in diameter. This size molecule is large enough that it will stay on the surface of the stratum corneum and not penetrate into the layers of the epidermis. In addition, the microsilver BG molecule is porous and adheres very well to the skin and will stay in contact with the skin until mechanically washed off; this allows for sustained anti-microbial effect. The silver molecule is also present in their seborrhea and anti-itch products.

Osurnia®
This is an otic gel with 10 mg florfenicol, 10 mg terbinafine, and 1 mg betamethasone acetate per mL that has been manufactured for the treatment of yeast and bacterial canine otitis externa. It is prepared in a 1ml sterile flexible soft tip applicator and one tube should treat one ear. The medication must be refrigerated upon arrival to the hospital and to increase patient comfort it should be warmed up slightly before use. The medication is then instilled in a clean and dry external ear canal and then the base of the canal is massaged to allow for the product to adhere to the lining and then also travel down the ear canal. This entire administration is then repeated in one week. This medication can be used for a suspected otitis externa with mainly cocci and/or yeast found on cytology. However, if the cytology confirms the presence of mainly rods this medication has been shown to not be very effective given the antibacterial medication present. This medication, like claro™, offers many advantages to the client and veterinarian in that all administrations could theoretically occur in the clinic. The medication would be administered at the initial visit and then the one week follow up. This increases client compliance and allows for the infection to be rechecked in a timely manner. Using a gel topical product also decreases the ability of the medication to exit the ear canal by intense head and ear shaking during the application process.

After application of this product it is recommended to not clean the ear for a total of 45 days. This recommendation stems from an ear swab depletion study that was performed with this medication in normal dogs. Normal dogs were administered the medication on day 0 and then repeated at day 7 and then drug concentrations of florfenicol, terbinafine, and betamethasone were gathered over the period of 45 days. It was concluded that after 45 days therapeutic concentrations of osurnia remained present in normal ears. However, it is suspected that concentrations of these medications in inflamed ears may be decreased due to increased absorption through the disrupted skin barrier and drug degradation secondary to inflammation.

This medication has not been tested in patients with a perforated tympanic membrane, or in animals that are pregnant or lactating. Safety studies have shown that when the 1ml product is re-administered once weekly for a total of five weeks there has been mucosal necrosis and ulceration seen of the lining of the middle ear cavity. At the recommended dosage administration patients have experienced elevations in aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), vomiting and hearing loss.

Claro™
This is an otic solution that contains 15.0 mg/mL florfenicol, 13.3 mg/mL terbinafine and 2.0 mg/mL mometasone furoate. It is prepared in a 1ml sterile tip applicator and one tube should treat one ear no matter what the size of the patients ear canal. Just like Osurnia™, this medication is mainly used for the treatment of otitis resulting from Malassezia pachydermatis and Staphylococcus pseudintermedius. If rods are seen on cytology and Pseudomonas spp. are suspect this medication should not be used.

This medication should be applied once in the veterinary hospital and does not need to be refrigerated. This medication has been found to remain active in the ear canal for 30 days so re-administration is not necessary.

This medication has not been tested in patients with a perforated tympanic membrane, or in animals that are pregnant or lactating. Safety studies have shown that when five times the recommended amount of medication is applied every two weeks for three applications patients can experience a dose dependent suppression of the adrenal cortical response to ACTH stimulation and have clear ear exudate and ear wetness. At the recommended dosing administration, no elevations were seen in the liver enzymes but thickening of the tympanic membrane was noted in one patient.

Sublingual immunotherapy (SLIT)
Allergen specific immunotherapy in veterinary and human patients for many years relied on the administration of subcutaneous injections. However, recently in both fields there has been evidence that allergens administered directly into the oral cavity can be well tolerated and effective for the treatment of spontaneous atopic dermatitis. In the veterinary field the clinical studies are limited to one in particular out of the University of Wisconsin where 10 dust mite sensitive dogs with Atopica dermatitis underwent a 6-month trial of SLIT. During the initial phase of this study, corticosteroids were needed to provide temporary comfort for patients while the immunotherapy was being introduced. However, after 4-6 months into the immunotherapy 4/10 patients stopped steroids all together and maintained comfortable and another 4/10 had a reduced steroid intake.
In the another clinical trial, 49% of 47 dogs that had failed injection immunotherapy responded to SLIT that was started with the same ingredients after they failed the injection route. This is consistent with experimental evidence that shows that the mechanism of SLIT is somewhat different than that of injection immunotherapy. Side effects seen with SLIT include facial pruritus, vomiting/diarrhea, and increase in clinical signs.

**Prescription Diet® Derm Defense™ made by Hills**

The goal of nutrition management for canine atopic dermatitis is to inhibit inflammatory response, stabilize the skin barrier and support skin and coat health. Hills has recently released this diet to aid in the treatment of the atopic patient and is meant to be used once adverse reactions to food has already been ruled out. This diet has been fortified with what hills is calling the Histaguard Complex™ which is a proprietary blend of whole egg, antioxidants, Vitamin E and polyphenols. These ingredients are meant to stabilize inflammatory cells and to decrease their histamine and cytokine release. Components within eggs have been shown to have an immunomodulation and anti-oxidant effect. Hills et al performed an internal study where dogs were divided into three groups; one ate a diet without egg, another group ate a diet without egg and was given an immunosuppressive doses of steroid, and the last group ate a diet with egg. This study was for a period of 12 weeks and the group that ate the diet enriched with eggs and the steroid receiving groups each had significant decreases in their wheal diameter and thickness.

Polyphenols, which can be found in the histaguard complex™ have been found to play an inhibiting role in the presentation of allergens to the immune system, an inhibitory role in T cell release of cytokines, inhibition on B cell production of IgE and inhibition of degranulation of mast cells. In addition, these polyphenols have anti-oxidant activity limiting the free radical cell injury that can occur.

This diet is also fortified with Vitamin E which has been shown to be clinically effective for the treatment of atopic dermatitis. One study reported low serum Vitamin E concentrations in canines with atopic dermatitis. When these patients were supplemented with 8.1IU/lb of Vitamin E they developed lower CADESI scores over time.

Omega Fatty acids levels also play a critically important role with this diet. Omega 3 and 6 fatty acids are important in skin healing and its resistance to producing inflammatory cytokines. When choosing a diet or a supplement one would want low total Omega6 to omega 3 ratio because this is considered more anti-inflammatory. While total omega 6 intake can be important for minimizing transepidermal water loss and repairing epidermal defects. In terms of actual fatty acid amount, it has been discussed that 180mg/10lb is the ideal amount of EPA levels for allergic patients and per feeding recommendations Derm Defense™ has 252mg/10lbs.

This diet has undergone several clinical studies, with the main one being an 8 week feeding study of atopic patients. During this study all patients were allowed to be on concurrent allergy medications (except oclacitinib) and the diet was part of the multimodal approach to therapy. At the end of the 8 weeks 65% of veterinarians and owners felt the diet made enough of a difference to warrant continued use.

**References**

13. MORRIS DJDaM. Multicentre open trial demonstrates efficacy of sublingual immunotherapy in canine atopic dermatitis. 7th World Congress of Veterinary Dermatology, July 24–28, 2012.
The Pemphigus complex is a group of autoimmune skin diseases that can affect dogs, cats, horses, people, and rarely goats. By far the most common disease of this group is pemphigus foliaceus (PF), with pemphigus vulgaris (PV), pemphigus erythematosus (PE), paraneoplastic pemphigus (PNP) and pemphigus vegetans (PVeg) being considered rare. PF was first seen in the canine species in 1977 by Halliwell and Goldschmidt and the first reported case of Feline PF was in 1982. PF in animals is a pustular and crusting disease rather than a vesicular disease as seen in humans.  

Incidence/prevalence
When looking at the Incidence of this disease it is difficult since there are only a few studies and there may be differences based on regions. It is suspected that PF accounts for up to 1/3 of all autoimmune diseases seen in the canine. Canine breeds that genetically predisposed include: Akitas, Chow Chow, Bearded collie, Newfoundland, Schipperke, English bulldogs and Dobermans.

Pathogenesis
PF is associated with acantholysis which occurs when there is a loss of adhesion between keratinocytes. This loss of adhesion results from disruption of desmosome junctions. Cadherins are the structures that bridge the gap between two adjacent keratinocyte cell membranes and are very important adhesion proteins. They consist of desmogleins (Dsg1–3) and desmocollins (Dsc1–3). These are the targets in pemphigus with the major antigen in canine PF appearing to be Dsc1.

Clinical lesions
The main clinical feature are pustules (vary in color) that develop in waves and evolve rapidly into crusts and sometimes erosions. They are present on the face, dorsal muzzle, peri-ocular skin, pinnae and planum nasale. Foot pads can also have extensive hyperkeratosis/crusting and fissuring. Pruritus can be present in 25-50% of cases and generalized erythema can also be seen. Some patients can also present with more systemic signs including anorexia, fever, depression and weight loss.

Diagnosis
Diagnosis requires biopsy. Since dermatophytosis can sometimes mimic clinical signs and histopathology (especially in cats) sometimes special stains are needed. In-house cytological examination of pustule contents will demonstrate acantholytic keratinocytes either individually or in rafts. There may also be extensive amount of non-degenerative neutrophils.

Treatment
The first step in the treatment of any autoimmune disease will be to perform baseline serum chemistry, complete blood count and a urinalysis in order to have a reference once treatments are started. In addition, once must ensure that any recently used medications that could have been implicated as a cause of a drug induced pemphigus reaction are stopped.

Antimicrobials
Many times at initial presentation these patients are actively infected with either bacterial or yeast infections. Ideally I like to base my antibiotic choice based off culture given these patients are going to be immunocompromised for quite some time and so medications may need to be extended. Many times patients will appear to not respond to initial coarse of immunosuppressive medications and it is because their secondary infections have not been properly addressed.

Glucocorticoids
The main stay and the first drug of choice when dealing with pemphigus patients. One of the few times steroids should not be considered as first line therapy is if a patient is concurrently diabetic which does occur on occasion and represents a clinical challenge. Generally, once the diagnosis is established that patient is started at immunosuppressive doses of a glucocorticoid in order to get that patient into remission. The choice of glucocorticoid depends on the patient and the clinician. If that patient already has a tendency to develop PU/PD on steroids or has concurrent heart disease, I will tend to gravitate towards the medications that have less or no mineralocorticoid activity. Also many times it is it not uncommon for a patient to have a better clinical response with one steroid over another.

Dose
Prednisolone/Methylprednisolone/Prednisone are used between 2.2-6 mg/kg/day but this author rarely goes over 3mg/kg/day. The immunosuppressive doses of triamcinolone is considered to be 0.2-0.6mg/kg/day and dexamethasone at 0.2-0.4mg/kg/day. When used as sole therapy it is ideal to get to 1mg/kg/EOD for prednisolone/methylprednisolone; triamcinolone to 0.1-0.2 every 2-3 days.
and dexamethasone at 0.05-0.1mg/kg every 2-3 days at maintenance. It is not uncommon for feline patients to require significantly higher dose of oral steroids to achieve remission, immunosuppressive dosages range from 2.2 to 8.8 mg/kg/day for prednisolone. Two studies have shown that 33-38% of canine patients can respond with the use of glucocorticoids alone5,6. I personally feel that felines many times will respond to steroids alone and this percentage may be higher is this species (around 65% or higher).7

**Monitoring**

In the ideal situation the immunosuppressive doses are continued for 10-14 days and then gradually tapered to maintenance level over a period of 6-12 weeks. This requires recheck examinations every 2 weeks for the first 2-3 months in the best case scenario. At each recheck I recommend serum chemistry/complete blood counts to be performed and a urinalysis and culture done at 2-3 months into therapy. The urine culture is to ensure that a patient has not developed a urinary tract infection that can commonly occur with long term steroid use8. The serum chemistry and CBC is to ensure there are no signs of hyperglycemia or severe hepatic dysfunction. At each recheck cytology is performed to evaluate the presence or absence of acantholytic cells and bacteria/yeast. If a large number of acantholytic cells are found generally I will continue the immunosuppressive doses for 2 more weeks and then recheck the patient two weeks later.

If unable to taper the dose of steroids due to lack of improvement of clinical signs or worsening of clinical disease upon taper one must either add in additional immunosuppressive medications or change the formulation of steroids.

**Adverse events**

Complications with steroids are vast given their general mechanism of action. Given the haptic changes that occur with glucocorticoids and many of the other immunosuppressive drugs it may be beneficial to also start hepatic support medications (SAM-E) at the time of diagnosis. Many patients will also suffer PU/PD/PP/panting, muscle atrophy, poor dull scaly hair coats, wt gain, behavior changes, increased risk for infections (bladder infections, demodicosis, dermatophytosis), comedones, atrophic skin, calcinosis cutis, atrophic scars, milia GI ulcerations, diarrhea and and decreased thyroid hormone, adrenal gland suppression, Diabetes mellitus.

<table>
<thead>
<tr>
<th>Medication</th>
<th>Glucocorticoid activity</th>
<th>Mineralocorticoid activity</th>
<th>½ life (hours)</th>
<th>Equivalent dose mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortisol</td>
<td>1</td>
<td>1</td>
<td>8-12</td>
<td>20mg</td>
</tr>
<tr>
<td>Prednisolone/ prednisone</td>
<td>4</td>
<td>0.8</td>
<td>12-36</td>
<td>5</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>5</td>
<td>0.5</td>
<td>12-36</td>
<td>4</td>
</tr>
<tr>
<td>Triamcinolone</td>
<td>3-5</td>
<td>0</td>
<td>24-48</td>
<td>0.5-1</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>25-30</td>
<td>0</td>
<td>36-72</td>
<td>.75</td>
</tr>
</tbody>
</table>

Azathioprine (Imuran®)

Azathioprine (AZA) is considered an antimetabolite agent whose main mechanism of action involves mimicking natural molecules utilized in DNA and/or RNA replication. As a group they are most active in the ‘S’ phase of the cell cycle (when DNA is being synthesized). Immuran serves as fraudulent purine bases during DNA and RNA synthesis, resulting in dysfunctional nucleic acid strands in proliferating cells. The T-lymphocytes, T-cell dependent antibody synthesis, and cell mediated immunity) are inhibited, with very little direct effect on B-cells. AZA is metabolized into 6-mercaptopurine (6-MP) by the liver and then 6 MP is metabolized by three different enzymes. Two of these enzymes are xanthine oxidase and TPMT (thiopurine methyltranferase) which produce inactive compounds. In general, patients with low TPMT activity, have a greater incidence of bone marrow suppression, but also greater immuran efficacy. As a species cats have low activity of TPMT, hence this medication is not recommended for these patients. Dogs have variable amounts of TMPT activity levels similar to that seen in humans, which may explain why some canine patients respond better and/or develop more myelotoxicity than others. Giant Schnauzers are known to have very low TMPT whereas Alaskan Malamutes have very high TMPT activity1,9.

**Dose**

When used in combination with oral steroids the dose varies from 1 to 2.5mg/kg Q24 to 48 hours) or 50 mg/m2. Supplied as 50mg tablets and there is a very slow onset of action. Typically, beneficial response in seen within 6-12 weeks

**Monitoring**

CBC/chem after 2 to 3 weeks, then again in 1 month, then quarterly. Some clinicians monitor more frequently (Q2 weeks for the first 8 week). Watch the lymphocytes and platelet counts for decreasing trends, which may indicate when to decrease the dose.
Adverse events
Include bone marrow suppression and hepatopathy (contraindicated in cats). There has been an association with pancreatitis when used concurrently with prednisolone. Diarrhea is the most common side effect along with opportunistic infections. There has been rare hepatotoxicity that does respond to drug withdrawal.

Chlorambucil
This medication is considered to be an alkylating agent that affects disease by physiochemical interaction with pre-formed and developing DNA and RNA. These medications as a group exert their effect (cross-links, strand breaks) on all stages of the cell cycle (i.e., do not require an actively proliferating population). As a group they are cytotoxic to all lymphocyte populations (including B-cells) and very effectively suppress immunoglobulin secretion. The new formulation requires refrigeration. It is considered to be the drug of choice for cats. It can also be used in conjunction with steroids.

Dose
0.1-0.2 mg/kg q 24-48 hrs ONLY 2 mg tablets

Monitoring
CBC at 2 weeks and CBC chem. 4 weeks, then CBC at 8 weeks; Delayed action 2-4 weeks.

Adverse events
Myelosuppression, anorexia, vomiting, diarrhea

Cyclosporine
Cyclosporine is considered a calcineurin inhibitor that leads to the blocking of IL-2 transcription which results in impaired T helper and T cytotoxic lymphocytes (remember the principal action of IL-2 is T cell proliferation). Reduces production of IL-2, IL-3, IL-4, G-CSF and TNF-alpha as well as reducing the clonal proliferation of the cell. This leads to decreased clonal proliferation of B lymphocytes and indirectly also effects other cells, such as granulocytes, macrophages, NK cells, eosinophils and mast cells. Although initial studies have shown that food affects absorption when clinical efficacy studies were done with atopic patients no change was seen.

Dose
5-10mg/kg Po SID

Monitoring
CBC/chem/UA after first 1-2 months and then every 6 months there after

Adverse Events
GI disturbances (vomiting, diarrhea, decreased appetite), gingival hyperplasia, papillomatous growths, increased susceptibility to opportunistic infections, hypertrichosis

Tacrolimus
The topical calcineurin inhibitor preparation is used mostly in veterinary medicine for localized lesions of PF and PE. It is the first macrolide immunosuppressant discover. it was found in a soil fungus, although it is produced by a type of bacteria, Streptomyces tsukubaensis.

Dose
Generally used twice daily

Adverse events
Minimal

Tetracycline/doxycycline and Niacinamide
The mechanism of action of this pair of medications is not exactly known. Tetracycline/doxycycline have been known to have anti-inflammatory properties affecting complement activation, antibody production, chemotaxis, prostaglandin synthesis, and suppressing lymphocyte blastogenesis. Niacinamide blocks antigen and immunoglobulin E induced histamine release, inhibits mast cell degranulation and phosphodiesterase protease release. This pair does have a delayed onset of action and generally beneficial response is seen after 6-12 weeks.

Dose
Doxycycline 5mg-10 mg/kg Po BID and Niacinamide is dosed at 250mg PO TID less then 10kgs; 500mg MG/KG greater then 10kg

Monitoring
Serum chem and CBC every 6 months

Adverse events
Vomiting, diarrhea are the most common Doxycycline can also cause esophageal stricture in cats and dogs
Mycophenolate Mofetil

Derived from the fungus *Penicillium stoloniferum* and is metabolized in the liver to mycophenolic acid (MP). This compound is a potent and reversible uncompetitive inhibitor of inosine-5’-monophosphate dehydrogenase (IMPDH). This inhibition leads to the the synthesis of guanine being blocked and prevents DNA and RNA synthesis. Cytotoxic to cells that rely on *de novo* purine synthesis (such as T and B lymphocytes)\(^1\).

**Dose**

22-39 mg/kg daily divided into q8 hour dosing; available in 250 and 500 mg. tablets

**Monitoring**

No clear protocol set, Complete blood count and serum chemistry q2-4 weeks for the first 2-3 months then every 6 months

**Adverse events**

Myelosuppression, Gastrointestinal upset: vomiting, diarrhea, anorexia and Increased risk of infections (urinary tract, skin, etc.) The concurrent use of mycophenolate and azathioprine is not recommend based off their similar mode of action\(^12\).

Leflunomide

Is a pyrimidine synthesis inhibitor that works by inhibiting the mitochondrial enzyme dihydroorotate dehydrogenase. This enzyme is involved in the *de novo* synthesis of the pyrimidine ribonucleotide uridine monophosphate (rUMP). Also Antagonizes action of IL-3, IL-4 and TNF-\(\alpha\)

**Dose**

2-4 mg/kg per day\(^13\)

**Monitoring**

No set protocol, CBC serum chem UA after 2 weeks and then every 3 weeks for 3 months. In one paper leflunomide dosage was decreased by 25% every 4 weeks for the first 4 months in order to achieve a trough level of approximately 20 micrograms/mL (leflunomide trough levels were based on studies of the canine renal transplantation model); then the dosage was decreased every 8 weeks until discontinuation after 10 months of therapy\(^14\).

**Adverse events**

Hepatotoxicity, myelosuppression (leukopenia, anemia and thrombocytopenia), recurrent infections, pneumonia and cutaneous drug eruptions

Human IVIG

Sterile purified IgG that is pooled from human plasma, that may also contain traces of IgA and IgM\(^15\). The exact mechanism of action is not known so there are several theories on how this medication works. Blocks the Fc receptors on antibiotics and eliminates circulating immune complexes, suppressing anti-idiotypic autoantibodies, inhibits complement mediation damage, and blocks the cell surface death receptor Fas have all been discussed\(^16,17\).

**Dose**

0.5-2.2 g/kg given slowly IV over 6-12 hours\(^14,18\).

**Monitoring**

Has a similar set up and monitoring as a blood transfusion to ensure no signs of anaphylaxis.

**Adverse events**

Allergic reaction, In human’s hypertension, nausea, tachycardia can occur. There has only been limited studies on the re-administration of IVIG to canine patients and this should be done with caution.

References

Managing Chronic Otitis: The Keys to Getting Started on the Right Foot
James Noxon, DVM, DACVIM
Iowa State University
Ames, IA

The 2013 and 2014 data from Veterinary Pet Insurance lists ear infections as the number TWO reason that dogs went to veterinarians (after “skin allergies”) for veterinary care. In addition, Banfield data indicates that otitis was the second most common diagnosis made in affiliated hospitals in 2011. This data has been similar every year since 2005, with otitis being the #1 or #2 most common presenting complaint in dogs, year after year.

There are many, many important concepts about otitis that can literally make the difference in practice. Knowledge can, in fact, change your entire attitude about dealing with ear disease.

Information needed to manage otitis (getting started on the right foot)

#1 – Understanding structure and function

The ear consists of the pinna, the external ear canal, the middle ear, and the inner ear. There are major variations in the anatomy from breed to breed, especially with respect to the length and diameter of the external ear canal. These variations will affect predilection for disease, diagnosis, and treatment. For example, it can be very difficult to fully examine the external canal of the ear of an Irish setter, for it can be very long!

The external ear canal consists of skin overlying the auricular and annular cartilages. It has a vertical component and a horizontal component. The vertical component is formed by the auricular cartilage. The annular cartilage is the rolled, tube-like cartilage that extends from the auricular cartilage at the base of the vertical ear canal to the temporal bone. The auricular cartilage overlaps the annular cartilage with a fibrous band, which allows for flexibility in movement.

Anatomically, the vertical canal is more open and larger in volume than the horizontal ear canal. There is a depression or pocket at point where the auricular and annular cartilages overlap (i.e., the “opening” of the horizontal canal). The entrance to the horizontal canal is often elevated and requires manipulation of the otoscope in order to pass it into the horizontal canal. There is actually a fold of skin (overlying cartilage) on the dorsal aspect of the canal that must be bypassed in order to slip the otoscope into the horizontal ear canal. Mechanical irritation (e.g., during otoscopic examination) of this fold will cause startle the patient and result in poor patient compliance with otoscopy.

The skin lining the ear canal has sebaceous glands and apocrine (i.e., ceruminous) glands throughout the length. Sebaceous glands are found in the superficial part of the dermis with the apocrine glands located deeper. These apocrine glands can open directly onto the surface of the skin or in the hair follicle. Hair follicles are found throughout the length of the ear canal in most breeds, but there is breed variation as to the type of follicles and their density.

Ear wax is the mixture of apocrine (cerumen) gland secretions, sebaceous secretions, and epithelial cells. There is a natural movement of sebum outwardly in the normal ear, facilitating natural cleaning and removal of sebum.

The lipid portion of ear wax is derived from sebaceous glands and contains various waxes and fatty acids, many of which are bacteriostatic and fungistatic. The lipid portion of cerumen is responsible for controlling microorganisms. The apocrine secretions (from “ceruminous glands”) produce a water-based secretion that contains phospholipids and IgA, which also contributes to the defense of the ear. Epithelial cells contribute to the texture and consistency of the wax. Increased epithelial cell production in the ear will produce a thicker, pasty ear wax.

The tympanic membrane is at the end of the external ear canal. On otoscopic examination, the tympanum appears as a vertically aligned structure, but it actually is sloped at approximately a 30° angle, with the top towards the viewer. The tympanic membrane consists of two parts. The pars tensa is the tightly stretched, clear to opaque whitish section of the tympanic membrane. Embedded within the pars tensa is the handle (aka manubrium) of the malleus, the largest ossicle of the middle ear. The malleus is curved, with the concave section pointing rostrally. The pars flaccida is the dorsal-rostral component of the tympanic membrane. It appears pink and there are often small capillaries visible on the surface of the membrane. The pars flaccida often bulges out and may be seem moving with respiration, in a movement that resembles the bulging throat of a bullfrog!

The tympanum in the cat is much more transparent, and thus is often thought to be absent. The malleus is straighter than in the dog and the pars flaccida is generally not visible. Cats also have a bony septum in their middle ear that runs rostral to causal….and this septum tends to obstruct the view of the middle ear during otoscopic examination and creates an obstruction for materials inside the middle ear. The two-chambered nature of the middle ear in the cat impairs our ability to clean and perform various procedures in the middle ear in cats.
#2 – Understanding the pathophysiology of otitis

By now, everyone should know about the concepts on the pathophysiology of otitis as introduced by Dr. John August. He recommended dividing the pathogenic factors of otitis as follows:

1. predisposing factors: these are conditions that “set the ear up” for inflammation. They include conformational changes, behavior, and previous treatments.
2. primary factors: these are those conditions that initiate inflammation in the ear. They include allergic diseases, foreign bodies, ectoparasites, autoimmune and other inflammatory skin disorders, and trauma.
3. perpetuating factors: these factors keep the inflammatory process active and often make it significantly worse. Perpetuating factors include bacterial infections, yeast infections, hyperplastic changes, and otitis media.

Simply put, there is a “WHAT” and a “WHY” when dealing with ear disease. Clinicians must address both or the problem will fail to resolve or recur.

#3 – Understanding pathologic changes in the ear

Once the otitis has begun, certain pathologic changes occur that initiate a cascade of events that make the ear more hospitable for microorganisms and reduce the lumen size of the ear canal. Inflammatory changes are accompanied by pain, and progressive disease leads to loss of hearing. It has been determined that the pathologic changes in the ear do reduce acuity of hearing, and that some of that hearing loss is reversible, as the pathologic changes are reversed.

With inflammation comes edema and infiltration of inflammatory cells. Secretion of various growth factors will result in epidermal hyperplasia and hyperkeratosis, resulting in macrofissures on the surface of the skin and increased deposition of cornified keratinocytes in the lumen of the ear. As inflammation progresses, there is fibroplasia (i.e., fibrosis) of the dermis and subcutis. Chronic inflammation of the cartilage will result in ossification of these structures.

Within the dermis, it has been shown that apocrine glands increase in size in otitis externa. The intense inflammation around apocrine glands, combined with epidermal hyperplasia (papillary proliferation) results in occlusion of ductal openings on the skin and hair follicles and may predispose the gland to rupture. When the apocrine glands rupture, there is infiltration of lymphocytes, neutrophils, mast cells, and macrophages into surrounding tissue. It would appear that the disruption of these glands significantly contributes to the inflammation, pain, and fibrosis. Interestingly, sebaceous glands remain the same size, even in chronic otitis externa, though there is a qualitative change in sebum production. The net result is decreased lipid content of cerumen in ears with otitis externa. Since lipid secretions of the skin have barrier and antimicrobial functions, there is speculation that this change further contributes to secondary infections in otitis externa.

Finally, biopsy of the ear canal in chronic otitis externa will reveal folliculitis and furunculosis. With furunculosis there is release of keratinized materials into the dermis, and the net result is a foreign body-type reaction. Furunculosis is common in ceruminous otitis externa associated with familial seborrhea of the American cocker spaniel.

#4 – Knowing the goal: Restoring defense mechanisms of the ear

The ear does have an effective defense system. First there is an inherent self-cleansing mechanism. Debris, including desquamated keratinocytes and wax, naturally moves from deep into the canal to the opening of the canal. Anything that blocks this movement, such as a foreign body or scar tissue, will predispose to infections. Second, ear wax is an amazing antimicrobial material, along with its other functions. Third, the hair in the canal and at the opening of the canal does help to restrict access into the canal form the outside. (On the other side of things, it can also cause problems by holding material in the canal that should be extruded.) Fourth, the very conformation of the ear (canal and pinnae) serves to restrict access into the canal. Again, this has both good and bad aspects.

Diagnostic approach to otitis

Collection of a thorough dermatologic history is crucial to evaluate the patient for the primary factor (i.e., underlying cause, or the “why”). When it comes to managing the perpetuating factors (e.g., current infections), it is helpful to know what medications have been used in the past. This includes amounts, frequency, and duration of each treatment. The physical examination includes inspection and palpation of the entire ear canal. The mouth should be opened wide to evaluation for bullae pain, one possible indicator of otitis media.

Otoscopy should be performed on all cases, and repeated at each recheck of the patient. Both ears should be examined, even if the client believes the problem is unilateral (one ear is often worse that the other). Handheld otoscopes are very useful and there are different styles that have different levels of magnification. Several commercial video otoscopes are now affordable and they provide much better visualization down the canal.

Cytology is the key diagnostic procedure in otology. Cytology should be done on both ears and repeated at every recheck examination…because things to change in the canal. Samples are usually collected by passing a cotton-tipped applicator gently into the ear canal to the beginning of the horizontal canal. If resistance is encountered while passing the swab, it should not be advanced further! The swab is gently rotated then withdrawn and used to make “roll preps” on a clean glass microscope slide. The slide is then stained (with the stain of choice in your practice) and examined under the microscope.

275
A couple of tips for cytology:
1. Use a clean glass slide (wipe the slide with a gauze to make it is clean)
2. Use firm pressure to roll the swab (this will increase the adhesion of material)
3. Dip or place slides into jars of stain or fixative VERY gently. Do not move the slide up and down after the initial placement…you may gently sway the slide in the jar to distribute stain, if needed.
4. Rinse the slide immediately after the thiazine (blue) stain (when using Diff-Quik stain), BUT do not let the rinse water hit the sample directly.
5. Air dry or use a blow dryer with the heat coil turned off to rapidly dry the slide. Do not overheat (or the sample may be ruined!)

<table>
<thead>
<tr>
<th>Tips:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Make two ear prep slides on each case and examine before cleaning the ears, in the event that a culture is indicated.</td>
</tr>
<tr>
<td>2. Stain one slide with Diff-Quik and save the other for a Gram stain, to be done if rod-shaped organisms are present on the initial slide.</td>
</tr>
</tbody>
</table>

A normal ear may contain low numbers of bacteria (usually cocci) and yeast. However, the absolute number (e.g., number of organisms per field of view) is not important, since we all make slides differently. The cytologic findings are correlated with the clinical findings and a decision made to treat is based on all data.

Bacterial culture is indicated when: 1) the cytology shows a uniform population of rod-shaped bacteria (probably *Pseudomonas* spp.), 2) the infection has failed to respond to “standard-of-care” therapy, 3) when you have a known resistant organism (generally based on previous culture results). Imaging of the ear can also be very helpful. Radiography may help identify bony changes in the bullae that might reflect otitis media. Computerized tomography provides much better detail and is the author’s imaging of choice, due to relative low cost and high degree of detail provided. Magnetic resonance imaging is also very helpful, however the cost is significantly higher than CT scanning.

**Client education and communication**

Client education starts on day 1….the first time you see a client/pet with otitis. Client education should include:
1. Some basic information about the pathophysiology of otitis (really important),
2. Information about your plan for their pet (i.e., identify secondary issues, treat those, then look for the underlying cause),
3. Diagnostic findings on their pet at the first visit,
4. Why the recheck exam is important and what will happen at that appointment (repeating diagnostics, switching from treatment to a maintenance plan, additions testing for primary factors, etc.),
5. The long-term picture of otitis

It is very helpful to use analogies when speaking to clients. The author uses the analogy of archeology: dermatology and otology problems are like archeology. That is, clinicians must keep on digging until they find the underlying civilization (i.e., primary factor). If the clinician does not address the underlying problem, then the perpetuating (i.e., secondary) factors will fail to respond to treatment or will recur. So, it makes sense to explain this to clients at the beginning, understanding that it is unlikely that a client will give consent to spend a lot of time and money searching for a cause of first-time otitis. But….you plant the seed by giving them the education about the pathogenesis of otitis. That way, when the problem recurs (notice I didn’t say “if”), they just may remember that you tried to explain this to them.

Ear models are great for explaining otitis. Several companies have provided these to veterinarians in the past, so ask your reps about one! It is especially helpful to explain the “L” shaped ear canal and why we have to medicate the way we do.

Last, video otoscopes also help the clients be more involved. Clients LOVE seeing their pet’s ears before and after cleaning or before and after treatment. Letting clients see the ears will definitely help to convince them that cleaning and medications are warranted.

The clinical effects of client education include: better client compliance, more cooperative clients, and better success. Everybody wins.
Topical therapy is the most commonly used treatment for otitis externa. Selection of active ingredients and treatment protocols for veterinary otic preparations tend to have been driven by the pharmaceutical industry based on guidelines to facilitate approval by various governmental and regulatory agencies. The term best practices implies a method or technique set forth by an authority that has consistently shown superior results to those achieved with other means, and that are used as a benchmark. Ideally, these serve as clinical treatment guidelines and are integral to evidence-based practice of medicine.

Important concepts prior to treatment
1. A reminder of the structure and function (anatomy and physiology) of the ear is crucial. Specifically, the shape of the ear canal provides some challenges for topical therapy.
2. A reminder of the pathophysiology of otitis is also important: we have predisposing factors, primary causes (or underlying factors), and perpetuating factors (secondary causes) in otitis. There is a difference between short-term management (and success) and long-term management (and success).
3. Client education is paramount. It is essential that clients understand the two points listed above AND the goals and expectations of treatment.
4. We need to have collected the right information to allow us (the veterinarian) to “choose wisely” the best topical medication for each possible combinations of problems that may be factors in each patient. We need to know “what” is going on in the ears.

Cleaning the ears: “Preparing to succeed”
Cleaning the ears is an important and crucial component of effective management of chronic ear disease in dogs and cats. Cleaning the ears is important for the following reasons:
1. Cleaning removes debris, such as wax, that may cause irritation of the ear canal.
2. Cleaning removes debris that will block movement of medication into the horizontal canal and the self-cleansing mechanism.
3. Cleaning removes debris (e.g., pus, biofilm) that can interfere with the activity of topical (and systemic) otic medications.
4. Cleaning may help to lower the burden of bacteria in the ear.
   The cleaner you get the canal, the better the chances are that your topical medication will work. Keep in mind that the efficacy of some topical medications, such as polymyxin B sulfates and some aminoglycosides, is dramatically reduced in the presence of pus! So, it is to your patient’s and client’s advantage to start with an ear cleaning.
   It is your choice, as the veterinarian, on which type of ear cleaning you select. For mild cases, it may suffice to use a basic technique of filling the canal with cleanser, massaging the canal, then removing excess cleanser and debris with a cotton ball…repeated until otoscopic exam confirms that most of the debris has, in fact, been removed. However, I recommend a deep ear cleaning (or ear flush) with the patient under general anesthesia if you are unable to definitively see the ear drum...or at least enough to confirm that it is intact.

Best practices for topical management of otitis externa
Overall, the long-term success of medical management of otitis externa depends on the following considerations:
- Obstructions, such as hair and wax, should be removed to allow distribution of medications deep into the ear canal
- Topical medications should be selected based on consideration of the active ingredients and data supporting the use of that agent for secondary infections or perpetuating factors
- The integrity of the tympanic membrane should be considered when selecting topical medications
- The formulation of the medication should allow the product to distribute deep into the canal and provide adequate coverage of the surface area of the ear canal
- Topical medications must be administered using proper technique to ensure delivery of medicine throughout the full extent of the external canal. This often includes “positional instillation” of medicine, which means positioning the animal (on its side, for example) to allow deeper movement of the agent into the ear canal.
- Adequate volumes of topical medications must be administered to reach the deeper aspects (proximal) of the ear canal
Treatment of infections should be continued until the infection is cleared. Generally, this requires a treatment period of 3-4 weeks.

Ear medications are most often in the form of an ointment (emulsions of lipid in water) or as a solution (aqueous or other carriers). Emulsions containing lipids will enhance penetration of the active ingredient into the skin of the ear; however, most of these ointment formulations are so viscous, that they fail to penetrate down deep into the ear canal. They are especially ineffective in the presence of a heavy growth of hair in the canal. Less viscous medications are more likely to allow medication to distribute deeper into the canal, especially when there is significant hair in the ear canal or when the canal is hyperplastic. There is little data on the overall effect of viscosity on “spreadability” or distribution of topical medications over the skin that lines the ear canal.

In all cases when topical therapy is used, the owners MUST be educated about application of medications. This should include having the owner instill medication, IN THE PRESENCE of the veterinarian or technician. Owners should be taught to massage ears for 15-30 seconds after instilling medications…and to use proper amounts of medications. Once-daily treatment is generally sufficient for most cases of otitis, though severe infections may benefit from twice daily treatment. Treatment should be continued until there is no clinical or cytologic evidence of active disease. The minimum recommended treatment time (with topical therapy) is 30 days.

**Dose (volume) recommendations**

- Small dogs (<15 kg) 0.4-0.5 ml
- Medium dogs (15 – 20 kg) 0.7-0.8 ml
- Large dogs (> 20 kg) 1.0 ml

The volume of medication applied into the ear during treatment appears to be critical. Dosing syringes work well to accurately measure volumes of otic medications. Failure to apply sufficient quantities to penetrate to these areas seems to be a major cause of treatment failure. Volumes recommended in this paper to achieve adequate penetration down the canal are based on existing literature and pilot studies performed by the author. You may increase movement of otic medicine deeper into the canal by using “positional installation” and by massaging the ear for 15-30 seconds after instillation.

Keep in mind that higher volumes of otic medication may increase the likelihood of absorption of otic medications, especially glucocorticoids. It is important to understand that there may be systemic side effects as more potent glucocorticoids are used.

**Table 1. Commercial veterinary otic preparations**

<table>
<thead>
<tr>
<th>Product</th>
<th>Manufacturer</th>
<th>Drops/ml*</th>
<th>Label dosing</th>
<th>Maximum tx time (days)‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aurizon®**</td>
<td>Vetoquinol</td>
<td>?</td>
<td>10 drops once daily</td>
<td>7-14</td>
</tr>
<tr>
<td>Baytril® Otic</td>
<td>Bayer Animal Health</td>
<td>30</td>
<td>&lt;35 lbs: 5-10 drops twice daily</td>
<td>14</td>
</tr>
<tr>
<td>easOtic®</td>
<td>Virbac Animal Health</td>
<td>NA</td>
<td>1 pump daily</td>
<td>5</td>
</tr>
<tr>
<td>Mometamax®</td>
<td>Intervet/Schering Plough Animal Health†</td>
<td>40</td>
<td>&lt;30 lbs: 4 drops once daily &gt;30 lbs: 8 drops once daily</td>
<td>7</td>
</tr>
<tr>
<td>Otomax®</td>
<td>Intervet/Schering Plough Animal Health†</td>
<td>37</td>
<td>&lt;30 lbs: 4 drops twice daily &gt;30 lbs: 8 drops twice daily</td>
<td>7</td>
</tr>
<tr>
<td>Posatex™</td>
<td>Intervet/Schering Plough Animal Health†</td>
<td>39</td>
<td>&lt;30 lbs: 4 drops twice daily &gt;30 lbs: 8 drops twice daily</td>
<td>7</td>
</tr>
<tr>
<td>Surolan®</td>
<td>Vetoquinol</td>
<td>45</td>
<td>5 drops twice daily</td>
<td>7</td>
</tr>
<tr>
<td>Tresaderm®</td>
<td>Merial</td>
<td>40</td>
<td>5-15 drops twice daily</td>
<td>7</td>
</tr>
</tbody>
</table>

* Determined manually by author. Estimates ± 2 drops/ml. ** Not available in USA  † Merck Animal Health USA   ‡ Label instructions
<table>
<thead>
<tr>
<th>Product</th>
<th>Manufacturer</th>
<th>Active ingredients</th>
<th>Labeled dosing</th>
</tr>
</thead>
<tbody>
<tr>
<td>KetoCort®</td>
<td>TrilogenPharma</td>
<td>Ketoconazole, hydrocortisone</td>
<td>Clean ears and dry. Instill adequate amount and repeat as necessary.</td>
</tr>
<tr>
<td>Osurnia®</td>
<td>Elanco</td>
<td>Florfenicol, terbenifine, betamethasone</td>
<td>Clean ears and dry. Instill one tube, massage 1-2 minutes. Repeat in one week.</td>
</tr>
<tr>
<td>Claro™</td>
<td>Bayer</td>
<td>Florfenicol, terbenifine, mometasone</td>
<td>Clean ears and dry. Instill one tube.</td>
</tr>
</tbody>
</table>

The integrity of the tympanic membrane is critical in determining the best treatment options for a patient with otitis. The possibility of ototoxicosis is greatly enhanced if the medication is instilled directly into the middle ear. The best practice is to avoid topical therapy, if the tympanic membrane is torn or absent. However, there are some clinical indications, based entirely on anecdotal evidence, that vinegar: water (1:2) and enrofloxacin (parenteral formulation) are fairly safe. Topical therapy is considered sufficient to manage most cases of otitis externa, if the principles of therapy discussed early are followed. In general systemic therapy is indicated when:

- The infections are recurrent and severe
- There are concurrent infections elsewhere, such as the skin, that would respond to the therapy
- When the owners are incapable of treating topically (e.g., arthritis, elderly owner)
- When the patient is entirely uncooperative
- When there is severe hyperplastic changes in the canal that preclude the ability of topical medications to distribute deeper into the ear canal

Systemic antibacterial therapy is indicated when inflammatory cells are seen on cytology, when a pure infection of a gram-negative bacteria is present, in recurring bacterial infections, when ulcers are present in the external ear canal, or when systemic signs accompany the otitis. Systemic therapy may or may not be indicated when otitis media is present. The antibiotic selection depends upon the organism isolated. Drugs should be dosed at the high end of the recommended range—always go up on pill size, never skimp on systemic drug doses! Drugs should be administered for a minimum of three weeks, then the patient re-examined and evaluated with cytology and/or culture.

Lastly, you should consider the goal of your therapy. Practically speaking, it is the improvement of the clinical condition of otitis: reduced swelling, erythema, pain, and restoration of function. However, for longer-term success in managing ear disease, it is important to CLEAR the infections. This generally requires longer treatment periods and higher doses.

**Future considerations**

There are several areas where additional studies could be greatly beneficial. For example, there is little data on contact times required, in vitro and in vivo, for effective killing/clearance of various bacteria and yeast. In addition, it would be helpful to better understand the distribution of topical medications, both immediately after instillation and after 12 and 24 hours following administration. We have little data about the duration of inhibitory concentrations of antimicrobials over time after topical application.

**Selected references and recommended readings**

Most difficult problems in otology can be resolved if best practices are followed, however, there are several conditions which seem to be considered more difficult and frustrating, depending on the situation. They include:

1. management of allergic ears
2. management of recurring yeast infections
3. control of specific bacterial infections, such as Pseudomonas infections
4. management of ceruminous otitis (seborrheic ear disease)
5. control of severe hyperplastic changes
6. treatment of otitis media

In this session, we’ll address Pseudomonas infections and hyperplastic changes and talk about strategies to prevent recurrence.

**Pseudomonas infections**

*Pseudomonas aeruginosa* is a hydrophilic, beta-lactamase producing, gram negative bacterium that is commonly associated with otitis externa and media in the dog. Many strains of Pseudomonas (up to 40% of isolates) are known to be potent producers of biofilm, a matrix that coats the surface of the tissue and “protects” the organisms from antimicrobial activity. Biofilm-producing bacteria had significantly higher MICs for common pathogens isolated in canine otitis. Biofilm is known to physically block penetration of compounds, such as antibiotics and antiseptics, and create concentration gradients of these agents that reduce efficacy and may lead to antimicrobial resistance. Remove or reduction of biofilm is a key component of managing patients with *Pseudomonas* infections.

Proper cleansing of the ear, systemic therapy with an appropriate antimicrobial agent, and management of the primary factor are also part of managing *Pseudomonas* infections of the ear! Aggressive and thorough cleaning of the ear is crucial to remove the biofilm, and thus allow the treatment of choice to be effective. There are limited studies reported at this time demonstrating the effectiveness of various cleansers or otic medications in the presence of biofilm.

**Antibiotic therapy of Pseudomonas otitis**

Antibiotic treatment of recurring *Pseudomonas* infections (or other resistant gram negative infections) should be based on cytology and culture results. Appropriate antibiotic stewardship is strongly encouraged when making the clinical decision to use an antibiotic.

Some topical treatment options include:

- Gentamicin (Otomax/Mometamax/Posatex-ScheringPlough-Merial) is an effective antimicrobial for many *Pseudomonas* infections. Unfortunately, the labeling on this product in the USA minimizes its effectiveness (dose volume, maximum treatment period).
- Topical tobramycin (available as generic ophthalmic drops)
- Polymyxin B (Surolan®-Vetoquinol). Many *Pseudomonas* isolates are sensitive to this antibiotic; however, polymyxin B sulfates are not active in the presence of suppurative inflammation. Synergy of polymyxin B and miconazole against *E. coli* and *Pseudomonas* isolates (but not *Proteus* isolates) from dogs with otitis externa has been demonstrated in vitro.
- Topical fluoroquinolone antibiotics (Baytril® Otic-Bayer, Aurizon®-Vetoquinol) are often effective for *Pseudomonas* infections.
- Other antibiotics from which topical otic medications may be formulated include amikacin, (1-2%), ceftazidime, imipenem and meropenem. The latter two drugs have restricted use in most hospitals (for life-threatening infections) to prevent resistance. Their use should be as a last resort and therapy should follow all principles of antimicrobial use to avoid contributing to bacterial resistance to these drugs.

Additional topical therapy includes agents that may not have direct antibacterial activity, but that are used to support other antimicrobial products.

- Tromethamine (Tris) edetate disodium dehydrate (EDTA), known more commonly as Tris-EDTA solution, is commonly used as adjunctive therapy for bacterial otitis. Several commercial products (e.g., TrizEDTA™ Aqueous Flush-Dechra, and T8 Keto® Flush-DVM) contain this solution. There is good evidence that the Triz-EDTA is highly effective for *Pseudomonas* when used concurrently with an appropriate antimicrobial (some fluoroquinolones or aminoglycosides), silver sulfadiazine, or chlorhexidine. Triz-EDTA alone is bacteriostatic in vitro, but is not bactericidal. Triz-EDTA has been shown in vitro to reduce the MICs for neomycin and gentamicin (but not enrofloxacin or polymyxin B) for biofilm-embedded bacteria. Additional studies show that Triz-EDTA enhances antibiotic efficacy of marbofloxacin and gentamicin against multidrug-resistant *Pseudomonas in vitro*. Clinically, these products are often
administered into the infected ear 15-30 minutes prior to an antibiotic; however, data suggests they may be administered concurrently. Tris-EDTA appears to be safe when instilled into the middle ear, but there is no evidence to support that clinical observation.

**Antiseptic therapy for Pseudomonas otitis**

Antiseptics are attractive alternatives to the use of antibiotics for control of bacterial skin and ear diseases. However, most studies involving their use for otitis are in vitro studies looking at MIC values. It is likely that the ultimate effectiveness of antiseptics will involve selection of the proper concentrations (to exceed MICs or minimum bactericidal concentrations) and also consider the contact time.

- Silver sulfadiazine (SSD), (Baytril® Otic-Bayer) or as a 1:9 dilution of the 1% silver sulfadiazine cream. SSD has been shown to be effective in vitro against *Pseudomonas*. Based on two studies, it appears that the MICs for *Pseudomonas* have increased in the past 30 years (from 7.5 ug/ml to 23.4 ug/ml); however, they are still low enough to easily treat ears topically with available products. Note: The addition of Tris-EDTA to SSD has been shown to decrease the MIC even lower.
- Acetylcysteine has been shown to have anti-*Pseudomonas* activity *in vitro*, with the MIC values for six isolates calculated to be 10.3 mg/ml. Clinical trials (in vivo studies) have not been reported.
- Aluminum acetate: Burow’s solution has been demonstrated to have activity against *Pseudomonas in vitro* and in some animal models of *Pseudomonas*-associated otitis media. Clinical studies are ongoing in dogs with *Pseudomonas otitis*. Interestingly, aluminum acetate is a component of many commercial products in the USA that are used for managing otitis.
- Chlorhexidine and other antiseptics / biocides have efficacy against *Pseudomonas* and have been combined in various ear cleansers with TrisEDTA for enhanced activity. There have been conflicting reports of the ototoxicity of chlorhexidine.

One very important key to successful treatment of *Pseudomonas* otitis, is the concurrent use of glucocorticoids, preferably systemically. Glucocorticoids reduce the pain that is associated with this condition- and thus will make application of topical medications easier and more effective. In addition, glucocorticoids reduce the inflammation, which also reduces the discomfort and swelling that accompanies this condition. The recommended dose of prednisone in dogs is: 1-2 mg/kg, PO once daily for 5-7 days, then every other day for 5 doses, then half of the dose every other day for 5 additional doses. Naturally, any allergy testing should be done prior to initiation of glucocorticoid therapy.

Patients with *Pseudomonas* infections tend to get other secondary infections, most often yeast infections, immediately after the *Pseudomonas* is cleared. Therefore, we often initiate prophylactic anti-yeast therapy as part of our maintenance therapy as soon as the bacterial component of the otitis is controlled.

Lastly, control of the underlying cause (or primary factor) is very important to prevent recurrence, and in some cases, may be necessary to get the problem under control.

**Hyperplastic changes**

Swollen ear canals are a major threat to the survival of the ear! Hyperplastic changes of the external ear canal include epidermal hyperplasia (e.g. lichenification), fibrosis, edema, glandular hyperplasia, and inflammation, especially folliculitis and furunculosis. Hyperplastic changes are perpetuating factors. They promote a microclimate favoring microbial growth (increased temperature and humidity) and physically prevent distribution of topical medications deep in the ear. In addition, they reduce the ability of veterinarians to adequately examine or clean the ear. Closure of the ear canal may be due to 1) edema and inflammation or 2) fibrous changes, including calcification of the canal. It is difficult clinically determine whether the hyperplastic changes are reversible (due to edema and inflammation) or permanent (fibrosis). To make that determination, the following is recommended:

1. Potent topical glucocorticoids are administered to reduce inflammation. The glucocorticoid is should in a vehicle that allows and facilitates deep movement into the canal (e.g., Synotic®-Ft. Dodge containing DMSO and flucinolone). An adequate volume should be instilled 1-2 times daily to reach the deeper areas of the ear canal. If flucinolone is not available, mometasone (Claro-Bayer) may be infused into the ear if the canal is patent enough to allow infusion.
2. Since distribution of a topical drug may not reach deep into the canal, concurrent administrations of a systemic glucocorticoid is recommended to reduce edema and allow for a proper examination or to allow medication to gain access to the ear. Assuming there are no medical conditions that may preclude their use, prednisone or prednisolone may be administered orally (1-2 mg/kg daily for 5-7 days, then q 48 hour for 5 doses, then half the dose every other day for 5 additional doses).

Patients are re-examined in 3-4 weeks. If the ear canal has opened (indicating the changes were primarily edema and inflammation), efforts should be directed towards identifying and managing the primary and perpetuating factors. If the canal does
not significantly open with topical and systemic administration of glucocorticoids, triamcinolone may be injected (0.05 ml/site) in a spiral manner in the most severe areas, in an attempt to reduce edema and inflammation. Alternatively, long-term administration of cyclosporine may benefit some of these ears. It is unclear whether any effect of cyclosporine is due to anti-inflammatory actions or control of underlying / primary factors of otitis. However, if the canal has become calcified, a total ear canal ablation is recommended.

**Preventing recurrence**

An important strategy for ALL ear infections is to aggressively treat and clear the infection using best practices as described previously. However, the next step in management of otitis is to recheck and re-evaluate the patient to determine if the infection has been reduced/suppressed, or cleared. There is a big difference.

A recheck examination should be performed in each patient at an interval when the veterinarian feels the infection should be cleared. At that time, the examination should include 1) history since treatment was initiated, 2) physical examination, 3) otic examination, 4) cytology of the ear, and in cases with recurring infection or gram negative bacterial infections, 5) repeated culture. If cytology and culture (when performed) are negative, we proceed to the next step.

Maintenance therapy is always begun on patients with chronic otitis as soon as the recheck examination suggests the infection is cleared. The goals of maintenance therapy include 1) keeping the ears clean, 2) control or decreasing pain and pruritus, 3) control or decreasing the number of infectious agents, and 40 promoting “normalization” of the ear. The principles include the intermittent use of cleansers and non-antibiotic therapeutics (e.g., antiseptics, non-antibiotic agents) to prevent recurrence of the infection OR to reduce the severity and frequency of secondary infections. Options maintenance therapy include use of cleansers proven to have antimicrobial activities (e.g. EpiOtic Advanced-Virbac; Malacetic Otic-Dechra). Ingredients with antiseptic properties include salicylic acid, boric acid, parachlorometaxylenol, and chlorhexidine. Other ear products and “flushes” that contain benzoyl alcohol (T8Keto-Bayer), aluminum acetate (Burrow’s solution, CortAstrin-VedCo) also have antibacterial and/or antifungal activity. Some otic products (MalAcetic Ultra-Dechra) contain azoles for managing yeast infections. We do not fully comprehend the ability of Malassezia pachydermatis to develop resistance to intermittent exposure to these agents, so caution should be the rule when looking for long-term maintenance of yeast infections.

**Ultimate control**

In the final analysis, identification and control of the underlying or primary factor of the otitis will lead to the best long-term management. However, some clients are unwilling or unable to pursue those factors due to financial consideration, medical philosophy, distrust of the motives of the veterinarian, or a lack of will. Maintenance therapy is ALWAYS combined with client education to achieve the best results for each patient.

**Summary**

Most difficult cases of otitis externa are not due to resistant organisms or strange circumstances. Most difficult cases develop when there has been a breakdown in communication or failure to strictly adhere to the best practices of ear management. Proper and thorough cleaning of the ears is a necessity in the management of chronic otitis externa. Infectious components of otitis can be managed and controlled, though in some cases, repeated trials may be required to identify the best treatment. Long term control of otitis externa or media requires identification and management of the primary factors.

**Selected references and recommended readings**


