Proudly Presents:

DERMATOLOGY

With:

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DERM DIAGNOSTICS: USING SIMPLE TESTS FOR MAXIMUM YIELD

The words tape, scrape and DTM are synonymous with veterinary dermatology. These procedures are routinely performed in everyday practice and provide value to the patient. Uncertainty about proper technique is commonly expressed when interacting with veterinarians of all experience levels. This presentation will utilize a series of photos to demonstrate techniques and tips for tape cytology, superficial and deep skin scrapes, DTM, sample collection for bacterial culture/sensitivity testing and biopsy.

**Tape cytology** is a useful tool to ruling out secondary infections. One of the first studies to tout the importance of cytology was published in 1979. To quote from two of the author's favorite sources: “An enormous amount of vital diagnostic data can be obtained by microscopic examination of stained material, such as smears of tissues or fluids, during a clinical exam ... often supplies sufficient data to narrow a differential diagnosis and develop a diagnostic plan.”

From a more recent publication on feline dermatology: “Cytology can give rapid results and may help to suggest or even confirm a diagnosis.” This invaluable tool helps the practitioner make informed decisions about proper therapy which in turn benefits the patient and improves client satisfaction.

**Bacterial Culture and sensitivity** is utilized frequently in the author’s practice. Pustules are easy lesions to sample. Ideally, at least two will be present, one for cytology to confirm the presence of bacteria and one for sample collection. A sterile needle can be used to open the pustule and cotton tipped applicator can be touched inside the open pustule. Epidermal collarettes can also be sampled. The tightly adhered crusts can be lifted with a sterile needle and a cotton-tipped applicator can be used to swab underneath the lifted crust. A study published in 2005 demonstrated that dry sterile cotton swabs rolled across epidermal collarettes and submitted for aerobic C/S produced isolates of *S. (pseud)intermedius* from 18/22 dogs. In the same study, samples were collected from the healthy abdominal skin from 24 healthy dogs. *Staphylococcal (pseud)intermedius* was not isolated from any of the control dogs. Finally, with deep pyoderma or lesions of papular dermatitis, a biopsy for macerated tissue culture may be necessary. Prep the surface by lightly clipping, if necessary, and lightly brushing with antiseptic. Please do not perform a heavy surface prep. Chose the papules you would like to biopsy and inject local lidocaine. I recommend ring block due to the presence of confounding studies in the medical literature as to whether lidocaine will hinder bacterial growth of *S. aureus*. Perform punch biopsy and submit sample in sterile red top tube.

**Skin scrapes:** Deep skin scrapes are useful for diagnosing the follicular mites such as *Demodex* species *canis, inui* and *cati*. You may need to clip the pelage in order to start working right at the surface of the skin. Squeeze the skin before scraping; envision pushing the mites upwards from deep inside the hair follicles. Place mineral oil on the blade and scrape in the direction of
hair growth until capillary bleeding is noted. Place the material on a slide, turn the condenser down on your microscope and examine at 10x magnification. Superficial skin scrapes are useful for *Sarcoptes scabei*, *Cheyletiella* sp., *Notoedres cati*, *Demodex gatoi*, *Otodectes cyanosis* and lice. You may need to consider clipping affected area(s) but try not to dislodge scale and crust as this may decrease your ability to find the parasite. Mineral oil can be placed directly on the blade or on the pelage/skin itself. The area is then gently scraped collecting material from the stratum corneum, no need to draw blood since these parasites live on or within the surface layers. Turn the condenser down on your microscope and examine at 10x magnification. Scabies can be difficult to find. Improve your chances by scraping several sites, typically ear margins, elbows, hocks and ventrum.

**DTM** (dermatophyte test medium) results can be optimized by following these steps. Sample collection can be enhanced by using a Wood’s lamp to collect hairs that fluoresce. Keep in mind this method is neither sensitive nor specific. A lack of fluorescence does not rule out dermatophyte since approximately 50% of *M. canis* strains will not glow. Additionally, positive fluorescence does not automatically confirm infection as fluorescing scale and debris can be distracting. Hairs can be collected by plucking with sterile hemostats or with the Mackenzie toothbrush technique. The best lesions to sample are new or expanding lesions and areas with scale, crust or broken hairs. The author’s clinic uses Dermaoplate-Duos. Package inserts recommend plates be kept cool prior to use (36-77°F), protect from light and warm to room temp before inoculation. Plates are monitored daily for growth of white or light colored cottony to powdery colonies at the same time as media color change. Dermatophyte colonies are never green, gray or black. The author tends to wait a few days to allow the colony to mature before opening the plate for identification. Remember some dermatophytes are zoonotic. Ideally, all plates should be handled under a laboratory hood and gloves should be worn. Use clear acetate tape and gently touch the surface of the colony. Apply the tape to a slide over a drop of blue stain (methylene blue, lactophenol cotton blue, blue Diff-Quik) and observe at 100x power.

**Identification**

- *Microsporum canis*
  - Contagious amongst pets
  - Macroconidia: Spindle shape, thick wall with 6 or more internal cells, terminal knob
- *Microsporum gypseum*
  - Originates from the soil
  - Macroconidia: Spindle shape, thin wall, 6 or fewer internal cells, no terminal knob
- *Trichophyton mentagrophytes*
  - Originates from rodent/rabbit nest
  - Macroconidia: Cigar shape, thin walls may also see spiral shaped hyphae and small grapelike clusters of microconidia
**Biopsy** is best performed on lesions that have been non-responsive to medical therapy over a period of time, ideally before chronic changes occur. The author also makes sure to treat secondary infections before biopsy. The author obtains samples from multiple sites that represent lesions in different stages of development. Skin biopsy does not need any surgical prep, to be sure cleaning and scrubbing is likely to remove valuable diagnostic material. Use a sharpie to circle or mark the four corners of the sites you would like to biopsy. The need for sedation is determined by patient personality but local lidocaine block is a must. Inject approximately 0.5 – 1 cc of lidocaine under each site. Keep in mind that each patient has a maximum lidocaine dose that can be injected. Wait at least 5 minutes before performing biopsy. A punch biopsy tool is placed vertically over the skin lesion. Rotate the punch in one direction with firm pressure until it moves into the subcutaneous tissue. Remove the punch, use forceps to grasp the sample deep near the panniculus tissue then cut with blade or scissors. Avoid grabbing the dermis/epidermis. Blot the sample with gauze to remove blood. Place in formalin. Close with simple interrupted or cruciate suture. Send the sample to a dermatophistopathologist and provide a thorough history and a list of your differential diagnoses.

**References**

GOT ATOPY?

Atopic dermatitis (AD) is defined as follows: a genetically predisposed inflammatory and pruritic allergic skin disease with characteristic clinical features associated with IgE most commonly directed against environmental allergens. Knowledge has grown over the years that we now understand AD is a result of a complex interaction between genetic and environmental factors. Research has shown that AD is multifactorial and polygenic with almost 50 genes implicated (genes that influence inflammation/immunology, cell cycle, apoptosis, repair or lesion formation, transport and regulation and barrier formation). We also understand it involves a complex mode of inheritance. All these factors together explain the variation in severity & response to therapy between patients.

Historically, atopic dermatitis was viewed as a disorder within the immune system. This hypothesis is termed the inside to outside hypothesis. Simply stated, it suggests a shift from a T helper lymphocyte type 1 (Th1) profile to a T helper lymphocyte type 2 (Th2) profile, which results in increased IgE production, which in turn predisposes an individual to increased skin inflammation and secondary infections. Others support an outside to inside hypothesis which suggests that the initiation of AD begins with impaired barrier function of the stratum corneum, allowing the outside (allergens) to cross inside (the skin barrier) thus initiating the shift from Th1 to Th2, followed by an inflammatory response, followed by the seemingly endless cycle of secondary infections and further barrier dysfunction and inflammation. Most clients don’t need the complicated version of the pathogenesis of the disease. It’s much easier to say that allergy leads to inflammation which predisposes a pet to secondary infections. We also know that there are basic differences in the skin biology of an atopic individual that contribute to the allergy. For the visual learners I like to show photos from a study published in the last 5 years that illustrate the difference between skin from an atopic dog versus a non-atopic dog. The brick and mortar analogy is easy for clients to understand. The skin cells are the brick, the lipids are the mortar. With fewer lipids, the barrier function is weak and predisposed to invaders such as pollens. Additionally, studies have shown that pets with AD have greater transepidermal water loss which contributes to dry, dull, itchy skin.

A series of articles were published from 2001 through 2011 by the International Task Force on Canine Atopic dermatitis. These reviews consolidated research on canine AD. From them we learned about breed and age predisposition. Most dogs begin to show their allergic signs between 1 and 3 years of age. One recent study indicates that the Boxer, Dalmatian, French Bulldog, German Shepherd Dog, Golden Retriever, Jack Russell Terrier, Labrador Retriever, Shar pei and West Highland White terrier are predisposed. The author is in complete agreement with this list and frequently performs allergy testing on terriers of all varieties, Lhasa Apsos, Pit bulls/mixes and absolutely any breed with a short nose (Boxer, American and English bulldog, Frenchie, Boston, Mastiff).
Clinical clues that help support the diagnosis of atopic dermatitis include
- Initial response to antihistamine that eventually leads to the need for steroids
- Face, feet, generalized dermatitis/pruritus
- Initially steroid responsive, may become less so over time
- Initially seasonal that becomes perennial
- First signs between the age of 1-3 years
- "Front end" disease

This list is certainly not all encompassing as we have all seen patients who don’t respond to antihistamines of any type. Allergies can also manifest at interdigital furunculosis, non-pruritic relapsing superficial pyoderma, periocular dermatitis, recurrent otitis externa/media or any number of other clinical signs. Canine atopic dermatitis is a diagnosis of exclusion, and it is essential to eliminate ectoparasites and evaluate the role of food. The intradermal allergy test is considered the gold standard of allergy testing for atopic dermatitis. Although some veterinary dermatologists do perform serum allergy tests, the methodology is far from ideal. The author routinely sees patients referred with negative serum IgE test results when the clinical history and physical exam clearly support AD.

Atopic dermatitis is a disease to be controlled, not cured, and multiple therapies are often necessary for management of the disease. Veterinary dermatologists recognize allergen specific immunotherapy (ASIT) as the "only proven treatment for allergies that actually works against the underlying immunopathogenesis of the disease instead of merely covering up clinical signs with anti-inflammatory therapies". This occurs by inducing a shift backwards from a Th2 profile to a Th1 profile. ASIT has traditionally been injection based. Recent studies have shown efficacy with oral immunotherapy. In the interest of time we will discuss oral immunotherapy in more detail in hour five (What’s New Doc?). One early study showed immunotherapy improves approximately 59% of allergic pets. Anecdotally, in the author’s practice, the expectation is set that 80% of allergic pets should respond to immunotherapy and it is reasonable to expect a 50-80% improvement in overall condition. Because immunotherapy rarely provides a complete cure, other therapies may be needed to further improve overall comfort.

Antihistamines are thought to be helpful in a low percentage of atopic patients. It has been suggested that combining an antihistamine with fatty acid therapy may increase efficacy. High dose fatty acid is recommended and clients of ADRC are directed to find a product that provides EPA (eicosapentanoic acid) at 180 mg per 10 pounds of body weight. Antihistamines are more likely to be of benefit when pruritus scores are mild to moderate. When pruritus escalates over 5/10 the author is more inclined to prescribe a stronger anti-itch medication and investigate the presence of secondary infections such as superficial staph pyoderma and Malassezia
Dermatosis. Diagnosing and treating secondary infections is paramount to overall success with patient comfort and client satisfaction.

The following chart is adapted from a popular dermatology text book and summarizes the doses of antihistamines used in previous studies.18

<p>| Antihistamines used for trials with atopic dermatitis |
|--------------------------------|------------------|------------------|</p>
<table>
<thead>
<tr>
<th>Name</th>
<th>Dog dose</th>
<th>Cat dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline</td>
<td>1-2 mg/kg every 12 hr</td>
<td>0.5 – 1 mg/kg every 12 hr</td>
</tr>
<tr>
<td>Cetirizine</td>
<td>1 mg/kg every 24 hr</td>
<td>5 mg/cat every 24 hr</td>
</tr>
<tr>
<td>Chlorpheniramine</td>
<td>0.4 mg/kg every 8-12 hr</td>
<td>2.4 mg/cat every 12 hr</td>
</tr>
<tr>
<td>Clemastine</td>
<td>0.05 – 0.1 mg/kg every 12 hr</td>
<td>0.68 mg/cat every 12 hr</td>
</tr>
<tr>
<td>Cyproheptadine</td>
<td>0.3 – 2 mg.kg every 12 hr</td>
<td>2 mg/cat every 12 hr</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>2.2 mg/kg every 12 hr</td>
<td>2.2 mg/kg every 12 hr</td>
</tr>
<tr>
<td>Loratidine</td>
<td>1 mg/kg every 12 hr</td>
<td></td>
</tr>
</tbody>
</table>

Steroids may be necessary for short to mid-term control of allergic pruritus. The two most common topical steroids noted in medical records from the Dallas, TX area are Genesis® spray (0.015% triamcinolone acetonide) and GenOne spray (betamethasone valerate equivalent to 0.284 mg betamethasone). The author recommends Genesis® spray as it is in the low strength (category six of seven) in regards to steroid potency while GenOne is in the upper mid-strength (category three of seven) and can cause dramatic side effects on the skin such as atrophy, comedome formation, etc19.

Topical therapy will not be useful for pets with generalized pruritus and ease of application decreases as the coat length increases.

Decision making regarding systemic administration of steroids is of course an art and science and many factors must be considered such as underlying health conditions, likelihood of side effects and ease of administration. The author encourages oral therapy as often as possible given the ability to taper therapy faster if side effects (especially increased appetite, increased water intake and increased urine output) are severe and can’t be tolerated by the pet parent(s).

Commonly used products are Temaril-p®, prednisone/prednisolone, dexamethasone and triamcinolone. As a general rule of thumb the author typically starts with Temaril-p® at label doses, prednisone at 0.5 mg/kg once or twice daily (depending on severity of pruritus) and tapering on 4-7 day intervals. Dexamethasone doses are calculated by determining desired prednisone dose and then dividing by 10 to obtain desired dose. For example, 5 mg of prednisone would calculate to 0.5 mg of dexamethasone. Triamcinolone doses are calculated by determining desired dose for prednisone and then dividing by 1/2 to 2/3 to obtain desired dose. For example,
5 mg of prednisone would calculate to 2 – 3.3 mg of triamcinolone. The author never uses dexamethasone or triamcinolone twice daily, only once daily tapering to longest possible interval.\textsuperscript{20}

Injectable steroids are popular with practitioners in the Dallas, TX area. The greatest concerns are for side effects and pruritus that does not respond to the steroid injection, yet knowing the duration of adrenocortical suppression, for example, to methylprednisolone acetate (depo) lasts for 3-9 weeks depending on the dose administered.\textsuperscript{21}

The following chart is adapted from a popular dermatology text book and contains the doses of injectable steroid formulas.\textsuperscript{22}

<table>
<thead>
<tr>
<th>Betamethasone acetate</th>
<th>Betasone</th>
<th>D: 0.2-0.4 mg/kg</th>
<th>IM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dex SP</td>
<td>Azium</td>
<td>D: 0.25 - 1 mg /dog</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td>Generic</td>
<td>C: 0.125 mg/cat</td>
<td></td>
</tr>
<tr>
<td>Flumethasone</td>
<td>Flucort</td>
<td>D: 0.06 - 0.25 mg/dog</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C: 0.03 - 0.125 mg/cat</td>
<td>IM or SQ</td>
</tr>
<tr>
<td>Methylprednisolone acetate</td>
<td>Depo-medrol</td>
<td>D: 2-40 mg /dog</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C: 10-20 mg/cat</td>
<td>IM</td>
</tr>
<tr>
<td>Triamcinolone</td>
<td>Vetalog</td>
<td>D: 0.2 mg/kg</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C: 0.2 mg/kg</td>
<td>IM</td>
</tr>
<tr>
<td>Prednisone</td>
<td>Meticortin</td>
<td>D: 0.5 - 2.2 mg/kg q 24 h</td>
<td>IM</td>
</tr>
<tr>
<td></td>
<td>Generic</td>
<td>C: 0.5 - 2.2 mg/kg 1 24 h</td>
<td>IM</td>
</tr>
</tbody>
</table>

Two FDA approved anti-allergy medications are now available: the calcineurin inhibitor Atopica® and the janus kinase inhibitor called Apoquel®. Allergic pets can be allergy tested while on either medication. Over the years we have gained a level of comfort with Atopica® and rarely see changes on routine lab work.\textsuperscript{23,24} Atopica is often combined with ketoconazole to take advantage of drug interactions and use less medication.\textsuperscript{25} Apoquel will be discussed in greater detail in hour five (What’s New Doc) and more information can be found in those notes. Briefly, Apoquel reduces pruritus as fast and as effectively as prednisone and dexamethasone. Adverse effects: GI disturbances in 2.3%, lethargy in 1.8%, loss of appetite in 1.4%.

The World Congress of Veterinary Dermatology was held in the summer of 2012 and many dermatologists were talking about therapy to improve barrier function. There was not solid research presented at this meeting but the author expects that over the next few years we should be learning more. Shampoo therapy with medicated shampoo and topical products containing skin lipid complex\textsuperscript{6} are utilized routinely for patients of the author’s practice.
**How itchy (pruritic) is your pet?**

This scale is designed to measure the severity of itching in pets. Itching can include scratching, biting, licking, chewing, nibbling, or rubbing.

Read all the descriptions below **starting at the bottom**. Then place a mark on the vertical line that runs down the left hand side to indicate the point at which you think your pet's level of itchiness (pruritus) lies. Different regions of the body may have different severity scores.

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>Extremely severe itching/almost continuous: Itching does not stop whatever is happening, even in the exam Room (needs to be physically restrained from itching)</td>
</tr>
<tr>
<td>9</td>
<td>Severe itching/prolonged episodes: Itching might occur at night (if observed), but also when eating, playing, exercising or being distracted</td>
</tr>
<tr>
<td>8</td>
<td>Moderate itching/regular episodes: Itching might occur at night (of observed), but not when eating, playing, exercising or being distracted</td>
</tr>
<tr>
<td>7</td>
<td>Mild itching/ a bit more frequent: Wouldn't itch when sleeping, eating, playing, exercising, or being distracted</td>
</tr>
<tr>
<td>6</td>
<td>Very mild itching/ only occasional episodes: The dog is slightly more itchy than it was before the skin problem Started</td>
</tr>
<tr>
<td>5</td>
<td>Normal dog</td>
</tr>
<tr>
<td>4</td>
<td>I don't think itching is a problem</td>
</tr>
</tbody>
</table>

References


19 Scott et al. Dermatologic Therapy. Muller and Kirk’s Small Animal Dermatology. 7th ed. 2013:127-128
21 Scott et al. Dermatologic Therapy. Muller and Kirk’s Small Animal Dermatology. 7th ed. 2013:130
FOOD ALLERGY: IT’S WHAT’S FOR DINNER

The following topics will be covered: epidemiology and clinical signs, pathogenesis, testing for food allergy, cleansing phase (what foods to use for food trial) and the challenge phase. Food allergic dermatitis is a non-seasonal dermatitis associated with the ingestion of a substance found in the diet and may manifest as pruritus +/- relapsing infections +/- gastrointestinal signs.

**Epidemiology and Clinical Signs:** One recently published study from our Swiss colleagues looked at over 250 dogs and gave us valuable information regarding allergic dogs. For example, 31% of dogs in the study improved on elimination diet, 85% improved completely while 15% only partially improved (indicating both food allergic and atopic dermatitis). The Boxer, German Shepherd Dog, Pug, Rhodesian Ridgeback and Westie were over represented breeds. Thirty one percent of dogs had gastrointestinal signs in addition to dermatologic signs. Age of onset was noted to be less than 3 years of age for 83% and less than 1 year of age for 48%, supporting our belief that dogs can develop food allergies at a very young age. Another study identified older dogs develop food allergies also. A gender predisposition has not been found for dogs or cats. Cat breeds prone to food allergy are Birmans, Siamese and their mixes and the mean age of onset is 4.5 years. From a clinical standpoint, food allergy is the main reason felines of any breed present to the author’s practice. It is rare that veterinary studies involve large numbers of patients but one recently published multi-center study included 502 cats. This study took the perspective of categorizing allergic felines based on the 4 major allergy patterns: miliary dermatitis, eosinophilic dermatitis, self-induced symmetrical alopecia and head and neck excoriations.
Sixty four percent of the food allergic cats had head and neck pruritus. Only 25% of the cats with eosinophilic granulomas had food allergy. Concurrent GI signs were noted in 21% of the cats in the study. Finally, investigators look at statistics based on age of onset and determined the following:

- Age of onset before 3 yrs of age
  - 72% of Atopics
  - 52% of Food allergic
- Age of onset after 6 yrs of age:
  - 26% of food allergic
  - 12% of Atopics

The take away message from this large study population is that no specific sign is considered pathognomonic for any one allergy. Some “leaning” can be done in that a feline patient with head & neck dermatitis/pruritus is more likely to be food allergic with atopic dermatitis being a close second. Later age onset: think food allergy first.

**Pathogenesis:**
There are numerous “layers” inside our bodies to help prevent the development of a food allergy including a) peristalsis, b) epithelial cells held together by tight junctions with mucous over the top help block the passage of large molecules, c) plasma cells release IgA which binds antigens which are then removed from intestinal mucus or circulation, and d) dendritic cells are able to neutralize allergens that cross the barrier via paracellular spaces, finally e) those allergens are presented to T helper lymphocytes which travel to the lymph node to start the process of an immune response.\(^5\) A 2011 review summarized the complicated steps towards developing a food allergy as follows: \(^6\)

- Sensitization to a food allergen develops after the initial exposure with formation of IgE to specific portions of the allergen. Released from activated B cells, IgE binds to high affinity receptors for IgE located on the surface of mast cells and basophils. Upon re-exposure to an antigen IgE binding brings Fc RI receptor on cell surfaces to proximity that allows cross-linking between receptors. Once receptor cross-linking occurs, several tyrosine kinases, including Lyn, Syk, and Fyn, are activated within the cell providing both positive and negative regulation of the signal cascade. Calcium influx controlled by both positive and negative regulation is essential to mast cell degranulation. Mast cells and basophils release preformed mediators including histamine, heparin, tryptase, chymase, and tumor necrosis factor α (TNF-α). They also release newly synthesized inflammatory mediators such as platelet activating factor, nitric oxide, TNF-α, cyclooxygenase products of arachidonic metabolism, and lipoxygenase products of arachidonic metabolism (leukotrienes LTC4, LTD4 and LTE4). Production of interleukin-4 (IL-4), IL-5, IL-13, and granulocyte macrophage colony-stimulating factor (GM-CSF) may continue for several hours.
It makes sense that diseases such as gastroenteritis (bacterial, viral, parasitic), pancreatitis, or genetic conditions such as enteropathy of Irish Setters would compromise the gastrointestinal tract and allow exposure to large molecules and predispose to food allergy.

Most AFR's appear to be IgE mediated and typically linked to allergens usually greater than 10,000 daltons, (10,000 - 70,000 daltons). Decreasing the protein allergen size should decrease binding to IgE. Most human hydrolysate based diets are less than 5,000 daltons and good evidence exists for use of diets in which the allergen is less than 3,500 daltons. What does this imply for our practices? A hydrolyzed diet may help a pet with IgE mediated food allergy.

What are the top allergens in Veterinary Medicine?

- Dogs: review results of 7 independent studies
  - Beef, cow's milk, soy, corn, wheat
  - Chicken, turkey, mutton, pork, rabbit, herring, egg, potato
- Cats: review results of 3 independent studies
  - Fish, beef, dairy, egg, wheat, corn, barley, chicken, lamb, rabbit, whale meat, others

Food Allergy Testing: The following tests have been investigated in humans and pets: serum IgE testing, intradermal allergy testing, patch testing, blood lymphocyte testing, gastoscopic food sensitivity testing, colonoscopic allergen provocation test (COLAP), histopathology, and limited ingredient food trials. Let’s look at the medical literature for each. Serum IgE testing: Correlation to clinical reality is poor. A 2012 study showed that sensitivity was 6.7%, meaning there is a high likelihood of false negative test results. Serum allergy testing also yields false positive results in most normal dogs, most dogs with other skin disorders and also dogs with food allergy, but not always to the allergens determined by ingredient challenge. A colleague recently summarized serum IgE testing for food in this manner: “published studies of food allergen-specific IgE assays in dogs found them to be insensitive, nonspecific, and unreliable for diagnosis of adverse food reactions”. Intradermal allergy testing: A limited number of studies have published data regarding this form of testing for food allergy. The first study included 100 suspected allergic dogs, skin-tested with 9 food extracts. Forty-eight of the dogs had positive reactions to 1 or more food extracts. Thirty of the food extract-positive dogs were fed a restrictive hypoallergenic diet. Of these 30 dogs, 3 improved (10%). Allergy signs worsened when the dogs were challenge-exposed with the original diet. Fifty-two dogs did not have skin test reactivity to any of the 9 food extracts. Of these 52 dogs, 35 were fed a restrictive diet. Six (17%) improved. Allergy signs worsened when the dogs were challenge-exposed with the original diet. The conclusion of the study was “skin-testing with selected allergenic food extracts was not useful in identifying food-sensitive dogs”. A second study involving 13 patients came to the conclusion “On the basis of these results, skin testing, and anti-IgE ELISA cannot replace an owner-prepared food elimination diet for food hypersensitivity testing in dogs.” Patch Testing was conducted by one veterinary group. In this study patch testing was considered to have high sensitivity and specificity. Blood lymphocyte proliferative studies: three have been published to date. There may be hope for this form of testing in the future based on the latest set of data. Gastoscopic food sensitivity testing utilize endoscopy to drip food extracts onto the dependent
aspect of the body of the stomach. Reactions appeared as localized mucosal swelling and erythema within 2-3 minutes and correlated to reaction upon oral challenge. Colonic allergen provocation – COLAP accurately determined 18/23 (73%) positive oral challenge reactions in dogs with food allergies and was negative in healthy dogs. Biopsy for dermatohistopathology: allergy looks like allergy whether food or atopic dermatitis so this is not helpful test. This leaves us with restricted food trials as the only way to diagnose a food allergy.

What to feed? Anything the animal has not previously eaten and a good history is absolutely necessary. Options include home cooked diets and commercially available pet food. Considerations include time investment, financial investment and safety. One website that can be utilized is www.balanceit.com. The author has not used this website but found it in the most recently released dermatology reference.

The following options exist for commercially available diets: Hydrolyzed diets are tolerated by most but not all dogs. Novel Protein diets are popular amongst vet derms in the United States. One recently released food is both novel protein and hydrolyzed. It seems availability of certain diets waxes and wanes, the author will share with the audience the brands/names currently prescribed at her practice during the presentation. The author cautions against using over the counter (OTC) “hypoallergenic” foods as a manufacturer may contract with multiple pet food companies and produce multiple foods on one production line. A recent study analyzed four OTC venison diets and found unlisted proteins: 3/4 contained soy and 1/4 contained beef. How long should a restricted diet be fed? At some point during training the author learned the following statistics regarding length of food trial: 21 day duration: 26% diagnosed, 8 week duration: 70% diagnosed and 12 week duration: 100% diagnosed. Whether this is fact or dogma is unknown as I have been unable to locate this reference. It is not surprising that improvement can take weeks given the complicated pathophysiology.

The Challenge Phase: It is preferred that the pet parent add individual ingredients one at a time to better identify flares. The ideal method is to add one new ingredient every other week. Another method is to reintroduce the pet’s previously fed food in week one, if a flare is noted you can then go back and scrutinize for ingredients likely to cause a flare. Using the list generated you can challenge individually with each. Previously administered flavored heartworm prevention can be reintroduced with time as can previously fed treats. Pruritus typically relapses within 3-7 days, in which case you should instruct the pet parent to discontinue diet. Typically the dermatitis resolves quickly but a steroid rescue may be necessary.

Between 1998 and 2006, four open studies were published. A combined one hundred ninety eight pruritic dogs were fed hydrolysate diets for 6-8 weeks. Complete remission was achieved in 18-34% of dogs while partial remission was noted in 27-69% of dogs.
A retrospective study from France investigated the prevalence and causative allergens of food induced AD.\textsuperscript{28} Food challenges resulted in flares to

- Zero food items: 12/50 (24%)
- One food item: 22/50 (44%)
- Two food items: 11/50 (22%)
- Three food items: 3/50 (6%)
- Four food items: 2/50 (4%)

This study also detailed the causative allergens as

- beef: 16/50 (32%)
- chicken: 13/50 (26%)
- lamb: 10/50 (20%)
- pork: 8/50 (16%)
- dairy product: 7/50 (14%)
- rice: 3/50 (6%)
- wheat: 1/50 (2%)

References


5. Wang et al, Food Allergy: J Clin Invest 2011;121:827-835


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STAPHYLOCOCCUS, ANTIBIOTICS, RESISTANCE: KNOWLEDGE IS POWER

Staphylococcal bacteria are normal inhabitants of the skin of humans and pets. *Staphylococcal pseudintermedius* is responsible for approximately 96% of superficial pyodermas on dogs. There must be some break in barrier function or change to skin biology for these commensals to become pathogens. Diseases such as atopic dermatitis, food allergy, hypothyroidism, cushing’s disease are commonly complicated by secondary staph infections.

Scientist Alexander Ogston first coined the term Staphylococcus in 1882 for the spherical organisms he viewed under the microscope from suppuration associated with abscess in the skin. Modern scientific techniques have allowed investigators to determine that these seemingly simple organisms have quite complex characteristics. Of concern is the bacteria’s {extensive arsenal of} virulence factors and its ability to overcome antibiotic therapy. Antimicrobial resistance was documented in the human medical literature shortly after the introduction of antibiotics. The first published report of antimicrobial resistant staph in companion animals was in 1999. A recent review listed 18 genes responsible for contributing to antimicrobial resistance in staph bacteria. One such gene is the mecA gene which confers resistance to the beta lactam class of antibiotics. The mecA gene is contained in a genomic island called the SCCmec. Under normal wild type conditions, a beta lactam antibiotic will impair the staph bacteria’s ability to build a cell wall thus killing the bacteria. A staph bacteria will no longer be susceptible to degradation once the the SCC mec gene island containing the mecA gene has been incorporated into a bacteria’s DNA. The bacteria then replicate and share the resistant genetics. Simply put, the current threat of acquiring methicillin-resistant strains of Staphylococcus is from exposure to a MecA positive Staphylococcus. Our patients are acquiring resistant bacteria strains from exposure to a carrier or fomite. The mecA gene is just one example of acquired antibiotic resistance that leads to methicillin resistant strains of staph bacteria. Bacteria can acquire higher levels of genetic resistance leading to multidrug resistant strains of bacteria.

Recurrent staph infections are frustrating for the practitioner and pet parent. Methicillin and multi-drug resistant strains can be downright distressing. As veterinarians we have a responsibility to be good stewards of antibiotic use so as to reduce contributions to the increasing incidence of antimicrobial resistance. The first and most important step is to prove a staph bacterial infection is present and that antibiotics are warranted. The author sees cases frequently in which antibiotics are administered for Malassezia dermatitis, pemphigus foliaceus or sarcoptic mange. Simple derm diagnostic tests such as tape and scrape can help you make informed therapy decisions. This is beneficial for everyone involved!

Second, utilize topical therapy as often as possible for focal infections such as otitis externa, facial or tail fold pyoderma, puppy impetigo of the ventral abdomen, etc. A series of studies was published in 2010 and 2011 and a review published in 2012 that provide evidence based medicine for topical therapy. Good evidence exists for using shampoos that contain 2-3%
chlorhexidine for bacteria, 2% chlorhexidine + 2% miconzole for bacteria & yeast and 2-3% Benzoyl peroxide for bacteria. Based on one study that included both owner and investigator observations, a 2% chlorhexidine acetate was shown to be as effective as a 4% chlorhexidine gluconate formula when dogs were bathed using 5 ml per 150 cm² body surface (~ 1.5 ml for 22 # dog) using the following protocol: gently wash with warm water, soak for 5 min, rinse & towel dry, bathe twice weekly. This publication included a second set of results which demonstrated efficacy of topical therapy against resistant strains of staph in 8 dogs. In an open trial study, dogs with a suspected methicillin resistant staph pyoderma were bathed with 2% chlorhexidine (Malseb: 50 ml per 30 kg (0.95 m2) by the following method: gentle washing, soak for 5 min, rinse and towel dry, twice weekly for 2 wks pending C/S results. The dogs were evaluated 2 weeks later and scored by the investigator. Methicillin resistant Staphylococcus pseudintermedius was isolated from all 8 dogs. Results of the study showed that 5/8 dogs improved without the need for oral antibiotic, 1/8 improved with some need for oral antibiotic, 2/8 had no apparent improvement while 0/8 had worsening of clinical signs during treatment. A follow up to that study was published the following year which investigated the effective dose/volume of shampoo to use. Briefly, 27 dogs were divided into three groups of 9 dogs each. The dogs in each group were bathed every other day with Nolvasan surgical scrub with a different volume: 57 ml/m², 29 ml/m² or 19 ml/m². All groups showed statistically significant improvement. The best response per owners and blinded investigators was group 2 in which 89% showed excellent to good improvement. Only 2 dogs in group 3 showed deterioration.

Not all patients and not all infections are candidates for topical therapy and systemic antibiotic therapy is often necessary. We often think of choosing an antibiotic based on a classification of first, second and third tiers. It is common practice to reach for Convenia®, Simplicef®, Clavamox® or cephalexin for first time infections. It is acceptable to continue to reach for these antibiotics for relapsing infections when previous infections cleared readily and completely. A recent systematic review article provided the following conclusions:

- Good evidence for high efficacy:
  - 1-3 consecutive subcutaneous injections of cefovacin at 8 mg/kg given 2 weeks apart
- Fair evidence for moderate to high efficacy of the following:
  - Amoxi-clavulanic acid at 12.5 mg/kg, BID, 21-28 d.
  - Cefadroxil, 22-35 mg/kg, BID, 28-42 d.
  - Clindamycin, 5.5 mg/kg, BID, 21 d.
    - The author would like to highlight another study and encourage the use of clindamycin at a higher dose of 11 mg/kg BID, especially since it is often employed for treating methicillin resistant strains of staph.
  - TMPS, 30 mg/kg, QD or BID, 42 d.
  - Sulfasalazine, 55 mg/kg day 1, 27.5 mg/kg thereafter, 21-42 d.
- Comparing duration of treatments:
  - 80% considered cured 14 d after single cefovacin injection at 8 mg/kg
  - 70% considered cured 14 d after course of cefadroxil at 22-35 mg/kg, BID
We want to set our clients up to succeed when treating a superficial pyoderma. Evidence based medicine published in 2011 lists the top barriers for owner compliance\(^9\). A complete list of those barriers is included at the end of these notes. The number one barrier to client compliance is frequency of dosing. We can help our clients by choosing therapies that need to be given less frequently. The 4\(^{th}\) barrier to compliance is a long duration of treatment. Treating for the shortest period of time will not only make our clients happy but will also decrease the time our patients spend in the “mutant selection window” (a term that is defined later in these notes). Treating for the shortest period of time does NOT mean 7 or 10 days. Using the evidence based statistics above: one injection of convenia is an adequate time frame for 80% and treating with cefadroxil for 21 days is adequate time frame for 70%. Use the practice of treating for 5 days past resolution of the infection, this way therapy is tailored to the individual. One final practice we can use to maximize successful resolution of superficial infection is to use antibiotics at their highest recommended dose. This utilizes a concept called the mutant prevention concentration (MPC). It is simply not enough to target killing 90/100 strains of a staph bacteria (MIC\(_{90}\)) instead we want to use antibiotic doses that will achieve concentrations to quickly kill all bacteria and kill bacteria with decreased susceptibility\(^{10}\). This mutant prevention concentration needs to exceed the MIC\(_{90}\) but needs to be lower than the maximum safe concentration (MSC). Between the MIC\(_{90}\) and the MPC is the mutant selection window (MSW). Placing antimicrobial concentrations inside the window is expected to enrich resistant mutant subpopulations selectively while placing antimicrobial concentrations above the window is expected to restrict resistant selective enrichment.\(^{11}\) Future studies are needed to find the concentration of each antibiotic with each bacterium at which no mutant is recovered both \textit{in vitro} and \textit{in vivo}. This will help us not only control infection, but decrease resistance.

The patient that has rapidly relapsing superficial pyoderma or an infection that is not responding to appropriate first line antibiotic therapy may have acquired a resistant strain of bacteria. The author highly encourages repeating skin cytology to confirm the presence of the bacteria followed by submission of a sample for aerobic culture and sensitivity testing. Use aggressive topical therapy pending C/S test results. Chose an appropriate antibiotic based on test results. Antibiotic commonly used for resistant staph infections are Primor\textsuperscript{®}, TMPS-SMZ, Clindamycin, Marbofloxacin, Enrofloxacin and Chloramphenicol. Doxycycline is commonly identified as an appropriate choice for resistant staph but the author cautions anecdotally of multiple treatment failures when using this drug class.

Fluoroquinolones (FQs) should never be used as a first line choice for treating superficial pyoderma. Four FQs have been approved for use in veterinary medicine: enrofloxacin, orbifloxacin, difloxacin, and marbofloxacin. Laboratory reports of sensitive versus intermediate versus resistant are based on interpretive criteria provided by Clinical Laboratory Standards Institute (CLSI) and are based on pharmacokinetic data (such as Cmax, AUC) and pharmacodynamic data (such as MIC). The CLSI has provided these values for pets for the 4 approved FQs but \textbf{NOT} for ciprofloxacin. Therefore, labs use interpretive criteria for humans to
report S, I, or R. We can all agree that bacterial pharmacodynamics & drug pharmacokinetics are not necessarily similar in dogs & humans nor in cats & humans. Additionally, ciprofloxacin bioavailability studies show the following: 70% in humans, 33-40% in dogs, 0-20% in cats. As summarized by Dr. Boothe in this 2006 publication: “As such, extrapolation of human interpretive criteria as a basis for an "S" versus "R" designation for cipro and canine pathogens is questionable.” Dr. Boothe makes 4 additional conclusions that the author feels are very important to share with practicing veterinarians

- An isolate designated as R to one FQ is likely to be resistant to all
- Emphasized using high dose FQ
- With FQ use in companion animals increasingly being scrutinized by regulatory agencies and the public, continued use of cipro despite availability of 4 veterinary FQ's might not be prudent
- Use of generic human products markedly undermines incentives to pursue new animal drug approvals

Other investigators, including the CDC in 2006, have also published studies that warn again the use of FQs as a first line antibiotic and emphasize that the FQ’s should only be used when directed by C/S test results.

To summarize, employ antimicrobial practices that

- resolve the infection rapidly & completely
- utilize a protocol with high probability of success from the start
- Once you decide to use antibiotics, go with the best in class antibiotic at optimal dose

One final point that is incredibly important to make after all this discussion of infections and resistance is to remember that the infections are secondary to something else. The infections will continue to relapse until you identify and address the underlying cause.

**Barriers to Compliance**

1. Frequency of dosing; administering treatment more than once or twice daily
2. Administering multiple medications
3. Difficulty getting pet to take the medication
4. Long duration of treatment
5. Not able to give medication with food
6. Lack of understanding about the disease being treated and/or the medication prescribed
7. Lack of client satisfaction with the time spent w/ DVM
8. Lack of client participation in treatment decisions
9. Client's unwillingness to ask questions
10. Client's busy lifestyle
11. Client's belief system, skepticism of value of western medicine
Hospital Infection Control

The author is by no means an expert in infection control but recommendations and resources are shared here for developing an infection control program for your hospital.

- Animal Cohorting and flow, hospital design
  - Maintain "like" groups
  - Derm patients separated from others

- Mixing in reception is source of contact
  - Educational campaign - posters to highlight need to keep pets from having contact
  - Limit time pets w/ active infection spend in waiting area

- Screening of veterinary personnel
  - Fraught with challenges, problems, controversial, rarely warranted

- Transmission:
  - between derm patients
    - Recent Study: 27% of dogs treated for NON-MRSP pyoderma were colonized with MRSP at time of recheck, a few weeks after clinical cure
  - to patients on other services
  - to clinic personnel
    - MRSP considered to have limited virulence
    - MRSP in vet personnel at reported rates of 0.7 - 8.8%
  - to owners
    - General hygiene principles, restricted contact
    - Isolation rarely needed

- Formal infection control program w/ infection control officer to oversee
  - Surveillance
    - Active
      - Screening at admission: expensive, time consuming, often not necessary
    - Passive
      - Use of already available data: collation of C/S results: helps identify infection trends. Potential bias b/c of case selection
    - Syndromic
      - Detection of syndromes like scratching
    - Environmental
      - Considered waste of time, $ and resources

- Environmental Cleaning and Disinfection

- Personal Protective Equipment
  - Lab coat changed regularly whenever potentially contaminated
  - Gloves and gown

- Hand Hygiene
  - Before patient contact….before aseptic procedure…after contamination of hands…after removing gloves….after patient contact
- Minimize exposure of susceptible dogs to resistant Staph
- Patients with history of resistant staph placed in room sooner
- Hand sanitizers in each room
- Strict hand hygiene - wash before and after
- Wear gloves
- No ties, scarves, necklaces, bracelets
- Cognizant of stethoscope, otoscope handle
- Routine cleaning of table tops, handles, drawer pulls, computer keyboards
- References to guide you

References

1 Dowling et al. Clinical significance of antibiotic-resitant bacteria. Am Med Assoc 1955;157(4);327-331


What's New Doc?

The Latest and Greatest to Help You Practice Your Best Derm!

Overview

• Apoquel®
  – Research, label & 3 month perspective
• Oral allergen specific immunotherapy
  – Research & one year perspective
• Review recent derm literature for clinically relevant information

Apoquel®

New therapy for itch
Apoquel®

- History - Concept of design - Spring 2007
- Label warnings - Should not be used in dogs
  - Less than 12 months of age
  - With serious infections
  - Breeding
  - Pregnant or lactating
- Increase susceptibility to infection & demodicosis
- May exacerbate neoplastic conditions
- not been evaluated in combo with steroid or CsA
- Most common side effects : vomiting and diarrhea
- Should not be used in dogs
- Safely used with other common medications including antibiotics and parasiticides and with vaccinations.

Apoquel®

- Cytokines are key players in K9 allergic skin dz
- Apoquel® (oclacitinib tablet), a targeted therapy
  - Janus kinase inhibitor
  - Inhibits JAK1-dependent cytokines involved in allergy
  - Rapidly reduces itching
  - Reduces inflammation in the skin, similar to glucocorticoids
  - Allows the veterinarian to diagnose the underlying cause of itch


The Complexity of Allergy
Single Dose Study

Low dose Apoquel® significantly reduced pruritus at all time periods between 1 and 5 hours after a single dose in a lab model of FAD


Single Dose Studies

Apoquel® -vs- prednisolone: 2 diff doses


Single Dose Studies

Apoquel® -vs- dexamethasone

Overdose Study

- One-year-old Beagle dogs
  - BID x 6 weeks, then QOD x 20 weeks
    - At 0.6 mg/kg (1X maximum dose, 8 dogs)
    - 1.8 mg/kg (3X, 8 dogs)
    - 3.0 mg/kg (5X, 8 dogs)
  - Eight dogs received placebo (empty gelatin capsule) at the same dosage schedule

Clinical observations considered likely to be related to Apoquel®
- Papillomas
- Dose-dependent increase in number & frequency of interdigital furuncyllosis (cysts) on one or more feet, lymphadenopathy of peripheral nodes of affected paws
- Five had mild pneumonia
- Mild, dose-dependent reduction
  - RBC, WBC, Total proteins

Vaccine Response Study

- Adequate immune response to
  - Killed rabies vaccine (RV)
  - ML canine distemper virus (CDV)
  - ML canine parvovirus (CPV)
  - Vaccination achieved in eight 16-week old vaccine naïve pups on Apoquel® @ 1.8 mg/kg (3X maximum dose) BID x 84 d
  - ML canine parainfluenza virus (CPI), 6 of 8 (75%) dogs achieved adequate serologic response
Vaccine Response Study

During the 3 month recovery phase to this study, dog (32-weeks old) was euthanized on Day 28
- Enlarged prescapular lymph nodes, bilateral epiphora, lethargy, mild dyspnea, and fever with elevated WBC count
- Necropsy: lesions consistent with sepsis secondary to immunosuppression. Bone marrow hyperplasia was consistent with response to sepsis.

Apoquel®

- Dosage and Administration
  - 0.4 – 0.6 mg/kg PO, BID x 14 days then qd
- Dosage Form
  - Scored caplets
  - 3.6 mg, 5.4 mg & 16.0 mg tablets
- Administered with or without food

Clinical Study 1

- Species: 436 dogs
  - Breed: Pure and mixed-breed
  - Age: 1-18 years
  - Size: small to large breed (6.60-135.7 lbs)
  - Sex: ♀ and ♂ dogs equally represented;
    - >88% were either spayed or neutered
  - Origin: Client-owned dogs enrolled at 26 vet practices throughout the United States
  - 24 General Practices and 2 Dermatology Specialty Practices

Inclusion

- The allergic dermatitis was attributable to at least one of the following:
  - Food Allergy
  - Contact Allergy
  - Allergy
  - Flea
  - Sarcoptic Mange
  - Atopic Dermatitis
  - Other Allergic Dermatitis (unless prohibited by exclusion criteria)

Exclusion

- Skin condition was attributable to:
  - Demodectic Mange
  - Bacterial Folliculitis
  - Fungal Dermatitis
  - Showed evidence of immune suppression
  - Diagnosed with a malignant neoplasia
  - Had been or were intended to be used for breeding
  - Enrolled in a previous study with Apoquel®

Clinical Study 2

- Species: 341 dogs
  - Breed: Pure and mixed-breed
  - Age: 1-15 years
  - Size: small to large breed (7.04-164.3 lbs)
  - Sex: ♀ and ♂ dogs equally represented;
    ▪ >90% were either spayed or neutered
  - Origin: Client-owned dogs enrolled at 23 Dermatology Specialty Practices across US
Clinical Study 3

- Species: 299 dogs
  - Breed: Pure and mixed-breed
  - Age: 1-13 years
  - Size: small to large breed (7.48-169.8 lbs)
  - Sex: ♂ and ♀ dogs equally represented;
    - >90% were either spayed or neutered
  - Origin: Client-owned dogs enrolled at 19 Dermatology Specialty Practices across US
  - On average, dogs gained 4% body weight

Safety Assessment

- No deaths or serious adverse events
- The majority of abnormal clinical signs resolved spontaneously with continued dosing
- A wide variety of concomitant medications were well tolerated

<table>
<thead>
<tr>
<th></th>
<th>Oclacitinib, n = 220</th>
<th>Placebo, n = 216</th>
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<tbody>
<tr>
<td>Diarrhea</td>
<td>5 (2.3)</td>
<td>2 (0.9)</td>
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<tr>
<td>Vomiting</td>
<td>5 (2.3)</td>
<td>4 (1.8)</td>
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<tr>
<td>Lethargy</td>
<td>4 (1.8)</td>
<td>3 (1.4)</td>
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<tr>
<td>Anorexia</td>
<td>3 (1.4)</td>
<td>0 (0.0)</td>
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<tr>
<td>Polydipsia</td>
<td>3 (1.4)</td>
<td>0 (0.0)</td>
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**Other Studies**

- Apoquel effect on IDAT
  - None, can allergy test while on Apoquel


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**Continuation Study**

- Program initiated – late 2009 after pet owners and DVMs made Zoetis colleagues aware that Apoquel® represented potential life-saving therapy for many of the dogs participating in the clinical trials
- Zoetis continued to provide Apoquel® to all enrolled dogs at least until commercial product is made available
- Owners and veterinarians must comply with strict visit window requirements and provide assessments of the dog’s response to Apoquel® administration

Continuation Study

- Data through 10/31/12 appears on product label
  - 249 dogs enrolled in an unmasked (no placebo control), continuation therapy study
  - Apoquel for an unrestricted period of time
  - Mean time on this study was 372 days (range 1 to 610 days)
- 177 (71%) remain
- 72 (29%) withdrawn
  - Mean time on study is 402 days
  - ~50% of the dogs have been on study for ≤1 year
  - ~50% of the dogs have been on study for 1-2 yrs
Label Warnings

- Should not be used in dogs
  - Less than 12 months of age
  - With serious infections
  - Breeding
  - Pregnant or lactating
- Increase susceptibility to infection & demodicosis
- May exacerbate neoplastic conditions
- Not been evaluated in combo with steroid or CsA
- Most common side effects: vomiting and diarrhea
- Safely used with other common medications including antibiotics and parasiticides and with vaccinations.

Human Counterparts

- FDA approved
  - Tofacitinib – JAK3 – Nov 2012
    - Psoriasis
    - Rheumatoid arthritis
  - Ruxolitinib – JAK1/JAK2 – Nov 2011
    - Psoriasis
    - Myelofibrosis
    - Rheumatoid arthritis
- In clinical trials: 5 more
  - Arthritis, lymphoma, acute myelogenous leukemia

Three Month Experience

- My ESTIMATIONS
- Highly effective overall for ~ 75-80%
- Partially effective for ~ 15%
  - Does well on BID but pruritus increases on QD
- Does not work at all for ~ 5%
- Reports of once daily therapy losing effectiveness after 14-21 days of QD dosing
Participating Derms

Jill Abraham, Massachusetts Veterinary Referral Hospital, Glen Burkett, Animal Dermatology and Allergy, Sarah Colombini-Osborn, Southwest Veterinary Dermatology, Chris Cook, Animal Allergy and Dermatology, Kimberley Coyner, Dermatology Clinic for Animals, Jenise Daigle, Austin Veterinary Dermatology and Allergy, Allison Kirby, Animal Dermatology Clinic, Tom Lewis, Dermatology Clinic for Animals, Jennifer Matousek, VCA Aurora Animal Hospital, Lindsay McKay, VCA Aurora Animal Hospital, Patrick McKeever, McKeever Dermatology Clinics, Inc., Colleen Mendelsohn, Animal Dermatology Clinic, Linda Messinger Veterinary 53, Karen Farver, Metropolitan Veterinary Associates, Cecilia Friberg, Animal Dermatology Center of Chicago, PC, Helen Globus, Veterinary Dermatology Service, PA, Dunbar Gram, Animal Allergy and Dermatology, Terry Grieshaber, Circle City Veterinary Specialty and Emergency Hospital, Craig Griffin, Animal Dermatology Clinic, Carolyn Kidney, Oakland Veterinary Referral Service, Brian Palmeiro, Animal Critical Care and Specialty Group-Dermatology, Sandra Sargent, Pittsburgh Veterinary Dermatology, Amy Shumaker, Dermatology for Animals, Mitchell Song, Animal Dermatology, PC, Laura Stokking, Veterinary Specialty Hospital, Tiffany Tapp, Veterinary Healing Arts, Inc., Sheila Torres, University of Minnesota Department of Veterinary Clinical Sciences

Oral Immunotherapy

Human Perspective

• 7th World Congress of Veterinary Dermatology – Vancouver – July 2012
  – Dr. Mary S. Morris
  – Sublingual Immunotherapy and Allergy: The Physician’s Perspective


Oral Immunotherapy

Human Perspective

• ASIT in use for over 100 years in U.S.
• Numerous studies, papers & publications
• Injection used more widely in U.S.
• Oral showing equal efficacy & superior safety from European studies
• Oral used widely in Europe with full regulatory and government backing

Oral Immunotherapy
Human Perspective

• Efficacy
  – Improvement of ~42% & medication ? of 43%

• Mechanism
  – Oral mucosal surface: “unique privileged immunological site…markedly higher conc of dendritic cells, large number of T-cells and very few effector cells (eos, masts, basos)
  ▪ Lower rates of adverse reactions
  ▪ Interaction between dendritic cells & naïve T lymphs
  ▪ Down regulation of Th2 response, ?IgE


Oral Immunotherapy
Human Perspective

• Safety
  – Oral / Facial pruritis
  – Gastrointestinal upset
  – Systemic reactions minimal
  – Side effects are dose dependent and may be reduced by dose reduction
  – “in more than 20 years of clinical trials there have been no fatalities reported”


Oral Immunotherapy
Veterinary Perspective

• 7th World Congress of Veterinary Dermatology – Vancouver – July 2012
  – Dr. Douglas DeBoer
  – Options for Allergen Specific Immunotherapy: An Update

Oral Immunotherapy
Veterinary Perspective

- Immunotherapy in general is the “Only proven treatment for allergies that actually works against the underlying immunopathogenesis of the disease instead of merely covering up clinical signs with anti-inflammatory therapies”
- Oral: Glycerin based
  - Protects and preserves allergen molecules from degradation


Oral Immunotherapy
Veterinary Perspective

- Initial pilot study by Dr. DeBoer using a protocol adapted from human SLIT that had been used for > 40 yrs
- Clinical improvement occurred in the majority (~60%)
- Clinical improvement in those who had failed or had adverse reactions to injections


Oral Immunotherapy

- My clinical experience
  - Works as effectively as injection
  - Seems to be working faster than injections
    - 2 month phone call from rDVM
    - 5 month recheck
  - Facial pruritis in 1
  - Loss of appetite in 1

Efficacy of cetirizine hydrochloride for atopic felines

- Mild to moderate pruritis
- Double blinded placebo controlled crossover
- 1 mg/kg QOD x 28 days
- 19 / 21 cats finished the study
- No statistically significant differences between cetirizine and placebo groups
- Pharmacokinetics have been established


Shelter Cats with M.canis Terbinafine + lime sulphur rinse

- Itraconazole, commonly used, effective but expensive
- Terbinafine, generic, well tolerated
- 85 shelter cats treated with either 14 or 21 days of terbinafine p.o. once daily w/food
  
  250 mg tablets
  
  <2.8 kg: ¼ tab
  
  2.8 – 5.5 kg: ½ tab
  
  > 5.5 kg: 1 tab


Shelter Cats with M.canis Terbinafine + lime sulphur rinse

- Other study aspects
  - LimePlus® dip from Dechra: twice weekly with commercial rose garden sprayer to thoroughly saturate coat and skin
  - No e-collars were placed
  - Housing: open floor model, 3 rooms (8-10 cats per room), bedding changed daily, daily sweeping to remove gross debris, washed with detergent then disinfectant applied daily (5.5% bleach 1:10 prepared daily)
  - Weekly cultures by Mackenzie toothbrush tech

Third feline Demodex mite?

- Cases:
  - March 2004 – 6 shelter cats
  - 2009 – 1 shelter cat in Wisconsin
  - Feb 2012 – 1 shelter in Nevada
  - April 2012 -1 shelter in Nevada
  - Dec 2012 – 1 client owned cat
- Shorter than D. cati but longer than D. gatoi
- Unknown if this is 3rd species of Demodex, a developmental stage of D. gatoi or variation of either species


Five observations of a third morphologically distinct feline Demodex mite

Atopica® for cats and dose tapering

- 88 client owned cats w/ non flea hypersensitivity dermatitis
- Atopica: 7 mg/kg PO once daily x 4 weeks
- 71 / 88 stayed in study
  - 50 / 71 (70%) successfully tapered to EOD x 4 w
    - 65 / 71 stayed in the study
  - 37 / 65 (57%) successfully tapered to twice weekly
- Adverse effects: 65% had adverse event, usually mild and self-resolving: V & D

Effect of ketoconazole on cyclosporine concentrations

- Results: No significant difference between in whole blood or skin [ ] of CsA between treatment
  - 1: CsA: 5 mg/kg
    and
  - 4: CsA: 2.5 mg/kg + keto: 2.5 mg/kg
- Conclusion: CsA + keto concurrently at 2.5 mg/kg each may be as effective as CsA alone at 5 mg/kg


Effect of ketoconazole on cyclosporine concentrations

- Treatment
  - 1: CsA: 5 mg/kg
  - 2: CsA: 2.5 mg/kg
  - 3: CsA: 2.5 mg/kg + keto: 5 mg/kg
  - 4: CsA: 2.5 mg/kg + keto: 2.5 mg/kg
- Randomized cross over study: 6 healthy dogs received each treatment by mouth once daily for 7 days
- Blood draws and punch biopsy

Malassezia Therapy

- Classically is Keto @ 5 mg/kg
  - I used to ÷ and give BID
- What about fluconazole?
- A non-inferiority clinical trial comparing flu or keto in combo w/ cephalexin for the treatment of dogs with Malassezia dermatitis

Malassezia Therapy

- Dogs with Malassezia and Pyoderma
  - Keflex @ 22-30 mg/kg⁻¹ BID
  - Keto or flu @ 5 mg/kg⁻¹ QD
- 32 dogs, 28 completed the study
- At week 3 on flu: 95.9% reduction in yeast
  on keto: 97.8% reduction in yeast
- Clinically & visually all dogs improved signif
- Flu is as effective as keto for treating yeast


References

2. McCandless et al. Production of IL-31 by canine Th2 cells and identification of inflammatory and neuronal target cells. Vet Dermatol 2012; 23(Suppl. 1): FC-64, p52
Itchy Pets: Case Based Dermatology

Smokie. 5 year old, Male, Neutered, Domestic Medium Hair

Notes: ____________________________________________
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The Nonresponsive Allergic Cat  
*Dana A. Liska, DVM, Diplomate, ACVD*

Smokie  
Neutered male domestic longhair cat, 10 pounds, 4 years of age on presentation in June.

**History**  
Smokie's owner indicated the primary complaint as “face is scratchy, red, and bleeding.” When asked to specify what helped relieve the cat's signs, the owner replied “nothing.” The referring veterinarian had given Vetalog (Fort Dodge Animal Health) injections in May 2 years earlier, in December of the previous year, and in January, 6 months before presentation. Oral prednisolone had been administered 3 months before the cat was presented. Neither treatment improved the condition.

**Clinical Signs**  
The veterinary dermatologist who initially examined Smokie noted:  
- Multiple excoriations.  
- No other clinical abnormalities.  
- Pruritus 10/10  

**Initial Workup/Laboratory Results**  

**Differential Diagnosis**  
- Food allergic dermatitis.  
- Feline atopic dermatitis.  
- Dermatophytosis.

**Next Steps**  
The treatment history of response to intermittent steroids strongly suggested environmental allergies; however, head and neck pruritus is a predominant feature of food allergy in cats. The attending dermatologist recommended the following approach, giving the client these directives:

- Start an elimination diet with Innovative Veterinary Diet Potato & Venison Cat Food (Royal Canin). No other food, treats, chews, flavored toys, or medications by mouth are to be given for the entire 8- to 12-week duration of the food trial. Do not give flavored heartworm preventive during the food trial. Compliance must be strict – 100% – to prove or disprove a food component as an allergen. Even an occasional transgression seriously limits the likelihood of reaching a diagnosis.
• If itch is resolved by the end of the strict food trial, please call and we will discuss the food challenge.
• If signs remain present despite a strict food trial, we need to recheck and discuss intradermal allergy testing for atopic dermatitis (environmental allergy).
• Dexamethasone will be administered to retest the steroid response. Give one 0.75 mg dexamethasone (0.17 mg/kg) tablet by mouth once daily for 10 days to retest steroid responsiveness.
• Use Soft Paws nail caps (Smart Practice) on the back claws.

**Return Checkups**

On his return visit 2 months later in the fall of that year, Smokie had improved dramatically. His facial pruritus was better (but did not resolve) with the food restrictions, and he was then responsive to oral dexamethasone. He underwent intradermal allergy testing and was found to have multiple positive reactions. In fact, he had multiple **STRONG** positive reactions to various allergens, which is an uncommon finding with feline intradermal allergy tests.  

Allergen-specific immunotherapy (ASIT) was started, he continued on the elimination diet, and a dexamethasone taper was repeated (one 0.75 mg tablet [0.17 mg/kg] daily for 10 days, then every other day for 10 doses).

Smokie was maintained on ASIT, a limited-ingredient diet, and dexamethasone administered sparingly until fall of the following year when he flared again and was seen for a recheck examination. Skin cytology of his face was completed and revealed sheets of degenerative neutrophils with large numbers of intracellular and extracellular paired and single cocci. This superficial pyoderma was treated with an antibiotic dosed at 32 mg subcutaneously (Convenia – Pfizer Animal Health).

After the fall flare Smokie no longer received oral dexamethasone but was given methylprednisolone injections by his regular veterinarian 1 and 2 years later in the fall. The latest steroid injection did not seem as effective, and he was given a second steroid injection that fall. Again, the owner felt the anti-allergy effect had limited duration.

**Referral**

Smokie was presented to our clinic 2 months later with an ongoing flare. Skin cytology was collected from his face and revealed sheets of degenerative neutrophils with large numbers of intracellular and extracellular cocci. This superficial pyoderma was treated with antibiotic therapy (Simplicef – Pfizer Animal Health; one half 100 mg tablet [10 mg/kg] by mouth once daily). The attending veterinary dermatologist recognized that Smokie had managed very well over the previous 4 years but that he seemed to be struggling more. Differentials included a new food allergy or new environmental allergies. In fact, when food was discussed the owner revealed that she had changed his food from the limited-ingredient venison diet that had been
recommended to an over-the-counter diet. Before this examination, however, she had returned to feeding Smokie the limited-ingredient venison diet.

Smokie did well until early spring of the following year when he flared with facial dermatitis and pruritus. Both Simplicef and dexamethasone therapies were initiated but proved unrewarding. When he did not respond to the Simplicef regimen, he returned to the office and I assumed supervision of his case. His lesions were even more severe than at the time of his first visit to the clinic.

A swab sample was collected for bacterial culture and sensitivity (C&S) testing. Pending the results, the following changes were made:
- Switched the diet from venison based to rabbit based as the owner reported Smokie's facial pruritus seems worse after he eats.
- One 4 mg tablet methylprednisolone (Medrol – Pharmacia & Upjohn) daily (0.88 mg/kg) for 7 days, then every other day, to test for steroid tachyphylaxis (a condition described in the human literature and observed in the animals we see).
- Dilute bleach bath solution (personal communication - Donald Leung, MD, PhD, during North American Dermatology Forum, Savannah, GA, April 2010): apply artificial tears ointment to both eyes. Soak cat's face with cool moist cloth to soften crusts, then follow with application of dilute bleach solution per recipe (1/4 cup bleach per 10 gallons of water).
- Elizabethan collar to prevent self-trauma.

C&S results were available one week later and showed *Staphylococcus pseudintermedius*, which was both methicillin resistant (MR) and multidrug resistant (MDR). On phoning to share the results of the C&S testing with the owner, Smokie was reported to be doing 70% better with topical therapy. Given that systemic therapy depended on the administration of amikacin or chloramphenicol, both of which can be associated with adverse effects, the decision was made to continue the topical therapy. Smokie continued to do well in regards to his skin but developed feline urinary tract disease.

**Final Diagnosis**
- Food allergic dermatitis.
- Feline atopic dermatitis.
- Relapsing superficial pyoderma that ultimately developed both methicillin resistance and multidrug resistance.

**Key Points**
- Cats with severe dermatitis can have secondary infections with *Staphylococcus* sp and yeast. This occurs less commonly than in our canine patients but is common in the specific subset of patients referred to our clinic. Other veterinary dermatologists concur.
Tape cytology is a useful tool in ruling out secondary infections. One of the first studies to tout the importance of cytology was published in 1979.14 To quote from two of the author's favorite sources: "An enormous amount of vital diagnostic data can be obtained by microscopic examination of stained material, such as smears of tissues or fluids, during a clinical exam ... often supplies sufficient data to narrow a differential diagnosis and develop a diagnostic plan."15 From a more recent publication on feline dermatology: "Cytology can give rapid results and may help to suggest or even confirm a diagnosis."16

Patients can have multiple allergies, and it takes time to work through them.

Cats can develop resistant *Staphylococcus pseudintermedius* infections.

Topical therapy can be beneficial in resolving even resistant *Staphylococcus* sp infections.

Changes of diet over time may be necessary for food-allergic patients.

**References**


Itchy Pets: Case Based Dermatology

Chip. 3 year old, Male, Neutered, Labrador Retriever

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Thank you for giving me my dog back
*Dana A. Liska, DVM, Diplomate, ACVD*

**Chip**
Neutered male, Labrador retriever, 67 pounds, 3 years of age on presentation in November 2011.

**History**
Chip's owner indicated the primary complaint as “itching of the face and armpits.” When asked to specify what helped relieve the dog's signs, the owner replied “steroids is really the only thing we have found that touches this.” The referring veterinarian (rDVM) had given antibiotics (Simiplicef) 5 times in 2011 and prednisone tapers were prescribed 7 times.

**Clinical Signs**
- Patchy alopecia and mild papular eruption
- Pruritus 10/10

**Initial Workup/Laboratory Results**
- Deep skin scrapes: negative
- Skin cytology: Cocci amongst neutrophils
- IDAT

**Working Diagnosis**
Atopic dermatitis with secondary superficial staph pyoderma

**Next Steps**
- Complete Simplicef as prescribe by rDVM
- Start allergen specific immunotherapy (ASIT) injections
- Discontinue Atopica due to GI upset and cost was not justifying response
- Prednisone, 20 mg, 1/2 tablet by mouth once daily for 5-7 days then every other day

**Follow up**
The owner phoned in late December that Chip finished antibiotic one week ago and seemed to be flaring with “red bumps” again. She was hoping to avoid oral antibiotics again. The decision was made to start topical therapy with Triz Chlor 4 spray since the staph infection was confined to the ventral abdomen. Another phone call was received in early January with the report that the infection was spreading, cephalexin was prescribed as give one 500 mg + one 250 mg capsule by mouth every 12 hours for 30 days.
On his return visit 2 months later in March 2012, Chip had again relapse with a papular dermatitis and he had patchy alopecia on his head, trunk and limbs. At the time of the visit he was receiving fexofenadine daily and 10 mg of prednisone every other day at night “so everyone can sleep”. The owner was giving Chip baths weekly with triz chlor 4 shampoo and was giving ASIT injections weekly. The rDVM had recently refilled a prescription for cephalaxin. Skin cytology showed the coccii shaped bacteria persisted despite cephalaxin therapy. A culture and sensitivity test was recommended but declined due to financial constraints. An empirical change of antibiotic was made to trimethoprim/sulfa: SMZ/TMP: 960 mg with the instructions to give 1 tablet by mouth every 12 hours initially. One refill was provided in case Chip was responding to therapy but the owner was advised that a culture and sensitivity would be necessary if the infection was not responding. Changes were made to the ASIT formula. Two weeks later the owner call to report that the “red bumps” were at least 60% improved and that his pruritus was waxing and waning.

Chip was maintained on ASIT and prednisone but the infection relapsed again in July. The owner inquired about a once daily medication, Primor ® (ormetiprim-sulfadimethoxine) was prescribed at 600 mg, give 1 + 1/2 tablet by mouth daily for 30 days. The owner phoned in September to request a refill of prednisone and reported that Chip’s last antibiotic was approximately 6 weeks prior. This was promising news but proved to be short lived as Chip relapsed in early October and another prescription of Primor was administered. In late November the owner reported yet another relapse and requested the “less expensive” twice daily trimethoprim-sulfa medication. This antibiotic was necessary for another relapse in January 2013.

Chip returned to the dermatology clinic in March 2013. His current medications included Gives fexofenadine each morning and benadryl each evening, prednisone, 10 mg at night before bed so he would sleep. By this time most patients have transitioned to ASIT injections every 14 days but Chip needed them every 7 days due to itch trends noted before each injection was given. Pruritus level was rated 5-6/10. On examination a papular dermatitis was identified and skin cytology confirmed the presence of coccii shaped bacteria amongst neutrophils. Deep skin scrapes were again negative. We had a prolonged discuss about therapy so far and explored important questions: namely have we used fewer antibiotics since starting ASIT (5 months on regular strength, 10 month on double strength for 10 months and the answer was no! We also asked whether he was less pruritus overall and needed less steroid, the answer was again no. The author may have encouraged another refill of ASIT; however, verbal and non-verbal cues clearly indicated frustration and financial constraints. The decision was made to start oral interferon as a possible tool to supplement Chip’s natural interferons which help fight secondary infections. ³ Prednisone was discontinued and changed to dexamethasone, 0.75 mg, 2 tablet by mouth daily for 7 days then every other day. ⁴,⁵
Chip continued to maintain a reasonable level of comfort when on dexamethasone but attempts to discontinue therapy resulted in spikes in pruritus scores. A limited ingredient diet with Royal Canin rabbit and potato was instituted, including a change to non-flavored heartworm prevention. Over the next few months the owner was able to determine that the following steroid regimen kept Chip comfortable:

Dexamethasone: 0.75 mg, 2 tablets every other day, alternating with ½ tablet every other day. The author felt this was a reasonable low dose steroid and the owner reported Chip was doing "very, very well" overall. The decision was made to continue the dexamethasone and interferon.

In November 2013 the owner phoned to report she was able to decrease the dexamethasone to 1.5 mg every other day and pruritus was approximately 3/10. When she tried every 3rd day dexamethasone therapy the pruritus increased to 6-8/10. The owner expressed concerned about weight gain and that Chip chewed a spot on the top of his tail to the point of hair loss. A recheck exam was recommended since this was a new lesion. An appointment was scheduled and the decision was made to continue interferon and try the new targeted itch therapy Apoquel®: 16 mg, give 1 tablet by mouth every 12 hours for 14 days then once daily for 16 days.

Three weeks later Chip visited ADRC. The following abnormalities were noted on examination: alopecia has progressed and Chip had a stripe of pelage along dorsum that was of course quality while the pelage on his lateral abdomen was softer and fluffier, much like a puppy coat. The dorsal tail had a patch of alopecia, erythema and hyperpigmentation with a prominent follicular pattern. The owner rated pruritus at 3-4/10 on twice daily apoquel but increased to 10/10 on once daily therapy. Testing this day consisted of deep skin scrapes which showed the tail patch to be positive for *Demodex canis* mites, moderate numbers in all life stages while scrapes from the shoulders back, head, and one paw to be negative. A discussion was held to discuss the demodex mites and how to proceed with therapy for Chip’s allergies. The author believed the low dose steroid was ultimately responsible and should be avoided. The owner was in favor of avoiding steroids given Chip’s weight gain from 65 to 77 pounds over time. Chip had previously received Atopica® for his allergies but gastrointestinal upset and the cost to low benefit ratio made this choice unfavorable for the owner. Apoquel® is contraindicated for dogs with demodicosis. The plan was made to continue interferon and continue apoquel®, 16 mg, but to try 1/2 tablet by mouth every 12 hours. Even though the lesion was localized the author recommended ivermectin at 300μg/kg, by mouth once daily.

One month later Chip returned for examination and he looked like a new dog. His coat quality was normal and full. His owner expressed her appreciation: "He is playing…like a different dog…like a puppy again". Repeat deep skin scrapes were negative for mites. The plan was made to discontinue interferon and monitor for decline in coat quality or relapse of superficial pyoderma. He will continue Apoquel® and ivermectin until he is seen in 3-4 weeks.
for repeat skin scrapes. Information regarding future follow ups will not be included in these notes due to printing deadlines but will be shared at the time of case presentation.

**Final Diagnosis**
- Food allergic dermatitis – not challenge proven yet
- Canine atopic dermatitis
- Relapsing superficial pyoderma
- Demodicosis – focal, likely secondary to low dose steroid administration

**Key Points**
- Most patients respond to ASIT, approx 20% do not respond
  - Apoquel is a new FDA approved allergy blocker, can't sustain high dose twice daily dosing due to concern for side effects
  - Apoquel contraindicated for patients with demodicosis. It was used in this patient in an off label manner
  - Skin can have changing dynamics over time, even if you've been working with a patient for years...don't forget new conditions may develop

**References**
Itchy Pets: Case Based Dermatology

Barkley: 7 year old, Male, Neutered, Airedale Terrier

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Will the Owner Do the Rechecks When I Ask?

Allergic Dog with Highly Resistant Staph Infection

Dana A. Liska, DVM, Diplomate, ACVD

Barkley

Neutered male Airedale terrier, 93 pounds, 7 years of age on presentation.

History

Barkley lived in the Dallas, Texas, area for the first 4 years of his life, moved to California for 3 years, and then returned to Texas. Medical records from his veterinarian in California show a history of intermittent dermatitis and pruritus responsive to cephalexin, tapering doses of prednisone, and Genesis Topical Spray (Virbac AH) consistent with atopic dermatitis.

Five months before his referral, Barkley experienced bilateral ear infections, which waxed and waned, along with waxing and waning skin infections, for 3 months. He was on and off topical and oral therapy for both conditions. The right ear infection responded to therapy, but infection in the left ear persisted. Three months before his referral a sample was collected from the left ear for bacterial culture and sensitivity, and growth showed coagulase-negative Staphylococcus bacteria. One month later a staph pyoderma was recognized as unresponsive to appropriate antibiotic therapy and was culture and determined to be Staphylococcus pseudointermedius sensitive only to amikacin. Because Barkley was moving to Dallas, no therapy was started.

Barkley’s veterinarian in Dallas tested him for hypothyroidism. When the thyroid panel was within normal limits, she promptly referred Barkley to the author's clinic where he was examined within 1 month of arriving in Dallas. At the time of referral he was eating a novel protein diet (Prescription Diet d/d venison formula – Hill's Pet Nutrition).

Clinical Signs

Barkley had active epidermal collarettes on his ventral abdomen. The interdigital skin (palmar, plantar, and dorsal) was moderately erythematous. An otoscopic examination of the left ear could not be performed due to severe stenosis and discomfort.

Initial Workup/Laboratory Results

Cytology of left ear: cocci bacteria too numerous to count (TNTC), with suppurative inflammation and a bipolar rod in each oil power field (1/OPF).

Skin cytology: Numerous cocci (extra and intracellular) among neutrophils from both the trunk and interdigital spaces.

Diagnosis

- Cocci bacterial otitis externa (left ear) – resistant Staphylococcus schleiferi.
• Superficial bacterial pyoderma – *Staphylococcus pseudintermedius* – methicillin (MR) and multidrug resistant (MDR).

**Differential Diagnosis for Recurrent Otitis and Dermatitis/Pruritus**

• Resistant organism – known.
• Reinfection from otitis media – unable to ascertain at time of referral.
• Secondary to food allergy – possible but less likely given the history is more consistent with waxing and waning dermatitis/otitis typical of atopic dermatitis
• Secondary to atopic dermatitis – historically more likely than food allergy
• Secondary to tumor in the ear canal.
• Perpetuated by chronic ear canal changes.

**Next Steps**

The history of waxing and waning pruritus, dermatitis, and otitis externa supported a working diagnosis of canine atopic dermatitis. Addressing the resistant infections was the short-term focus while working toward intradermal allergy testing. Barkley was eating a limited-ingredient diet, which allowed time to determine if he showed any degree of improvement with a diet trial.

Further short-term management included a simple ear flush (not a deep flush) to remove debris and infection, but the canal was so swollen that the author could not assess the tympanum. Topical therapy was started: antiseptic ear cleanser (Epi-Otic Advanced – Allerderm) as pretreatment against the cocci shaped microorganisms followed by ticarcillin/clavulanic acid (Timentin – SmithKline Beecham) therapy to address the infection specifically. Steroids are important for improving soft tissue swelling of severe otitis externa; therefore, prednisone at a dosage of 20 mg (0.5 mg/kg) was prescribed to be given as one tablet by mouth once daily until Barkley's recheck. His owner was counseled regarding side effects.

Regarding Barkley's skin, discussion included the high degree of antimicrobial resistance noted in the bacteria as well as starting amikacin injections and the possible side effects. Amikacin has long been known for its effects on the kidneys and middle ear/vestibular system. A daily bath with antiseptic shampoo (Hexadene – Virbac) was prescribed, with instructions to lather affected areas and allow 10 minutes contact time before rinsing. Additional topical therapy was prescribed for the opposite end of the day from the bathing; the owner was to apply chlorhexidine spray (TrizCHLOR 4 – DermaPet) to all lesions. A recheck examination in 2 weeks was recommended given the severity of the left ear infection. The owner was advised that multiple rounds of ear flushing might be required before it could be determined whether medical management was going to be effective.

As commonly occurs, the owner returned with Barkley 4 weeks later rather than the recommended 2-week interval. Otoscopic examination still could not be performed due to severe
stenosis and discomfort; however, the ear canal was opening, and Barkley was reportedly less painful at home. At this visit the author was able to pass a 10 French catheter for an ear flush. Barkley exhibited some coughing and swallowing during the flush, indicating that the eardrum was not intact. He had 3 active collarettes on his ventrolateral abdomen. The interdigital skin remained mildly to moderately erythematous.

Cytologic testing demonstrated the following results:

<table>
<thead>
<tr>
<th>Test</th>
<th>Initial Visit</th>
<th>First Recheck</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ear cytology</td>
<td>TNTC cocci bacteria with 6-10 cocci per OPF</td>
<td>6-10 cocci per OPF</td>
</tr>
<tr>
<td></td>
<td>1 bipolar rod in each OPF</td>
<td>No rods seen</td>
</tr>
<tr>
<td></td>
<td>Suppurative inflammation</td>
<td>Suppurative inflammation</td>
</tr>
<tr>
<td>Skin cytology</td>
<td>Numerous cocci (extra- + intracellular) bacteria</td>
<td>Low number cocci bacteria</td>
</tr>
<tr>
<td>From trunk and interdigital skin</td>
<td>amongst neutrophils</td>
<td></td>
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The ear cleanser (Epi-Otic Advanced), ticarcillin/clavulanic acid (Timentin), and oral prednisone at the same dosage were continued. A recheck examination in 2 weeks was encouraged.

Author's Note: At the time that Barkley was due for his next recheck the Dallas area experienced a severe winter storm with dangerous ice resulting in a "veritable shutdown of the city." Instead of seeing Barkley as anticipated, the owner stopped by the referral clinic after about 6 weeks, rather than 2, to refill the ticarcillin/clavulanic acid for treating Barkley’s ear infection. Barkley's owner reported that he was doing well until they ran out of prednisone and until they could not drive Barkley to the groomer for his daily bath during the ice storm. The owner mentioned that Barkley had not received prednisone for 10 days and that his affected ear had seemed worse over the previous few days.

The author saw the opportunity to take advantage of Barkley's period without steroids and formed a plan with the owner to wait 4 additional days and then perform intradermal allergy testing (IDT). The optimum time for corticosteroid withdrawal prior to IDT has not been established and probably varies in each clinical situation. In the absence of well-documented guidelines, current textbook recommendations for withdrawal of glucocorticoids prior to IDT are a minimum of 3 weeks for oral glucocorticoids and 8 weeks for injectable glucocorticoids.4,6

Further Treatment

Physical Findings
Management of Barkley's MDR staph infection had been possible with topical therapy alone and he was initially improving, but after bath therapy was discontinued he relapsed rapidly. Barkley's left ear continued to be inflamed and the author palpated more stenosis. While the canal was not
completely ossified, the left canal seemed less pliable than on previous visits. The canal showed moderate erythema and a thick otic exudate. Papular dermatitis with epidermal collarettes, crusts, hyperpigmentation, and subtending erythroderma had relapsed.

About 2 months after Barkley's first recheck an intradermal allergy test was performed. Results indicated positive reactions to grasses, molds, weeds, trees, and others such as house dust, staphylococcal antigens and flea antigen. He continued to show cytologic improvement in his left ear despite continued soft tissue swelling. The staph pyoderma had relapsed off topical therapy. A culture and sensitivity test was repeated on the epidermal collarettes on his skin.\textsuperscript{7} The author sees some patients in which avoiding systemic antimicrobial therapy for a prolonged period of time (several months) enables the staph bacteria to return to a less resistant state. In a recent publication, 31 dogs previously diagnosed with a clinical infection were sampled repeatedly for a minimum of 8 months or until two consecutive negative results were obtained. The overall median length of MRSP carriage was 11 months (range: 4.5-19).\textsuperscript{8}

Cytology at this visit demonstrated these results:

**Test: Ear cytology** – two cocci/OPF

Skin cytology – moderate number of cocci shaped bacteria and degenerated neutrophils

This was the second ear cytology showing low numbers of bacteria yet the continued presence of severe otitis externa ± media. The author began encouraging surgical referral.

Oral prednisone dosed at 20 mg (0.5 mg/kg) was continued as was an appropriate dose of fatty acids and various antihistamines appropriate for Barkley’s weight. The author and colleagues counsel clients to give 180 mg per 10 pounds of body weight of EPA (eicosapentanoic acid). Aggressive daily bath therapy Hexadene – (Virbac) was recommended pending culture results. Topical ticarcillin/clavulanic acid was continued to give the owner time to discuss surgical referral with the family.

**Working Diagnosis**
- Canine atopic dermatitis.
- Cocci bacterial otitis externa (left ear) – resistant *Staphylococcus schleiferi*. Numbers of bacteria continued to improve, but canal was swollen again.
- Superficial bacterial pyoderma – highly resistant *Staphylococcus pseudintermedius*. Sensitive only to amikacin; initially responded to topical chlorhexidine therapy but has relapsed.

**Differential Diagnosis for Recurrent Otitis**
- Resistant organism – known.
- Reinfection from otitis media.
- Secondary to food allergy – possible but less likely because Barkley is already eating a venison diet and history supports Atopic dermatitis.
• Secondary to tumor in the ear canal – no historical concern from family veterinarians.
• Perpetuated by chronic changes to the ear canal.

1 week after IDT: Bacterial culture and sensitivity test results were available, and the bacteria were sensitive to multiple systemic medications. Barkley's owner was updated and advised to administer 1,200 mg (28 mg/kg) of sulfadimethoxine/ormetoprim (Primor – Pfizer Animal Health) initially given as two tablets by mouth in a single oral dose. Then Barkley was to receive one tablet by mouth once daily for 30 days.

1 month later: Barkley's owner phoned to report that the lesions had dramatically improved. The sulfadimethoxine/ormetoprim antibiotic was refilled and continued at the same dosage for an additional 15 days. Prednisone at the 20 mg dose was also refilled, and the recommendation was to give it once every other day until the next recheck. The owner was asked to ensure a recheck before medications were completed.

2 through 3 months later: The owner missed and rescheduled appointments multiple times, although the sulfadimethoxine/ormetoprim antibiotic was refilled to enable continued therapy until the actual recheck. Long-term therapy with potentiated sulfas raises concerns about side effects, such as fever, arthropathy, blood dyscrasias (neutropenia, thrombocytopenia, or hemolytic anemia), hepatopathy consisting of cholestasis or necrosis, skin eruptions, uveitis, or keratoconjunctivitis sicca.

4 to 7 months later: Barkley basically continued on a low dose of prednisone administered every second to third day as well as topical ticarcillin and clavulanic acid, ASIT, and antihistamines. His owner reported that the ear was doing well and the skin looked great; however, at the end of the seventh month Barkley was presented again because his left ear was flaring with infection. Ear cytology showed TNTC cocci bacteria, and the author facilitated a referral to veterinary surgeons for a consultation regarding total ear canal ablation and bulla osteotomy.

The following month Barkley flared with Staphylococcus pyoderma. In most cases the author does not change the ASIT formula at the 6-month recheck because a majority of papers analyzing data about ASIT with aqueous allergens report that most dogs respond after 3 to 12 months of treatment. In Barkley's case, however, the author increased the concentration of his formula given the severity of his allergies.

Final Diagnosis/Case Discussion
About a month after his last flare, instead of experiencing another truncal superficial pyoderma, he flared with severe pododermatitis on 3/4 paws. Tape strip cytology revealed TNTC Malassezia, which responded readily to ketoconazole at a dosage of 200 mg given as one tablet (4.6 mg/kg) by mouth once every 24 hours for 30 days and prednisone at a dosage of 20 mg
(0.5 mg/kg) given as one full tablet daily for 5 to 10 days, then every other day therapy and preferably every third day therapy. Given Barkley’s history one might assume that this episode was just another flare of staph pododermatitis, yet a simple tape cytology test was beneficial in diagnosing *Malassezia* dermatitis and enabled an informed decision regarding appropriate antimicrobial therapy.

Barkley presently is seen by the author approximately every 5 to 6 months for allergic flares that result in staph pyoderma. He continues to respond to sulfadimethoxine/ormetoprim antibiotic therapy and tapering prednisone doses as previously prescribed.

**Key Points**

- Antimicrobial resistance patterns can improve if systemic antimicrobials can be avoided.
- Topical therapy for resistant staph pyoderma takes dedication on the part of the pet owner and can be rewarding.
- Ear infections do not recur because you have not found the right medication; they recur due to underlying allergy and chronic canal changes.
- Investigate and focus on the underlying allergy as a way to reduce the recurrent pruritus and relapsing infections.
- Refer recurrent otitis externa cases earlier rather than later to avoid an end-stage ear and the need for surgical intervention.
- Tape cytology is a useful tool in ruling out secondary infections. One of the first studies to tout the importance of cytology was published in 1979. To quote from two of the author's favorite sources: "An enormous amount of vital diagnostic data can be obtained by microscopic examination of stained material, such as smears of tissues or fluids, during a clinical exam ... often supplies sufficient data to narrow a differential diagnosis and develop a diagnostic plan." From a more recent publication on feline dermatology: "Cytology can give rapid results and may help to suggest or even confirm a diagnosis."

**References**


