Canine Atopic Dermatitis:
Integrating New Therapies into Your Strategy

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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 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, dermal 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

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 worse 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 needed but not as frequently as cytology. 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 farenhiet. 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

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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 chlortetracycline 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 for 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.

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

*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.

CPR for Sewer Ear:
How to Improve Your Outcome in Otitis Externa
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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 cause of otitis externa 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. <u>Is there an allergy and are you treating it now?</u> You may not treat allergy at the first visit for otitis externa. But, you should at least start the conversation about allergy.
2. <u>How much debris is in the ear canal?</u> 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. <u>How is the conformation of the ear canal?</u> 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. <u>What type of infection is present?</u> 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. <u>How much edema and erythema are present?</u> 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 or potency are as follows:
    a. <u>Prednisolone</u>
    b. <u>Betamethasone</u>
    c. <u>Mometazone</u>
6. <u>How much pain and anxiety are present?</u> 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?

Feline Allergy:
Beyond Depo-Medrol
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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 lgE 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 Jess 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 eat'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 extern a 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 extema 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 Shampoo

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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 bothyou 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 topic 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 1 0-15 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 isimportant. 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 inftammatory 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. Benozyl 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 direcUy 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 Novasomesn.t by Vetoquinol®, Spherulites ^{TM} by Virbac®, Triz EDTA from Dechra®, and ceramides. Novasomes TM 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 ^{TM} are somewhat similar. However, Spherulites TM have multiple layers of active ingredient and water. During bathing the Spherulites TM 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. Cholesteral and free fatty acids make up the rest of the lipid payer. 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 •tean" 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.

Unusual Doesn't Mean Uncommon:
Skin Diseases You Don't Want to Miss

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Calcinosis cutis

Calcinosis cutis describes the deposition of calcium salts into dermal tissue (usually calciumphosphate 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 hyperglucocorticoidism. 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 ormultifocal 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 ultrasonagraphers 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, Octreotride 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 (glucogonoma 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 500mlldog 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 2mglkg/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 straight forward 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. Acatholytic 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. Discreet 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 uremission" 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 6mglkg 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.

Crusted Cats
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Two of the most important aspects in assessing dermatology cases in dogs and cats are the ability to accurately describe and recognize primary and secondary skin lesions along with obtaining an accurate history. Most of the primary and secondary lesions may be easily distinguishable from each other; however, crusts and scales can be more of a challenge and may occur on the same patient.

Scale is an accumulation of loose fragments of the cornified cell layer of the skin. Scales have multiple appearances such as a fine powder, large flakes, greasy or dry, loose or adherent and may be various colors from white, silver, yellow brown or grey. Normal desquamation of the epidermis consists of invisible scale, so when larger flakes are detected, abnormalities in keratinization (including overproduction) or desquamation (abnormal retention) can be the underlying cause. Most of the scaling disorders in cats result from chronic inflammation and therefore are usually secondary.

A crust is an accumulation of dried exudate, serum, pus, blood or other cells, scale and mediations that adhere to the skin surface. Crusts often become thicken when associated with haired regions, as the hair and crust can matt and become tightly adherent. Like scale, crust can be variable in color. Hemorrhagic crusts may be reddish, purulent crusts may take on a greenish or yellow hue, honey colored crusts may be more infectious in nature, and crusts consistently predominately of keratinocytes and scale may be dark brown, slivery or black. Similar to scaling in cats, crusts are often associated with inflammation, excoriation and pruritus. Again, crusts are more often secondary types of lesions.

Like with most dermatologic cases, the presence of pruritus will also affect the diagnostic plan in cats with scale and crust. Evidence of pruritus may be difficult. Often the assessment by the owner can be influenced by the amount of time that the owner actually spends with the cat and how observant the owner is. Additionally, some cats can be "closet lickers" and be more secretive with their pruritic behaviors. To help determine if a cat is licking, a trichogram can be very informative. Plucking the hairs from regions of thinning hair or alopecia and microscopically evaluating the ends of the hair for trauma sets up the trichogram. Hairs with tapered ends are normal. Broken and blunted follicular tips points to the hair being sheared by overgrooming.

The diagnostic plan for cats with scales or crusting would be consistent with a routine work-up of most cases of feline dermatologic disease and includes skin scraping, flea combing, direct cytological impression smears, dermatophyte cultures, Wood's light examination, and histopathologic examination of the skin via skin biopsies. Finally, if all others have been ruled out, appropriate work-up for allergic skin disease should be pursued. This lecture will focus on non-allergic triggers of crusted disorders in cats.

Parasitic mites
Notoedres cati
Notoedric mange in cats is caused by the Sarcoptid mite, *Notoedres cati*. Like other Sarcoptic mites, these burrowing mites live in the epidermis and are obligate parasites, meaning they live their entire life cycle on the host, similar to *Sarcoptes scabiei* in dogs. This is a highly contagious mite and appears to occur more common regionally and in local microenvironments in the US. Clinically, crusts initially develop on the face and medial proximal edge of the pinnae with subsequent secondary clinical signs including erythema, scaling and pruritus. The areas affected may spread to involve the rest of the body over time. Skin scrapings may reveal all stages of these mites, including eggs, nymphs, larvae and adults. These mites are generally much easier to find than their counterpart in the dog.

Otodectes cynotis
A Psoroptid mite, *Otodectes cynotis*, causes Otodectic mange. Otodectes mites are also obligate parasites but not especially host specific. These mites may cause diseases and be transmitted to dogs and small mammals in the environment as well. These mites live predominately in the ear canal and occasionally on the face, neck or body. They cause disease both by direct mechanical irrigation and by hypersensitive reactions. Classic clinical signs include generally young age of onset (although any age may be affected) with a typical black brown ceruminous discharge that is usually bilateral. Pruritus can be severe with erosions and significant crusting on the face and ears from excoriations may be detected. This disease should be differentiated from relapsing *Malassezia* otitis externa associated with hypersensitivity reactions. Chronic relapsing cases of Otodectic mange are unlikely, and in cats that have recurrent ear disease investigation into underlying allergic skin disease needs be undertaken. These mites are also generally easily detected either by direct examination of the ear canal with a hand held otoscopic or video otoscopic machine, or can be visualized in direct smears of ceruminous debris onto a microscope slide with mineral oil. Skin scrapings of affected body parts may be more difficult to find the mites.

Demodex cati
Demodectic mange caused by the mite *Demodex cati* is a relatively uncommon disease associated with the proliferation of these mites within the hair follicle or sebaceous glands. The life cycle and stages of these mites are similar to *Demodex canis* in dogs. Localized or generalized conditions can occur, however the localized form in the cat is uncommon. Localized presentations are often limited to

the head, eyelids and face or as a ceruminous otitis externa. These may be self-limiting or require topical, but rarely systemic, therapy. The generalized form of the disease is the more common presentation although it is still relatively rarely seen. Burmese and Siamese cats are reported to be over-represented. Clinical lesions are the classical areas of alopecia, erythema, scale and crusting. The disease may or may not be pruritic. Generalized disease is most often seen in association with underlying metabolic immunosuppression, such as FeLV/FIV positive status, diabetes mellitus, hypercortisolism (either spontaneous or iatrogenic), and malignant neoplastic processes. Therapy for this condition is predicated upon resolution and control of the underlying disorder then the appropriate miticidal therapy. Often chronic management is necessary.

Demodex gatoi

The second condition of cats associated with demodicosis is with the *Demodex gatoi* mite. This short-bodied Demodex mite lives in the epidermal pits of the stratum corneum, as opposed to the hair follicles. The life cycle of these mites is less understood however they are suspected to live their entire life in the superficial layers of the skin. Clinically this condition can present as either non-pruritic cases of alopecia and scale with crusting to intense pruritic cases that have significant crusting with excoriations and trauma. The abdomen, lateral thorax, and medial aspect of the legs are generally affected. These mites appear to have geographic epizootic infestations in some areas of the US, specifically southern states and areas of higher humidity. These mites are small and translucent. They can be easily missed on skin scraping. In cases of pruritus, the cat can easily remove these mites. Fecal flotation may be helpful in finding these mites in cases when the skin scrapings are non-diagnostic. Additionally scraping along the margins of the areas of hair loss my increase the mite yield on superficial broad skin scraping. Routine miticidal treatments and anti-parasiticidal mediations are generally ineffective. Most cases will only respond to lime-sulfur baths or rinses performed weekly to twice weekly.

Cheyletiella blakei

Cheyletiella blakei is a mite specific to feline patients although on occasion other species of Cheyletiella (including *C. yasguri* and *C. parasitovorax*) can infest the cat. This condition is likely under diagnosed and can be particularly problematic in catteries. These mites live on the skin surface and feed on cutaneous debris. They are more often diagnosed in young cats but adults can be affected and sometimes asymptomatic. These mites present a zoonotic concern as this mite can trigger a pruritic papular rash in humans. Often called "walking dandruff", these mites are slightly larger than others and can be visualized as moving white spots in severely affected cats. Infestation will create significant scaling. Skin scraping or tape preparations can locate the mite. Since Cheyletiella is generally easily killed by most topical flea control products, areas in which fleas are less common and topical products no used are the areas that the author sees the majority of cheyletiellosis cases.

Bacterial infections

Although most textbooks and references label superficial bacterial pyoderma or folliculitis as "uncommon" or "rare" in cats, most dermatologists and even recent literature disagree with these statements. Superficial bacterial pyoderma is commonly undiagnosed and in many cases untreated. These secondary infections associated with primary skin disease in the cat are a common finding when one begins to look for it. Crusted papuler eruptions or miliary dermatitis are the most common presentation for folliculitis in the cat, however large areas of erythematous and erosions dermatoses can also be associated with large numbers of bacterial organisms. Bacterial infections are generally still considered a secondary complication of underlying disease, but management of the bacterial component can be a critical factor in achieving control and remission of the primary disease.

Dermatophyte infections

Dermatophytosis is most commonly caused by *Microsporum canis* in the cat. It is a common skin disorder that has a pleomorphic presentation. It can be characterized by either scale or crusting. Contact with the naturally infection stage, the arthrospore, is the route of infection. This is most commonly associated with contact with an infected animal or in homes or environments of infected cats. Normal grooming behavior may be an important first line of protection but the most commonly affected animal are ones that are young, older or immune compromised due to poor nutrition, ectoparasitic concerns or metabolic disease. In most healthy cat spontaneous remission occurs and treatment goals should be aimed at reducing environmental contamination and thus zoonotic potential. Recommendations for therapy and characterization of the disorder have undergone many changes over the years but recent evidence would suggest that since infected arthrospores can be found numerous centimeters from the obvious clinical lesions, most cases that do no spontaneously resolve should be considered generalized and treated and such. Treatment options for systemic therapy include the use of itraconaozle, fluconazole or terbinafine as the drugs of choice.

Pemphigus foliaceus

Pemphigus foliaceus (PF) is the most common auto-immune disease in cats. While primary lesions of PF in the cat are vesicobullous or pustular, these lesions are fragile and transient. Crusting, although secondary in these cases, may be the predominately recognized sign. Crusted lesions are generally found on the face, pinnae, and periocular areas as well as around the nipples. In addition, purulent discharge around individual or multiple claw folds can be a common manifestation of this condition in cats. The claw fold disease is a distinct difference to the clinical presentation of PF in the dog. This disease can have a waxing and waning course. It may respond

transiently to injectable corticosteroids and is often misdiagnosed as an allergic skin disease. Pruritus however is variable. Cytology can be suggestive with the finding of acantholytic keratinocytes, however biopsy sampling with histopathology is needed for definitive diagnosis in most cases. Acatholytic cells in the cat can occasionally be challenging to isolate on cytology or on histopathology and evaluation of multiple sectioning samples may need to be requested of the pathologist. In cases with a high index of suspicion, repeat biopsies may be needed for definitive diagnosis. Either way, focusing on lesions with heavy crusting can increase the diagnosis yield. Treatment with corticosteroids, cyclosporine, or chlorambucil is the most commonly used therapy for this condition. Prognosis is generally good although some cases can be challenging to achieve remission.

Exfoliative dermatoses

Exfoliative (or shedding of keratinocytes in scales) dermatoses can occur in the cat and has been associated with a number of different disorders. The scale produced in these disorders then to be large and sheet-like. There may or may not be associated erythema. In cats disease triggers can be associated with topical agents, FeLV/FIV infection, erythema multiforme, or toxic epidermal necrolysis. If receiving drug therapy, drug reactions or associated with infection due to glucocorticoid therapy are possible.

A specific well recognized syndrome in the cat is associated with the presence of a thymoma. Systemic signs include lethargy, weight loss, and anorexia may or may not be present. Larger masses may be associated with respiratory signs or regurgitation. Exfoliative reaction is generally observed at the head and neck initially with progression caudally. Thoracic radiographs or ultrasound will be diagnostic for the mass. Skin biopsy demonstrates cell poor interface dermatitis with exocytosis of lymphocytes onto the surface or follicular epithelium. Surgical excision of the thymoma is curative.

Paraneoplastic dermatosis

Paraneoplastic dermatosis is a syndrome presenting with progressive alopecia and scale. It is seen in association with malignant internal neoplasia. This syndrome is recognized in older cats with no breed or sex predilection. Pancreatic and bile duct malignancies are the most commonly associated cancer. Often the primary tumors and liver metastasis are not detected at the time of diagnosis. The neoplastic process dues not involve the skin directly, but the sin is a manifestation of the internal disease. The alopecia has an acute onset and large areas of hair are sloughed initially from the ventral abdomen and then the limbs and paws. The surface of the skin often ahs a "shinny" appearance and the remaining hair is of poor quality and easily to epilate. A generalized large sheet scale is often noted in association with the clumps of hair that are lost. Secondary colonization with *Malassezia* organisms can be observed with a dark brown discharge on the surface of the skin. Skin biopsy reveals cutaneous histopathologic changes suggestive of the syndrome but can be nonspecific. Ultimately ultrasound, imaging or exploratory laparotomy are necessary for definitive diagnosis. Because metastasis is often present at the time of diagnosis, progress is grave.

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Endocrine Alopecia
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Dermatologic diseases in small animal veterinary medicine comprise of roughly twenty percent of the caseload of a general practitioner.[1] There are many functions of the skin and coat but as the "largest organ of the body" it provides a marker of internal disease to the practitioner.[2] Endocrinopathies are on of the more common internal disease triggers of cutaneous disease seen in small animal practice. In general, most endocrine diseases affected the skin via their hormonal influence on the hair follicle, epidermis, and adnexal structures.[3] Often endocrine disorders trigger early entrance of the hair cycle into catagen and telogen phase. The growth phase, anagen, will become slowed or even stopped. These changes in the hair cycle results in atypical shedding cycles, easily to epilate hairs, and poor hair regrowth following clipping or trauma. Eventually these cases will develop a characteristic pattern of symmetric alopecia along the trunk, sparing the head and extremities. This is due to the regionalization of hormone receptor numbers or receptivity.[4] The severity and distribution of the alopecia will vary among breeds and individuals within the same breed. In addition to alopecia, other changes in the hair follicles can be detected. Coat changes including a dry, brittle or coarse coat can be detected. The pigment of the hair can change to a lighter color, with black dogs become more rust or brown. Finally, follicle plugs or comedones may develop. Additional dermatologic features of endocrinopathies include dry or oily seborrhea due to changes in epidermal kinetics. Skin pigmentary changes can be detected as well as secondary bacterial or *Malassezia* infections. Unlike allergic dermatitis, these cases are not pruritic. This lecture will focus on when the thyroid and adrenal glands impact the skin.

Hypothyroidism
Hypothyroidism is the most common endocrine disorder of the dog, with estimates of 0.2 to 0.8%; conversely, it is also the most commonly over-diagnosed endocrine disease.[5-7] More than 90% of all cases of canine hypothyroidism are due to acquired form. The two main causes of acquired primary hypothyroidism are lymphocytic thyroiditis and idiopathic thyroid necrosis and atrophy. In lymphocytic thyroiditis, also known as Hashimoto thyroiditis, there is a genetic predisposition. Early in the disease process thyroglobulin autoantibodies can be detected.[8] Both humoral and cell-mediated autoimmunities are involved in the development of lymphocytic thyroiditis. Some believe that idiopathic thyroid necrosis and atrophy may be an end stage presentation of lymphocytic thyroiditis. Naturally occurring secondary hypothyroidism accounts for less than 10% of all canine hypothyroidism. This is due to a failure of the pituitary gland to secrete thyrotropin (TSH).

Acquired hypothyroidism can affect any breed of dog but seems to occur with increase frequency in golden retrievers, Doberman pinschers, and Labrador retrievers.[6] Familial hypothyroidism has been suspected in Great Danes, Doberman pinschers, and German shorthaired pointers. There is no gender predilection however some studies demonstrate a higher risk for neutered male and female dogs than intact dogs.[9] There appears to be a higher risk to middle aged dogs between the ages of 6 and 10 years, even though any age may be affected. Large and giant breed dogs tend to be affected early at 2 to 3 years of age.

Due to the thyroid hormones widespread affects on the body, the clinical signs of hypothyroidism are many and varied, often involving several organ systems.[6,10] Dermatologic changes are seen in 60-80% of cases with canine hypothyroidism.[7] Alopecia in regions of trauma or wear, including the bridge of the nose, elbows, tail and trunk and a dry, dull, brittle coat which often demonstrations post clipping alopecia are classic cutaneous presentations of canine hypothyroidism.   Often the alopecia will evolve to symmetric truncal alopecia with a "rat tailed" appearance to the tail. Other classic cutaneous lesions include myxedema, variable hyperpigmentation, seborrhea, recurrent pyoderma or *Malassezia* dermatitis, and lack of pruritus. Less common cutaneous signs include poor wound healing, easy bruising, hyperpigmentation of the skin, lichenification, comedones and excessive mucin accumulation in the dermis.

Since there are many clinical signs that can be triggered by low thyroid production, the differential diagnosis lists is very large. Definitive diagnosis is achieved via thyroid biopsy; however, since impractical and invasive, practitioners rely on history, physical examination, hematology and serum chemistry, urinalysis, skin biopsy and thyroid function tests. Not one of these tests are specific for primary hypothyroidism. Histopathologic findings of skin biopsies often demonstrate non-diagnostic changes often detected with many endocrinopathies including orthokeratotic hyperkeratosis, epidermal melanosis, follicular keratosis, follicular dilatation, follicular atrophy, telogenization of hair follicles, excessive trichilemmal keratinization (flame follicles), and sebaceous gland atrophy.[11]

Clinical management with thyroid hormone replacement is often required for the remainder of the patient's life. Most dermatologic lesions will slowly resolve in most cases in a 3 to 4 month period after treatment initiation. Often apparent improvement in cutaneous lesions does not occur until after at least 4 weeks of therapy. Pressure point scarring tends to persist but no new lesions should develop.

Hypercortisolism

Hypercortisolism (Cushing's disease, Cushing syndrome) is a common disorder in the dog, associated with excessive endogenous or exogenous glucocoritcoids. Often in dermatologic practice, only cutaneous symptoms are apparent at presentation. Cushing's disease, as described by Harvey Cushing in 1932, refers to only one specific cause: an adenoma of the pituitary gland; however, current the term Cushing's is used to describe several different etiologies. Three classes of hypercortisolism are described: pituitary-dependent hyperadrenocorticism (PDH), adrenal tumor hyperadrenocorticism (AT), and iatrogenic hypercortisolism.

80 to 85% of dogs with spontaneous hypercortisolism are diagnosed with PDH often due to micro- or macroadenomas. The hypercortisolism results from excessive pituitary corticotropin (ACTH) secretion, which intern produces bilateral adrenocortical hyperplasia.[6] This form of hypercortisolism seems to be more common in Boston terriers, dachshunds, boxers, and poodles; but can occur in any breed. Less commonly spontaneous hypercortisolism may be triggered by a functional adrenal tumor. Literature reports a frequency of 15% to 20% of cases of canine hypercortisolism is due to either adenomas or malignant adenocarcinomas.[6] The author's practice tends to see identify AT much less frequently. Finally, injudicious use of glucocorticoids for therapeutic purposes is the most common trigger for clinical presentation of Cushing's disease. Long-steroid use in any form, whether it be oral, injectable, or topical, can produce significant adrenocortical suppression, elevations of hepatic enzymes and iatrogenic hypercortisolism in dogs.

Natural occurring canine hypercortisolism is often detected in middle-aged to older dogs, often greater than 6 years of age. Some studies have found that there may be a slightly higher frequency in female dogs; 55% of PDH cases and 60 to 65% of AT cases.[12,13] PDH tends to be more common in smaller breed dogs with 75% of dogs weighing less than 20 kilograms. AT is described more frequently occurring in larger breed dogs and seems to be more common in poodles, dachshunds, German shepherd dogs, and Labrador retrievers.

Like canine hypothyroidism, the clinical signs of hypercortisolism are many and varied. This can point to the length of time the disease is present. Some more astute owners may notice subtle changes in coat while others with less exposure to the pet, may present when the disease and clinical signs are more advanced. Systemic signs of hyperadrenocorticism include polydipsia, polyuria, polyphagia, abdominal enlargement, decreased exercise tolerance, panting, lethargy and obesity.

The cutaneous manifestations of canine hypercortisolism have been well described. Early changes often include a dry dull coat. With time, slow hair regrowth and hair loss can be detected. The alopecia is symmetric, involving the trunk and sparing the head and distal extremities. However, some cases can present with patchy hair loss on only the flank region or along the face.[10,12] Coat color change has also been described with black hairs becoming auburn or rust colored and brown hairs becoming tan or blond. Cutaneous changes including thin, hypotonic skin, hyperpigmentation, easy bruising, seborrhea, comedones, milia, poor wound healing, recurrent bacterial pyodermas, and calcinosis cutis are also associated with canine hypercortisolism. Often the dermatologic signs precede systemic disease. A review of 10 cases of Cushing's disease with only cutaneous manifestations found that non-pruritic alopecia and non-pruritic pyoderma were common to the cases investigated.[14]

Again the diagnosis of canine hypercortisolism, like canine hyperthyroidism, can be tricky and involves hemogram, serum chemistry, urinalysis, skin biopsies and adrenal function testing. Histologic features of hypercortisolism include, orthokeratotic hyperkeratosis, follicular keratosis, telogenization of hair follicles, follicular atrophy, excessive trichilemmal keratinization, follicular dilation, telangiectasia, epidermal atrophy and melanosis, sebaceous gland atrophy and dystrophic mineralization of collagen fibers and hair follicles.[11] Other screening tests for canine hypercortisolism include urinary cortisol:creatinine ratio, ACTH stimulation test, endogenous ACTH concentration, and dexamethasone suppression tests. Additional diagnostics including abdominal ultrasound and radiographs are recommend to determine if PDH or AT is present.

Clinical management of canine hypercortisolism is recommended for the improvement of the quality of life for the pet as well as the owner. Adrenalectomy is the treatment of choice for AT, while medical therapy with trilostane or mitotane/lysodern can be utilized to control PDH. Comparison of survival rates of dogs with PDH treated with mitotane or trilostane showed no difference between the clinical efficacies of the two treatments.[15]

Atypical hyperadrenocorticism

Steroid hormones other than cortisol can be synthesized and secreted by the adrenal glands. For the purpose of this handout/lecture, several clinical syndromes will be linked together: Alopecia X syndrome, hair cycle arrest, adrenal sex hormone imbalance, follicular dysfunction of plush-coated dogs, adrenal hyperplasia-like syndrome, growth hormone/castration-responsive dermatosis/alopecia, pseudo-Cushings syndrome, and adult-onset hyposomatotropism.[16] Abnormal adrenal corticies may secrete 11-deoxycortisol, deoxycorticosterone, aldosterone, progesterone, 17α-OH-progesterone, estrogens or androgens in excess. There appears to be distinct breed predilections, Pomeranian**,** Keeshond, Alaskan malamute**,** Siberian husky, chow chow**,** Samoyed, miniature poodles, which suggests heritability.[16,17]

The term 'Alopecia X' was coined to suggest that an endocrine etiology, but this has not been proven. Since mitotane therapy can cause hair regrowth in some dogs, a role for adrenal hormones is suggested. The disease process may be hormonal, but possibly derived from abnormalities in local estrogen or other hormone receptors at the level of the hair follicle.

Cases of atypical hyperadrenocorticism may present from 9 months to 2 years of age and usually at the onset of puberty. It may also be detected in dogs as old as 12 years. Like other endocrinopathies, the dermatologic symptoms are slowly progressive resulting in bilaterally symmetrical alopecia originating in frictional areas beneath collars, caudal thighs, and perineum. Initially, the primary hairs are lost, followed by a variable loss of secondary hairs. Additionally, post clipping alopecia and hyperpigmentation in areas of alopecia may also occur. End-stage disease results in total alopecia of trunk, neck and proximal legs, sparing head, distal legs and distal tail. Affected dogs appear to be otherwise healthy, with no concurrent PU/PD or other HAC signs. Diagnosis is made when history, physical examination, skin biopsy and sex hormone function tests are taken in to consideration. Hormone ACTH response offered by University of Tennessee is most well known and often utilized. Dogs are given ACTH; basal and 1 or 2 hour post samples are taken (depending on type of ACTH administered) and the following hormone levels are determined: cortisol, progesterone, 17-hydroxyprogesterone, dehydroepiandrosterone sulfate, androstenedione, testosterone, and estradiol-17β.

Therapy with trilostane and mitotane has been utilized with some success. Not all cases will regrow hair. Often treatment with either of these two medications is postponed or not pursued as most believe this disease process is a cosmetic problem. Some owners are concerned with potential adverse advents with either drug. Often melatonin supplementation is initiated. The exact mode of action is unknown. This naturally occurring hormone is found in most animals. Circulating levels vary in a daily cycle and melatonin plays a role in regulation of circadian rhythms. When dosed at 3 to 6 mg by mouth twice daily, it has been reported to stimulate hair regrowth in 40% of cases.[3]

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Methicillin-Resistant Staphyloccus

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Bacterial skin infections are very common in the dog and lesser so in the cat. *pseudintermedius* is recognized as the primary cutaneous pathogen of dogs, and probably cats.. An important property of stphaylococci is their capacity to become resistant antimicrobials. In human medicine, methicillin-resistant *Staphylococcus aureus* (MRSA) has been deemed as a major global crisis in human healthcare by the Centers for Disease Control (CDC). Currently MRSA accounts for anywhere from 30% to 40% of all hospital-acquired infections in humans, making it the most prevalent nosocomial pathogen worldwide. As we have seen an increase in resistant *Staphylococcus* in human medicine, several species of methicillin-resistant *Staphylococcus*, including *S. pseudintermedius, S. intermedius, S. schleferi,* and *S. hyicus*, have been detected in veterinary patients with increasing frequency. Methicillin-resistant *Staphylococcal* species (MRSS) have been reported in dogs, horses, cats, cattle, sheep, rabbits, chicken, pigs and parrots. As veterinarians, it is vital to an understanding of how to recognize and treat MRSS as well as client education on the risk of zoonosis.

What is methicillin-resistance?

In 1928, Alexander Fleming discovered penicillin. Soon after, penicillin was being mass- produced to treat bacterial infections, which up until this point was responsible for 25% of all deaths in the United States of America. Penicillin and related beta-lactam ring antibiotics bind and inactivate penicillin-binding proteins (PBPs) required for creating the bacterial cell wall. Interference with the cell wall results in osmotic lysis of the bacterium making this class of antibiotics bactericidal. However soon after the introduction of penicillin to the practice of medicine, *Staphylococcus* sp. developed beta-lactamases, which cleave the antibiotic ring, thereby avoding death by inhibiting the inactivation of the PBPs. To combat these new resistant strains of *Staphylococcus*, humans developed semi-synthetic penicillins that avoid degradation by the beta-lactamases. These early semi-synthetic penicillins include methicillin, oxacillin and dicloxacillin. In terms of practical usefulness, methicillin was short-lived and replaced by oxacillin and dicloxacillin, as these drugs provided better stability, prolonged activity and easier administration route. Methicillin was introduced in 1959 and by 1961 the first case of MRSA was reported.

MecA gene

Methicillin resistance is the most clinically important antimicrobial resistance mechanism detected in *Staphylococcus.* Resistance is conveyed by the *mec*A gene, which is carried on the mobile genetic element staphylococcal chromosome cassette *mec* (SCCmec). The source of the *mec*A gene is unknown but may have originated in *Staphylococcus sciuri* and undergone horizontal transfer to *S. aureus.* SCCmec can be transferred from one strain of *Staphylococcus sp,* to another, or even to a different species. SCCmec encodes for an altered penicillin binding protein (PBP2a). PBP2a has a very low affinity for all beta-lactam

Staphylococcus antibiotics. The presence of PBP2a confers complete resistance to all beta-lactam antibiotics, including penicillins, augmented penicillins, cephalorsporins, cephamycins, carbapenems, and monobactams.

SCCmec is used to help track resistance patterns in medicine. Five clonal SCCmec types have been described: SCCmec Type I, II, and II represent hospital acquired (HA-MRSA), while Types IV and V are associated with community acquired (CA-MRSA). An alternative way to classify MRSA is using pulse filed gel electrophoresis (PFGE). Using this technique, HA- MRSA strains are often identified as USA100 or USA200, while the most common CA-MRSA is USA300. In veterinary medicine, equine MRSA cases are most often USA500.

All of this becomes even more important since MRSS strains also demonstrate high-level resistance to antibiotics outside of the beta-lactams. This multi-drug resistance (MDR) phenomenon results from the way *mec*A is encoded in the *Staphylococcus* genome. As mentioned earlier, *mec*A transmission occurs via transfer of the entire SCCmec region. The SCCmec region may also carry adjacent antibiotic resistance genes. HA-MRSA strains are far more likely to have the MDR via these other antibiotic resistance genes. This is believed to occur due to the multiple antibiotic selection pressures in the hospital environment. There is also variation in the size of the SCCmec types. CA-MRSA (SCCmec Type IV) is the smallest and carries fewer drug resistance genes on top of the mecA. Conversely, HA-MRSAs (SCCmec Types II and III) are larger and carry the additional antibiotic resistance genes. In general, CA-MRSA will be susceptible to 3 of 5 of the following antibiotics: tetracyclines, macrolides/lincosamides, flouroquinolones, gentamicin, and trimethoprine sulfa antibiotics. Other ways for differentiating CA-MRSA and HA-MRSA strains include the double disk diffusion D-zone test for inducible clindamycin resistance and the presence of Panton- Valentine Leukocidin (PVL) exotoxin.

Veterinary perspective

MRSS adds a therapeutic challenge to our veterinary patients beyond just determining the right antibiotic therapy. There is a significant concern for transmission between patients, to owners and veterinary healthcare providers. Historically, *Staphylococcus* was believed to be very host-specific. Humans are colonized by *S. aureus;* dogs and cats are colonized by *S. psueudintermedius.* Currently,

S. aureus has been isolated from suppurative infections as well as subclinical carriage sites in dogs and cats. Healthy dogs and cats may be colonized by MRSA; however, this colonization may be transient, particularly in dogs. The organism may not be isolated on repeated sampling. The prevalence of MRSA colonization in healthy dogs or upon admission to veterinary hospitals ranges from 0% to approximately 3%.[2,3] For cats, the reported prevalence ranges from 0% to 4%.[3] Additionally, animals presenting for veterinary care were significant more likely to carry MRSA than were healthy animals.

There have been many studies evaluating the carriage sites of MRSS in veterinary patients. To detect MRSA colonization, optimal sensitivity is achieved when a combination of nasal and rectal or perianal swabs are obtained. A recent study found 8% of pets were positive for MRSA. The oral cavity (72% sensitivity) is the most sensitive location for recovery of MRSA in dogs with the combination of nares-mouth showing a 92% sensitivity. In general, mammals are nine times more likely to be positive for MRSA carriage than reptiles, fish and birds.

Canine patients are four times more likely to test positive for colonization with MRSA than felines. Again this numbers are for the colonization with MRSA, as clinical lesions are very rare.

Although several studies have suggested the possibility of MRSA transmission from colonized or infected humans to animals, or vice versa, true direction of transmission often cannot be proved. Current data suggests that transmission from direct contact with colonized humans is the most likely explanation for the presence of *S.* aureus on a dog or cat. In one study, contact with human hospitals and contact with children were significant factors for a dog's colonization with MRSA.[4] In studies of pets within households of MRSA infected people, animals (dogs- 1.5%, cats-0.0%) had lower rates of organism prevalence than their owners (people 3.3%).[3] Further more typing data strongly supports that MRSA in household pets has emerged as a result of MRSA in the humans.[3] Finally in terms of MRSA colonization in pets, it appears to be transient, likely because *S. aureus* is not naturally a commensal organism in these species.[3] This trend calls in the question to actively treat MRSA colonization as attempts to decolonize pets may not be necessary. The risk of direct pet-to-pet transmission appears to be low, especially among healthy colonized dogs.

MRSA is an emerging pathogen in horses and farm animals, particularly pigs. MRSA colonization in various horse populations in the community and upon admission to veterinary hospitals have been reported from 0-10.9%.[5,6] In North America, initial reports showed horses colonized by or infected with a clonal MRSA strain known as USA500 (or Canadian epidemic MRSA-5).[3] Although this strain was initially associated with nosocomial infections in humans, it has now become well adapted to horses, but may colonize or cause infection in humans with close horse contact.

Other species of methicillin-resistant Staphylococci

While we mostly discuss MRSA when talking about methicillin resistant strains of Staphylococci, in veterinary practice it is far more common to detect other species. MRSA has been identified as a well-adpated pathogen in dogs, cats, and horses, *S. pseudintermedius* and *S. schleiferi* are far more commonly associated with dogs and cats. Both can be native resident microflora as well as opportunistic pathogens. When it comes to zoonotic potential, an important difference with *S. aureus* is that *S. pseudintermedius* colonization is very uncommon in humans even among individuals with frequent contact with animals.

Recognizing methicillin-resistant Staphylococci

Methicillin resistant staphylococci detected in most dogs and cats are no more virulent or toxic that the methicillin-sensitive strains; they are just more resistant to treatment. The clinical signs of a methicillin-resistant staphylococcal infection are identical to that any staphylococcal infection. In dermatologic cases, folliculitis, superficial spreading pyoderma, deep pyoderma, impetigo, and deep folliculitis, furunculosis and cellulitis could all be triggered by either MRSS or MSSS. Other presentations for MRSP include abscess, postoperative wound infection, and nosocomial IV catheter site infections. Another common site for MRSP include orthopedic surgical implants. Testing for MRSS is indicated when coccoid bacteria is detected on cytology, if there has been a partial or incomplete response to first line antibiotic therapy, or if relapse of infection occurred within 1 to 3 weeks of antibiotic discontinuation. Additionally, culture is recommended in cases of deep bacterial infection or if mixed infection (both rods and cocci bacteria) is detected on cytological evaluation. MRSS presence should also be evaluated if there had been previous use of antibiotics that might predispose a case to methicillin resistance. For instance, fluroquinolone use has been identified as a risk factor for the development of MRSS colonization. Finally, another risk factor for the development of a methicillin resistant infection is if the owner has or had MRSA, recent hospitalization or linked to the human health care filed. Ultimately any time a MRSS is suspected, it is clinically important to perform bacterial cultures. Since methicillin is no longer commercially available in the United States, it does not appear on antibiotic susceptibility panel. Instead, oxacillin is the stand in. The true identification of MRSS is to detect the *Mec*A gene or expression of PBP2a via PVR, but in general, if an organism is reported to be resistant to oxacillin, assume it is a methicillin resistant strain.

Treatment of methicillin-resistant Staphylococci

Antibiotic treatment should be based on susceptibility testing and extend for 2 weeks beyond clinical resolution. If a surgical implant is present and associated with the infection, it should be removed. Regardless of what the laboratory report says, consider all oxacillin

resistant Staphylococcal strains to be resistant to all penicillins, cephalosporins, cephamycins, amoxicillin/ticarcillin-clavulanic acid, piperacillin, tazobactam, and carbapenems, including imipenum. Veterinary isolates have variable resistance to non-beta-lactam classes, including gentamcin, rifampicin, fluroquinolones, fusidic acid, and tetracyclines. Most commonly, strains are susceptible to amikacin, vacnomycin, chloramphenicol, trimethoprim sulfa, clindamycin, linezolid, and dapomycin. In addition to systemic therapy, topical therapy is very beneficial in these cases. It works to remove debris, has direct access to the bacterial organisms, and can have beneficial physical effects on the skin. With topical therapy, there is less dependence on sensitivity, absorption and adequate penetration. There is a lower concern for development of resistance. Often with these cases, a maintenance therapeutic plan can be instituted to reduce relapses.

MRSA prevention and management revolves around institution of schemes to break the chain of infections. Good hygiene and hand washing is the single most important factor for prevention. The CDC determined that alcohol gels containing at least 60% alcohol are the best agent for elimination of both gram-positive and gram-negative bacteria in health care settings. Other means to break the chain of infections including isolation of infected cases and follow-up screening for decolonization. Education about antibiotic use and strict avoidance of overuse and misuse of antibiotics is also vital.

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Pemphigus Foliaceus
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Pemphigus is an uncommon autoimmune disease process described in humans, dogs, cats, horses and goats. Initially described in 1964 by Beunter and Jordon when circulating antibodies to cell surface keratinocytes were detected in serum from patients with pemphigus vulgaris. Pemphigus is a vesicobollous to pustular disorder of the skin and mucous membranes characterized by acantholysis. Several varieties have been detected and reported in humans with about 5 varieties described in dogs and cats.

Pemphigus foliaceus is the most common form of pemphigus in the dog and cat. In general, pemphigus foliaceus affects the epidermis as well as hair follicles. Pemphigus foliaceus is even considered the most common autoimmune skin disease in the dog. There is no age or sex predilection but approximately 65% experience disease at greater than 5 years of age. Canine breeds that appear to be predisposed include akitas, chow chows, breaded collies, Newfoundlands, and Doberman pinschers. Additional breeds including Chinese Shar Pei, Collie, Finish Spitz, Schipperkes, English springer spaniels and Dachshunds also appear at an increased risk. In general pemphigus diseases are far less common in the cat than in the dog. Pemphigus foliaceus is seen at the author's practice at an incidence of 2% of referral cases, with the national average being about 1 to 1.5%.

Pathogenesis
The exact pathogenesis of pemphigus foliaceus in veterinary patients is unknown. In most canine cases, the disease appears to be idiopathic in nature. An idiopathic form is most commonly seen in chow chows and akitas.

There is a drug-induced form of pemphigus foliaceus reported in the Doberman pinscher and Labrador retriever. In humans, the role of drug eruptions in triggering pemphigus is well established as some medications can initiate acatholysis or causes disease flares in patients predisposed to the disease. The existence of drug induced pemphigus foliaceus has been questions. Recently 22 cases of a PF drug eruption were described following the topical administration of an ectoparasiticide containing amitraz and metaflumizone. Other drugs that have been associated with PF eruptions include trimethoprim/sulfonamides, penicillamine, phenylbutazone in dogs and methimazole, trimethoprim/sulfonamides and cephalexin in the cat.

Chronic disease, usually of an allergic nature, may also be a trigger of pemphigus foliaceus in the dog. In a study in California, a history of flea allergy dermatitis often preceded the development of pemphigus. A study out of Pennsylvania detected concurrent diagnosis of canine atopic dermatitis in 11.6% of studies. Other diseases that have been reported to be associated with PF include hypothyroidism, leishmaniasis, thymoma and systemic lupus erythematosus. UV radiation and sun exposure also appears to exacerbate the condition, however literature as presented conflicting results.

Clinical presentation
In humans, pemphigus foliaceus presents as scaly-crusted erosions affecting the face, scalp, and upper trunk. The primary lesion detected in human PF is a small flaccid blister. Unlike humans, in dogs and cats, PF does not have a vesicular phase. In our veterinary patients, PF is a pustular crusting disease. In general clinical lesions are variable and include pustules, crusts, erosions, ulcers and alopecia. Clinical presentations through will vary depending on breed, triggering factors and the cyclical nature of the disease. Some cases are restricted to the face, predominately dorsal muzzle, planum nasale, pinnae and periorbital lesions. Some cases may become or present as generalized disease. Pawpads may or may not be involved with fissuring and crusting. Dogs may develop claw disease but it is not a common feature. In addition, purulent discharge around individual or multiple claw folds can be a common manifestation of this condition in cats. The claw fold disease is a distinct difference to the clinical presentation of PF in the dog. Typically there is striking bilateral symmetry present. The degree of pruritus is variable with some cases demonstrating severe itching and self-trauma. Mucosal lesions are rare and a mucocutaneous distribution is not a feature of PF.

Pemphigus has an unpredictable course. It may wax and wane or it may present as rapidly progressive. Secondary *Staphylococcal* infections may be present and can result in partial responses to antimicrobial therapy. Additional systemic signs include lymphadenopathy, anorexia, fever, and depression. Often when the disease is active, the pet does not feel well.

Diagnostic methods
Pustular diseases have several differential diagnoses so performing the dermatologic minimum database is essential to exclude demodicosis, dermatophytosis, and superficial pyoderma. Examination of intact pustules by cytology may detect acantholytic cells. Acantholytic cells are rounded and deeply blue staining isolated keratinocytes and may occur in clumps or as individuals. Additional cytological findings include lack of coccoid bacteria and numerous non-degenerative neutrophils and eosinophils.

If pemphigus is suspected, tissue biopsies should be performed to confirm the diagnosis. Histopathologic findings of PF demonstrate intraepidermal or intrafollicular acantholytic pustules. These pustules are commonly detected in the corneal, granular or

upper spinous layers of the epidermis. The pustules are often infiltrated with neutrophils and eosinophils. The stratum corneum may be lost or may have adherent acantholytic cells within serosangious crusting.

Routine hematology and biochemistry should be performed to evaluate health as well as provide a baseline prior to starting therapy. Many of pemphigus cases can have moderate to marked leukocytosis and neutrophilia, mild nonregenerative anemia, mild hypoalbuminemia and hypergolubinemia.

Common therapeutics

Therapy for PF involves immunosuppressive or immunomodulating drugs. As with the clinical signs, the response to therapy is variable with some cases requiring life long multiple drug therapy and others resolving with a course of corticosteroids.

Glucocorticoids

Glucocorticoids are the first choice for the treatment of PF. Prednisone or prednisolone administered at 2 mg/kg/day until remission then tapering is most often performed. It is important to note that each pet may respond differently to different corticosteroids. Some cases may develop undesired side effects like polyuria and polydipsia on prednisone and not on another formulation like methylprednisolone. Often if no response to the initial dose of corticosteroid is detected in the first 10 to 14 days or if side effects become too bothersome, the type of steroid is changed or additional therapeutics are added. Ultra high doses of corticosteroids when used with a gastric protectant have been reported as successful at inducing remission. This technique involves using prednisone sodium succinate at 10 mg/kg IV or dexamethasone at 1 mg/kg IV while instituting oral therapy. More refractory cases may also benefit by using triamcinolone or dexamethasone orally. These corticosteroids are considered to be 6 to 10 times more potent than prednisone and the dose ranges are about 0.2 to 0.4 mg/kg/day.

Azathioprine

Azathioprine may be used as a sole or combination therapy of PF in the dog. It should not be used in cats, as it is more likely to trigger profound myelosuppression and fatal reactions. In canine patients, azathioprine is often used as a steroid-sparing agent with a synergistic effect when dosed at 1.5 – 2.5 mg/kg or 1 mg/m². Azathioprine is an antimetabolite, which interferes with the synthesis of nucleic acids and is cytotoxic to T cells. It does have a slow onset and usually takes about 4 to 8 weeks to start to see clinical effect. Adverse reactions include myelosuppression and hepatotoxicity. Initially monitoring every 2 weeks with complete blood cell counts and serum biochemistries is recommended for the first 3 months. As the medication is tapered to every other day or a few times weekly, the rates of adverse reactions reduce.

Chlorambucil

Chlorambucil is an additional steroid-sparing agent utilized in feline PF cases. Chlorambucil is an alkylating agent that functions by inhibiting the cross liking of DNA and is considered less toxic than other alkylating agents. It is dosed at 0.1 to 0.2 mg/kg every 24 to 48 hours and is an alternative to azathioprine in feline patients. Like azathioprine, myelosuppression is a concern so similar monitor is recommended.

Tetracycline antibiotic & niacinamide combination

Tetracycline antibiotics and niacinamide, either alone or in combination, have been reported to be therapeutic or act as steroid-sparing agents for may inflammatory skin diseases. This combination has been used with variable success in dogs and humans with pemphigus. The author finds that this combination may be more successful for localized cases of pemphigus foliaceus or pemphigus erythematosus. The most common adverse side effects described are gastrointestinal with vomiting, diarrhea, and anorexia. Since the discontinuation of tetracycline, the author will substitute doxycycline or minocycline at 5 to 10 mg/kg/day. Niacinamide is dosed at 500 mg for dogs weighing greater than 10 kgs and 250 mg for dogs less than 10 kgs every 8 to 12 hours.

Cyclosporine

Recently the use of cyclosporine has been evaluated. As a sole source of therapy, results have not been impressive; however when used as a combination therapy with other immunosuppressive medications may be helpful in more refractory cases. The author will often use cyclosporine to reduce the amount of glucocorticoids to control feline PF. It is dosed at 5 to 10 mg/kg. Additionally topical tacrolimus, which is also a calcinerin inhibitor, can also be used topically for localized forms of pemphigus or areas that do not respond to systemic therapy, ie the nasal planum in dogs.

Mycophenolate mofetil

Mycophenolate mofetil use has increased since the medication has become generic and decreased in cost in recent years. It acts by inhibiting *de novo* purine synthesis and therefore reduces the proliferation of B and T lymphocytes. Current reports on the efficacy of mycophenolate are variable with one author demonstrating a success rate of about 50% with some dogs completely weaned off of prednisone. The dosage has a wide range but the author uses the medication at 10 to 20 mg/kg twice daily. Further study is needed to evaluate its success as a steroid sparing agent or its use in conjunction with other immunosuppressive medications.

Prognosis

Canines exhibit a variable prognosis with pemphigus foliaceus. In one study of 31 cases, 71% were still alive with a mean follow up of 2.7 years. Previous studies found most dogs euthanized due to treatment failures, unacceptable side effects, or poor quality of life.

Immunosuppressive therapy is often continued long-term at the lowest possible dose to keep the disease in remission. The prognosis for feline patients appears to better than that in the dog. For the most part the author feels pemphigus foliaceus is a serious disease but by no means a death sentence. With so many therapeutic options and combinations available, stable disease can often be achieved with minimal side effects.

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Practical Cytology
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The dermatologic minimum database involves a trio of surface sampling techniques. It consists of cutaneous cytology, skin scraping, and dermatophyte culture. The goal of these tests is to identify surface infectious organisms and help guide a diagnostic plan to identify and treat the primary disease. A great deal of information can be obtained from these quick and easy-to-perform tests. Additionally, the needed setup is already in place at the clinic so no further equipment is necessary. To maximize the results of these surface-sampling techniques, practice and study may be necessary.

Cytology

Cutaneous cytology is one of the most valuable tools available in veterinary dermatology. It is inexpensive to perform, requires little equipment, and gives immediate information to the practitioner. Cytology can aid in the diagnosis of several dermatologic conditions from infectious diseases, neoplastic processes, and immune mediated diseases.

Equipment and techniques

The equipment required for collection and evaluation of cytologic samples includes: microscope, microscope slides, cover slips, syringes and needles, cotton-tipped applicators, cytologic stain, and a heat source. Additional equipment, although optional, includes transparent acetate tape and mounting media.

Microscope

It is imperative for proper evaluation of cutaneous cytology and skin scraping to have a good quality, well maintained microscope with multiple objectives (4X, 10X, 40X, and oil immersion 100X lenses). Binocular scopes with halogen bulbs are preferred over monocular lens scopes with incandescent light sources. Three main types of immersion oil are available: Types A, B, and NVH, each with different viscosities – Type A being least viscous and NVH being most.[1] Types A and B are far more common to use in-house with NVH more commonly used in a commercial or research laboratory setting.

To examine a cytologic sample, it is best to start with one of the lower objectives or low power. This allows the slide reader to identify types of cells and a location to examine under the higher objective or oil immersion. Often in the case of cutaneous cytology, the entire sample will be covered in keratin debris and corneocytes with the inflammatory cells present only in certain areas. With the lower power objectives (4X or 10X), the practitioner can find these cells and identify them. This area is then examined with the higher magnification to get a better idea of cellular morphology and the presence of microbes. For evaluating a cytology sample, the light condenser should be up and the iris diaphragm open to minimize the contrast.

Cytologic stains

A commercial modified Wright's stain like Diff Quik (Diff Quik Baxter Diagnostics, McGaw Park, IL) is the easiest stain to use in-house. This three-part stain should be kept clean with the staining tubs changed weekly, and a separate set for "dirty" samples like anal gland cytology and fecal cytology to reduce bacterial contamination. Other stains used in cytology, including New Methylene Blue, acid fast, Gamori methanine silver, and Giemsa, are often not used in-house, but can be performed by professional laboratories if looking for atypical bacterial or fungal infections.

Specimen collection

Depending on the location or the type of lesion, there are several different ways to obtain samples. Ear cytology is easily obtained using a cotton tipped applicator (CTA) applied to the vertical external ear canal. The CTA with ear exudates is then rolled on the microscope slide. CTAs can also be used to obtain moist exudative samples from skin folds or interdigital spaces. Cytology of crusts, exudative or purulent debris, and pustules are best obtained by directly impressing or firmly rubbing the microscope slide across the surface of the lesion. Clear acetate tape can be used to collect a cytologic sample from dry or scaly lesions. The sticky side of the tape is pressed firmly against the desired location. The tape can be stained directly (skipping the fixation solution of the Diff Quik kit) and pressed onto a microscope slide. A toothpick or end of a CTA can be used to collect samples from claw folds. For nodules or abscesses, these lesions are best sampled via fine needle aspiration.

Sample interpretation

Initially, the first step in learning to interpret cutaneous cytology is to evaluate normal skin. Normal structures found include squames or corneocytes (angular, anuclear keratinocytes), occasional nucleated keratinocytes, surface debris, and wax from ear canals. Additional findings include free melanin granules, keratohyaline granules within keratinocytes, rare coccoid bacteria and yeast.

Infectious organisms

The most common infectious organisms detected with cutaneous cytology are yeast and bacteria. *Malassezia pachydermatitis* is the most common yeast organism found on dog and cat skin. This organism has the classic "foot print" shape that is usually 3 to 5 µm in

diameter and stains purple with Diff Quik.[1] *Malassezia* is an inhabitant of the skin in normal dogs and cats; however, usually only 1 or 2 yeasts are found when 1-cm^2 sections of slide are examined.[2] In one study, average yeast counts of greater than 5 organisms per 40X high powered field (HPF) were considered significant.[3] Often one yeast organism per oil immersion field (OIF) can warrant treatment when the sample is from an inflamed ear or skin.

Cutaneous cytology is important in distinguishing between bacterial skin infections (pyoderma, folliculitis) and bacterial colonization or overgrowth. With cytology, the exact species of bacteria cannot be identified; for that, a culture is needed, but cytology can distinguish between cocci and rod bacteria. There is a considerable variety of bacteria that can be detected with cutaneous cytology; however, *Staphylococcus psuedintermedius* infection is the most common. *S. psuedintermedius* is a coccoid bacterium, 0.5 to 1.5 µm, and often found in pairs.[1] This *Staphylococcus* can be a normal inhabitant of the ear and skin of dogs and cats. Average otic bacterial counts greater than 25 cocci/HPF are significant.[3] For skin of normal dogs, the average number of cocci and rods per OIF is less than two.[2] When inflammatory cells are detected with intracellular bacteria, active pyoderma is present. Cytology can also reveal high numbers of extracellular bacteria, which can point to a bacterial overgrowth.

Inflammatory and epithelial cells

Often the identification of inflammatory cells with cutaneous cytology can give the practitioner a clue to the pathogenesis of the lesion. For instance, degenerative neutrophils with intracellular bacteria are indicative of pyoderma, and nondegenerative neutrophils point to sterile inflammatory processes like pemphigus foliaceus, primary allergic inflammation or irritant reactions. Eosinophils are commonly seen with inflammation secondary to ectoparasitism, feline allergic disease, food allergies, foreign body reactions, mast cell diseases or eosinophilic disease processes. Mast cells are often sparsely present in samples collected from parasitic diseases or allergic lesions. Large quantities of mast cells are indicative of a mast cell tumor.

Epithelial cells are normally encountered with cutaneous cytology. The most commonly detected are corneocytes or squames, which are nonnucleated keratinocytes. Nucleated keratinocytes can be detected to a lesser extent in normal skin samples, but are often found on samples obtained from mucous membranes. Acantholytic cells are nucleated keratinocytes from the lower layers of the epidermis that have lost their adhesion to neighboring keratinocytes. These cells are most commonly associated with pemphigus foliaceus, but can been seen to a lesser extent with deep pyoderma and dermatophytosis. Acantholytic cells are large, round cells with a centrally placed nucleus and stain blue with Diff Quik. In cytology from active pemphigus foliaceus lesions, they can be seen as singular cells or grouped together in rafts.

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Updates on Canine Atopic Dermatitis

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Canine atopic dermatitis (CAD) has been defined as a genetically predisposed, inflammatory and pruritic, allergic skin disease with characteristic clinical features, most commonly associated with IgE antibodies to environmental allergens.[1] Of course as with many diseases in veterinary medicine, it is not that simplistic as current understanding suggests that CAD is a multifactorial disease most likely resulting from a complex interaction between host and environment. Treatment of these cases, therefore, requires a multipronged approach utilizing both systemic and topical applications. CAD is also a progressive disease that generally requires lifelong management, benefiting from client education, compliance, and an inclusive treatment plans for success.

Pruritus is the defining feature of CAD but is a sensation in the skin that occurs with numerous skin diseases. The approach to the pruritic dog will be covered in another lecture. A variety of therapeutic or diagnostic trials are needed to determine the cause of the clinical signs in dogs with pruritus and often, it is a diagnosis of exclusion. Allergy testing (*in vivo* like intradermal testing or serum *in vitro*) is NOT generally considered a major tool in the diagnosis of CAD, but instead used to determine significant allergens to initiate immunotherapy.

Allergen-specific immunotherapy (ASIT)

Again, "allergy" testing must be undertaken in order to identify clinically significant allergens for the inclusion in the ASIT. However, independent of the tests, it is essential that allergens in the treatment extract are selected based on a careful correlation between the test results and the clinical history. Allergen-specific immunotherapy (ASIT, hyposensitization, desensitization, allergen therapy, specific immunotherapy, and immunotherapy) is the practice of administering gradually increasing quantities of an allergen extract to an allergic patient to ameliorate the signs associated with subsequent exposure to the allergen. It usually involves giving the allergens by an alternative rout of exposures, which in dogs, is usually the subcutaneous or oral route. The allergen extracts are solutions continue proteins from the pollens, molds, epithelia and insects that trigger allergy. It is important to realize that effective ASIT tends to be more economical long term that other treatment options and often once maintenance therapy is reached, less labor-intensive than oral and topical treatments. ASIT is not a "once and done" treatment, so it is important for clinicians learn to optimize efficacy by making changes.

ASIT via subcutaneously immunotherapy (SCIT) is considered to be efficacious and recommended for the control of chronic atopic dermatitis (AD) in dogs. It is reported to be the only therapy that may cure canine AD and modify the development of further allergies. In many dogs, the dose and frequency of allergen injections need to be tailored based on the individual response during the induction and/or maintenance therapy phases.[2] Some dogs demonstrate an increase in pruritus following the ASIT injection, which gradually resolves over the following few days. In these cases, the dose of ASIT should be decreased. The other pattern commonly encountered is that the dogs tolerate the injections well but the pruritus increases with time until the next injection is given. Once the next injection is administered, there is a reduction/resolution of the pruritus. In these circumstances, the injections should be administered more often. These types of adjustments can maximize the efficacy of the therapy but requires experience, patience, and excellent client communications.

Recently, sublingual immunotherapy (SLIT) has been utilized as a therapeutic option in human allergic disease with similar results to the traditional subcutaneous immunotherapy. In the past few years, SLIT has also been introduced to our veterinary patients. Based on unpublished data, SLIT is as, or more successful than SCIT in the treatment of canine atopic dermatitis (CAD).[3]

Symptomatic allergy therapies

Glucocorticoids

This class of drugs is the most commonly used and abused in the treatment of atopic dermatitis. Often, their use is required in about 50% or more of cases with about 60-80% of cases responding to oral glucocorticoids.[4] Treatment of atopic disease often requires long-term therapy and therefore short acting glucocorticoids (like prednisone, prednisolone, methylprednisolone) are preferred. In clinical practice, glucocorticoids are often used to help give immediate comfort but the goal of therapy is to try to identify a long-term plan and minimize side effects. Ideally, if steroids are needed for a prolonged period of time, giving the drug on alternative days at about the same time can reduce adrenal suppression.

Cyclosporine

Cyclosporine (Atopica®, Novartis) is an immunosuppressant agent used extensively in human and veterinary medication. The approved FDA formulation of Atopica has over 10 years of pharmacovigilance in its use for the treatment of atopica dermatitis and demonstrated to be a safe therapy.[5] Cyclosporine (CsA) is a potent inhibitor of T cell activation, which occurs by inhibition of intracellular calcineurin within T cells. Blocking calcineurin preventions the gene transcription necessary for the production of many interleukins and cytokines. CsA also affects canine keratinocytes and inhibits mast cell degranulation. It is widely distributed in most

tissues due to his lipophilic properties. CsA is metabolized by the cytochrome P450 enzyme system, specifically CYP3A4, in the liver and intestines. Drugs that inhibit CYP3A4 or compete with P-glycoprotein may alter CsA metabolism substantially. An example of this is ketoconazole. Ketoconazole will suppress the cytochrome P450 enzymes, thereby decreasing CsA clearance and increasing CsA blood concentrations. Concurrent administration of CsA with ketoconazole (5 – 10 mg/kg/day) has been estimated to result in a 50-75% CsA dose reduction.[6,7]

Atopica®, Novartis is the only FDA approved veterinary micro emulsion formulation that improves absorption of the drug and is available in capsule of 10 mg, 25 mg, 50 mg, and 100 mg. A liquid formulation is available, Atopica for Cats®, Novartis (100 mg/ml). The absorption cyclosporine can be variable depending upon the formulation; Atopica® and Neoral® are more readily absorbed than its predecessor Sandimmune®, Novartis. Atopica® is most consistently absorbed when given without food on a empty stomach. The most common reported adverse events associated with CsA are gastrointestinal with vomiting or diarrhea. Humans experience a high incidence of nephrotoxicity and hepatic toxicity, which is not commonly observed in dogs. Other side effects encountered in dogs include hirsutism, gingival overgrowth and hyperplastic dermatitis; these are rarely significant and often resolve with dosage reduction.

Oclacitinib

Oclacitinib maleate (Apoquel, Zoetis) is a new drug that has been developed for the treatment of allergic skin diseases in dogs. It is a synthetic drug with a novel mechanism of action, Janus kinase (JAK) inhibitors. This class of drugs falls under the category of tyrosine kinase inhibitors, which have been gaining in popularity in both human and veterinary medicine. JAK are responsible for transmitting intracellular signals from a bound cytokine that has activated a cell surface receptor. Oclacitinib predominately acts by inhibiting JAK1 enzymes, which are most sensitive to IL-31, IL-2, IL-13, IL-14 and IL-6. IL-31, the cytokine on which oclacitinib as the greatest effect, is an important mediator of pruritus sensation. Efficacy has been demonstrated in pruritus associated with allergic disease.[8] This drug is dosed at 0.4 to 0.6 ml/kg given twice daily for two weeks then once daily. It is available in 3.6, 5.4, and 16 mg tablets. Although a majority of the dogs control at once daily dosing, the author and other dermatologists have found that some cases need their once daily dosing divided twice daily for more optimal pruritus control. Details regarding specific studies and frequency of adverse events can be reviewed in the Apoquel product label information.[9] Most common reported side effects included diarrhea, vomiting, anorexia, and polydipsia.

Antihistamines

Evidence based review of antipruritic agents for AD did not report evidence to support the use of antihistamines.[10] However many believe that antihistamines can be beneficial as adjunctive therapy, especially since these treatments are relatively inexpensive and safe. Individual response to antihistamines can be variable so trials with different agents may be necessary. These medications tend to be well tolerated and seem to include minimal to no sedation.

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